Handout Early Detection and Early Intervention for Cerebral Palsy: Groundbreaking New Tools and Treatments

Presenters:
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Iona Novak PhD OT | Cerebral Palsy Alliance Australia
Alicia Spittle PhD PT | Murdoch Children’s Research Institute Australia
Linda Fetters PhD PT | University of Southern California USA

Purpose:
The purpose of this course is to examine the very latest research data on tools that accurately predict cerebral palsy early and the emerging evidence for new and novel early interventions that effectively treat cerebral palsy (CP).

Course Summary:
Registers’ indicate the average age for the diagnosis of CP is 19 months. Recent neuroplasticity literature suggests that intensive, repetitive, task-specific intervention for CP ought to commence very early while the brain is most plastic, which is almost never the case when “wait and see” monitoring is occurring prior to diagnosis. It is important for those managing the care of infants and young children with motor delay discriminate as early as possible between CP and other diagnoses. The choice of evidence-based interventions and prognostic messages now differs greatly depending on diagnosis. Early motor assessment tools, brain imaging, and neurological examinations all help in predicting CP, with the most promising of these tools the General Movements Assessment. With growing evidence regarding available tools and the potential neuroplastic benefits of early intervention, we propose a major change in diagnostic and intervention practice.

Timetable:

<table>
<thead>
<tr>
<th>TIME</th>
<th>WHAT</th>
<th>WHO</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.00</td>
<td>Introduction &amp; Aetiological Factors Informing Intervention</td>
<td>Iona Novak</td>
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</tbody>
</table>

Four distinct groups are at risk of cerebral palsy:
1) premature infants – whose risk increases as gestational age decreases;
2) infants with a stroke;
3) term born infants with neonatal encephalopathy (NE) – whose risk of CP increases with increased severity of NE; and
4) “healthy” term infants born with no identifiable risk factors at birth, but are numerically the largest group of children with cerebral palsy.

This section of the workshop covers the latest population prevalence data on these subgroup populations and the aetiological implications for considering the choice of interventions.
1.30 Early Detection/Diagnosis of Cerebral Palsy
An overview of evidence-based diagnostic, assessment, and prognostic tools for infants “at risk” of cerebral palsy, including: 1) preterms; 2) infants with stroke; 3) infants with NE; and 4) “healthy” term born infants will be discussed. Systematic review data on the tools that accuracy predicts cerebral palsy will be presented and compared. Clinical utility will also be discussed. In addition an overview of new assessments available will be provided. These data will be summarised using a video case-study and presentation of the associated child outcomes.

Alicia Spittle

2.10 Parent Perspective of Diagnosis
A video will be shown outlining: (a) parent perspectives on the impact of diagnosis; (b) their preferences for how to receive bad news; (c) plus a summary of the qualitative literature about the impact of diagnosis on parents and recommendations for diagnosticians.

2.20 Early Detection & Diagnosis - Summit Recommendations
The findings from the Early Detection and Early Intervention Summit in Vienna 2014, in terms of recommendations for early detection will be summarised, including recommendations for internationally agreed measures and agreed terminology.

Iona Novak

2.25 Early Detection - Questions
All

2.35 BREAK

2.50 Motor learning in Infants at Risk of Cerebral Palsy
Motor learning based interventions are highly effective for older children with cerebral palsy and developmental coordination disorder plus adults with stroke and are therefore considered best practice paradigm for learning movement skills in many diagnostic groups. Motor learning however has not been widely tested for effectiveness in infants with cerebral palsy, partly because late diagnosis has hampered researcher’s ability to recruit children with confirmed cerebral palsy to early intervention trials. However, new research is underway, plus leading researchers in the early intervention field, believe the application of motor learning to infants ought to be a major research priority.

Linda Fetters

3.20 Early Intervention Evidence Base and New Discoveries
Based on latest evidence, experts now recommend a shift away from referral for intervention following a formal (most often late) description of CP, to one of referral for intervention which occurs immediately once an infant is considered “at high risk” of CP.

A summary of the existing early intervention evidence base will be provided. Clinical pathways and decision-making trees that include assessment, treatment, and expected outcomes will be presented based on best-available evidence.

Cathy Morgan
### 3.50 Case Studies
Two new and novel interventions for infants at risk of cerebral palsy will be described, along with presentation of new data from rigorous international trials studying the efficacy of novel early intervention treatments.

Interactive video case studies will then be presented to assist participants to simulate planning treatment activities using these new novel interventions for unilateral and bilateral cerebral palsy, and infants born premature.

**Cathy Morgan**

/Alicia Spittle

### 4.30 Early Detection & Diagnosis - Summit Recommendations
The findings from the Early Detection and Early Intervention Summit in Vienna 2014, in terms of recommendations for early detection will be summarised, including recommendations for current clinical practice and future research.

**Linda Fetters**

### 4.45 Early Intervention Questions

**All**
References: Early detection of children at risk of CP

References: Motor Learning and Exploration

21. Meinecke L, Breitbach-Faller N, Bartz C, Damen R, Rau G, Desselhorst-Klug C. Movement analysis in the early detection of newborns at risk for...

References: Early Intervention


## Participant Worksheet

### Case Study  
**Cassie**  
**Diagnosis**: High risk of CP  
**Imaging**: Extensive infarct: posterior frontal & temporal, bilateral parietal, & occipital lobes  
WMI: frontal lobes & insular cortex  
**Age**: 6 months  
**Background**:  
- First child  
- Term born  
- IUGR  
- Feto-maternal hemorrhage  
- HIE  

### Goals for Intervention

**Canadian Occupational Performance Measure (COPM)**  

<table>
<thead>
<tr>
<th>Occupational Performance Problems</th>
<th>Performance</th>
<th>Satisfaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Independently rolling in both directions</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>Bringing toys together in the midline with her hands</td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td>Feeding herself; either with her hands or holding spoon</td>
<td>1</td>
<td>8</td>
</tr>
<tr>
<td>Sitting more independently</td>
<td>1</td>
<td>8</td>
</tr>
</tbody>
</table>

### Intervention Plan

**Active motor Interventions**  

**Parent Education**  

**Environment Enrichment**
## Participant Worksheet

**Case Study:** Zayd

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>High risk of CP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Imaging</td>
<td>Grade III intraventricular haemorrhage bilaterally with ventriculomegaly and subsequent development of hydrocephalus</td>
</tr>
<tr>
<td>Age</td>
<td>3 months corrected</td>
</tr>
</tbody>
</table>
| Background| - First child  
- 26 weeks GA, 915 g  
- E coli meningitis + ventriculitis and hydrocephalus (shunted)  
- Seizures |

### Occupational Performance Problems

<table>
<thead>
<tr>
<th>Problem</th>
<th>Performance</th>
<th>Satisfaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Head control when held upright</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>2. Reaching for toys</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>3. Taking weight through legs</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>4. Increasing weight via oral intake</td>
<td>7</td>
<td>7</td>
</tr>
</tbody>
</table>

### Proposed Intervention Plan

#### Active Motor Interventions

#### Parent Education

#### Environmental Enrichment
Case Study
Diagnosis
Imaging
Age
Background

Proposed Intervention Plan

Active Motor Interventions

Parent Education

Environmental Enrichment
Early identification and intervention in cerebral palsy

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Cerebral palsy (CP) is the most common motor disorder among children, affecting approximately 2 to 2.5 per 1000 live births.1–3 The term CP covers several disorders of movement, all attributed to non-progressive disturbances to the developing fetal or infant brain. The physical impairment is often accompanied by disturbances in cognition and perception.4 Among others, genetic predispositions, maternal disease, preterm birth, low birthweight and birth asphyxia are associated with an increased risk of CP.5,6 Most often, the pathology of CP in preterm infants can be ascribed to periventricular leukomalacia (PVL) or peri- or intraventricular haemorrhage (IVH), and in general, the risk of CP increases as gestational age decreases.6 Some cases of CP in infants born at term are caused by birth asphyxia or neonatal arterial infarction,7 but often a clear underlying pathology is not found. The incidence and prevalence of CP has fluctuated over time because of changes in prenatal and paediatric care, and advances such as avoiding kernicterus have contributed to preventing the subtype of athetoid CP. Improved care has led to an increasing number of surviving preterm and low birthweight infants at high risk of CP in Western industrialized countries.3,8

Severe CP can be predicted with high probability shortly after birth by cranial ultrasonography, magnetic resonance imaging (MRI) and other imaging techniques. This is not the case for mild to moderate CP. As the child develops, early warning signs include delay in meeting motor milestones, seizures, poor sucking ability, a persistently fisted hand, and decreased rate of head growth.9 However, the majority of cases do not present unequivocal symptoms early on and in current practice, most children with CP are diagnosed around the age of 1 to 2 years.1,2 A fundamental question is whether these children would benefit from being identified earlier and receiving specific, early intervention.

In this review, we summarize the existing knowledge regarding the significance of environmental stimuli on early, neuronal development and use this to argue that early intervention ought to facilitate functional development in early childhood. In the literature, ‘early intervention’ encompasses approaches initiated before term age, when the infant is a few months old and at approximately 1 year of age. A clear consensus on a definition of ‘early’ is lacking. There is no unequivocal, scientific basis arguing in favour of a better effect of intervention initiated at, for instance, 3 months of age as compared with 12 months, and clinical studies documenting an age dependency of intervention are absent.10 We have decided to focus on interventions aimed at infant motor development in which the infant shows active exploratory motor behaviour that can be externally facilitated through intervention. While the lower age limit of ‘early’ intervention in this context may be set at term equivalent age, the upper limit is more
difficult to delineate. We have somewhat arbitrarily limited the review to studies in which intervention was initiated before 6 months of age. Methods to identify infants with early signs of CP are discussed with a focus on the General Movements assessment (GMA) and neuroimaging. We subsequently review the existing literature on early intervention, pointing out that only a few studies have been performed on a selected population of infants with a high probability of developing CP. This may explain the overall lack of significant, long-term effects of intervention, since a large number of the infants included in the studies may be assumed not to have required the intervention. We end up by arguing that intervention should be initiated as early as possible and directed specifically towards infants selected on the basis of an effective neurodevelopmental evaluation. Thus, this review argues for a research agenda combining better identification and specific early intervention.

Postnatal human brain development

Human brain development is characterized by a significant extension into postnatal life and lasts much longer than in other mammals, including our closest relatives, chimpanzee, gorilla, and orangutan. In humans synaptic density in the prefrontal cortex peaks at 3 years 6 months to 10 years of age,\textsuperscript{11,12} in the auditory cortex at 5 months to 3 years 6 months,\textsuperscript{13} and in the primary visual cortex around 3 months of age.\textsuperscript{14} Analysis of gene expression has supported that synaptic growth and plasticity continues to increase in humans during at least the first decade.\textsuperscript{11,15,16} Following an initial increase in the expression of synaptic genes and other molecules involved in synapse formation and plasticity, a decline is seen late in childhood and early adulthood, but with a sustained abundance far above that seen in other species.\textsuperscript{11,12,16} It seems reasonable to relate this continued postnatal synapse formation and plastic moulding of neural circuitries in the brain to the protracted motor and cognitive development in human infants, children and young adults as compared with other species. Even basic motor abilities such as gait and hand function have been shown to develop and mature up to the age of 14 to 15 years\textsuperscript{17–19} and most cognitive abilities continue to develop for much longer. This is most likely to be related to continued maturation of the corticospinal tract throughout childhood and adolescence.\textsuperscript{20,21} In monkeys, the corticospinal tract establishes direct synaptic contacts with spinal motor neurons between birth and 8 months of age, which coincides with development of the ability of fractionated finger movements and precision grip.\textsuperscript{22–24} Human infants develop this ability towards the end of the first year of life, consistent with the generally protracted development of the nervous system in humans as compared with monkeys. Physiological observations suggesting establishment of connections between corticospinal fibres and spinal motor neurons before birth in humans are at variance with this and require independent confirmation.\textsuperscript{25}

What this paper adds

- Demonstration of an effect of early intervention requires early identification of infants with possible CP.
- The term ‘early intervention’ is used in many different ways, which impedes comparison of published studies.

Higher potential for recovery following neural lesions in infants than adults

It also seems reasonable to assume that the continued development of the brain well into adulthood creates a favourable environment for reorganization of internal connections and functional networks following lesions, whereas in adults reduced plasticity creates a somewhat less favourable environment.\textsuperscript{26} People who were born blind thus show significant reorganization of their visual areas, which may process tactile and other sensory information, whereas such reorganization is not seen spontaneously in people who have become blind as adults.\textsuperscript{27} It is also a general observation that surgical ablation of one hemisphere (in order to control epileptic seizures) leaves relatively mild impairments when performed before the age of 10 to 11 years of age.\textsuperscript{28} This is well in line with original observations on the increasing functional severity of lesions in monkeys of increasing age, known as Kennard’s principle.\textsuperscript{29,30} The observation that early brain lesions may cause more severe effects than later lesions\textsuperscript{31} does not necessarily challenge the idea that the plastic potential decreases with maturation. Such observations may as well be explained by the limited size and immature state of the nervous system at the time of lesion.

Critical periods and sensitive periods

It is unclear to what extent this also signifies that the development of neural circuitries undergoes a critical period, where the maturation of the circuits and their function in the adult brain depends crucially on the presence of specific environmental influences at a certain time in development. Since the original demonstrations of a critical period in the development of ocular dominance columns in the visual cortex of kittens by Wiesel and Hubel\textsuperscript{12,33} critical periods have been demonstrated in a number of different species, in different cortical areas, and for a number of different functions.\textsuperscript{34} For the motor system, Martin et al. have demonstrated that the development of the corticospinal system is impaired with severe functional deficits in adult cats when kittens are prevented from using their paw during a 1-week period, 2 to 3 weeks postnatal.\textsuperscript{35} For obvious reasons it is difficult to determine whether similar critical periods exist in humans. Significant controversy surrounds this issue, but most authors agree that critical periods may exist for the establishment of binocular vision between 3 to 8 months and for language acquisition in the first few years of life.\textsuperscript{14} In these cases it appears crucial to ensure the appropriate sensory stimulation very early, similar to what has been found in other species.
Considerably less controversy surrounds the existence of sensitive periods during human development. Sensitive periods are extended periods of time where children are more receptive to environmental stimuli than later in life. Accordingly there is every reason to assume that perceptual, motor and cognitive functions are more sensitive to environmental influences (i.e. training and other forms of stimulation) during childhood than later in life.\cite{36,37} However, we know little of the magnitude and time course of this higher sensitivity for individual functions, what determines its variability among children, and how it may be utilized in training and learning. Based on the findings from kittens,\cite{35,38} it may be speculated that the period where the corticospinal tract is in the process of refining its functional connections with the spinal motor neurons during development would constitute a sensitive period, where interventions would be especially efficient. In this case, the first year of life might be considered a sensitive period for motor development, but we have insufficient information to be able to conclude this with any certainty.

**Enriched environments**

This also relates to observations on the significance of an enriched environment during development.\cite{39,41} The concept of enriched environments was initiated with Hebb’s anecdotal observations in the 1940s of larger behavioural improvements in rats he brought home as pets as compared with their litter mates kept in the laboratory.\cite{42} In the 1960s, Rosenzweig et al. developed the concept into a testable scientific theory\cite{43} and subsequent work has demonstrated the stimulating effect of an enriched environment during development in experimental animals on a range of parameters related to plastic changes in the brain,\cite{44} and a meta-analysis recently concluded that interventions involving enriched environments are a promising tool for infants with or at high risk of CP.\cite{44} It is generally accepted that no single factor is responsible for the stimulating effect of an enriched environment but that it is the combination of complex inanimate and social stimuli which is important (i.e. larger cages with more litter mates and possibility of interaction with toys).

Although controlled experiments are unavailable for obvious reasons, irrational human behaviour has occasionally provided evidence of the significance of an enriched environment during human development. The most publicized case is probably that of Genie, who was locked alone in a room during her first 13 years and showed severely arrested motor and cognitive development, including failure to develop any significant language skills, when she was discovered in 1970.\cite{45} Although sad cases like that of Genie do not tell us anything about the amount of enriched environment necessary to guarantee normal human development, they do illustrate the significance of adequate stimulation during development. Most likely the relationship between stimulation and development follows the general law of decreasing returns: if a child is very deprived, a little stimulation will make a large difference, whereas if the child is well stimulated it will take a lot more to make a significant difference. It should also be mentioned that reduced environmental stimulation, as implemented by the Newborn Individualized Developmental Care and Assessment Program in preterm infants in the neonatal period, has been proposed to prevent childhood attention disorders, however, a recent systematic review did not find evidence of long-term neurodevelopmental effects of NIDCAP.\cite{46}

**Passive stimulation is insufficient—learning requires active participation**

Since Donald Hebb put forward his theory of the neural basis of learning, popularized as ‘what fires together—wires together’, it has been a fundamental idea that learning requires coordinated activity in neural circuitries.\cite{42} From a developmental perspective, this also relates to the notion that ‘successful’ neural circuitries, which produce an adequate model of the environment or an adequate behaviour, survive, whereas less successful circuitries are removed.\cite{47,48} This pruning of neural circuitries probably explains the gradual decrease in the thickness of the cerebral cortex throughout late childhood and adolescence.\cite{49} Essential to this idea is that the selection during development is based on a continuous testing of the efficiency of the neuronal circuitries’ ability to produce a given sensory feedback when interacting with the environment. In other words, the establishment of valid internal models and representations of the external world in the nervous system is based on continuous testing of the validity of these models. This is done by monitoring the success of the models in producing sensory feedback corresponding to that expected by the model.\cite{50} According to this idea, learning (i.e. alteration or selection of neural circuitries) happens when the internal model produces a behaviour that has sensory consequences different from what the model expects.\cite{50} In this case, the sensory information from the environment acts as an error signal which updates and alters the internal model.\cite{50} This is similar to the idea that learning only takes place in an action–reaction situation, or put differently, when the child actively explores the environment or participates actively (takes an interest) in the training. Therefore, an enriched environment, learning, and training do not involve passive stimulation, but rather require that the child plays an active part.

**Early identification of infants with signs of cerebral palsy is important**

As previously mentioned, CP is on average diagnosed when the child is approximately 1 to 2 years old. This is too late for early intervention as defined here to be initiated and therefore, early intervention requires early identification of infants that may develop CP. Additionally, the time from suspicion is raised and until diagnosis is made can be very stressful for the parents and should be minimized if possible.\cite{6} For the time being, techniques that can easily identify infants with early signs of CP are lacking. Infants with severe brain lesions are usually detected soon after birth on the
basis of neuroimaging such as ultrasonography and MRI and therefore they may benefit from intervention instigated very early. However, infants with severe lesions may require more intensive and long-lasting treatment efforts to achieve developmental effects. Age limits differ, but infants born after 28 to 30 weeks of gestation are not routinely examined with ultrasonography or MRI. This is partly due to the relatively low sensitivity of the modalities; ultrasonography: 66–79%,\textsuperscript{51} and MRI: 71–88%,\textsuperscript{52} and partly to restricted time and financial resources. Thus, a brain injury that does not present clear clinical signs can go undetected for a long period of time, resulting in an intervention being initiated late. Additional methods for early identification are necessary, and the General Movements assessment may be one such system. It consists of an observation of the quality of spontaneous movement patterns, where abnormal general movements indicate a high risk of developmental disorders such as CP. General movements are present during the neonatal period and disappear at around 5 months corrected age. From 8 to 9 weeks corrected age, a pattern termed ‘fidgety movements’\textsuperscript{53} is normally present, and absent or abnormal fidgety movements are associated with a high risk of later CP.\textsuperscript{54–57}

Since not all children with abnormal findings at neurological examination or on neuroimaging go on to develop CP\textsuperscript{58} several authors recommend combining MRI and GMA.\textsuperscript{59–61} Skiold et al. recently found definitely abnormal general movements to be significantly associated with CP at 30 months corrected age and that moderate-severe white matter abnormalities on MRI had an even stronger association with CP than the general movements. When combining the GMA and MRI findings, sensitivity and specificity of 100% was achieved.\textsuperscript{61} However, as the diagnostic value of MRI at term may not be much better than consecutive ultrasonography, and since MRI is demanding, routine MRI at term is unlikely to become standard practice. To our knowledge, studies combining ultrasonography and the GMA have yet to be performed.

Choice of imaging modality aside, a joint method seems appealing. However, the GMA requires ample training, upkeep of analytic skills and time for video analyses. The clinician must use the GMA regularly and considering the relatively low number of infants suspected of CP this may be challenging. One option is to computerize the GMA to identify infants who need a second opinion from a team of clinicians.\textsuperscript{62–64} Computerizing the analysis may even allow screening of infants at risk. As the high specificity and sensitivity of the GMA is deduced from groups of high-risk infants, more research on the validity of the GMA in low-risk populations of infants is needed. Thus, one caveat for the use of the GMA as a screening tool is that it appears to have low predictive value in a general population of new-born infants.\textsuperscript{65}

Despite novel methods for identifying infants who may develop CP, the diagnosis of CP is still made from clinical observations. The commonly accepted definition of CP from 2005 by Bax et al.\textsuperscript{4} reads: ‘Cerebral palsy (CP) describes 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. The motor disorders of cerebral palsy are often accompanied by disturbances of sensation, cognition, communication, perception, and/or behaviour, and/or by a seizure disorder.’ Finding a large IVH on neuroimaging or finding absent fidgety movements predicts the development of CP but does not allow the diagnosis. Even with perfect prediction of the final outcome of a developmental process, the clinical condition at the beginning of that process is different from that at the end. Strictly speaking, if the condition at the beginning and at the end were perfectly linked, then intervention could have no effect.

Unconvincing evidence of the efficacy of early intervention

Based on our knowledge of neuroplasticity and sensitive periods it seems apparent that early intervention ought to benefit infants with brain damage during development. However, from the vast amount of literature on the subject it is difficult to determine whether early intervention is effective or not. Several reasons for this may be proposed. As already mentioned, one is the matter of defining ‘early’. Another problem is that it is difficult to compare studies since a countless number of diverse ‘early interventions’ have been applied. This is a challenge for meta-analyses. Researchers have tried everything from teaching parents how to handle their preterm infant, improving the parent-infant relationship,\textsuperscript{66,67} specially educated staff,\textsuperscript{68} different physiotherapeutic approaches\textsuperscript{69–71} to acupuncture.\textsuperscript{72} Furthermore, the methods of measuring the effects are numerous, not all have been validated and some may not be adequate to measure the outcome in question.

Early intervention studies also face the challenge of actually achieving a genuine comparison of the intervention to no treatment, as it is difficult not to offer infants in a control group any treatment. Usually the solution is to provide training for the control group as well, although less frequently than the intervention group. Yet, the training of the control children is likely to mask the effect of the intervention. Additionally, it is well known that people may be disappointed when allocated to the control group,\textsuperscript{73} and if randomized to the control group some parents will presumably attempt to train the child themselves. Finally, the physician responsible for the children in the study may feel compelled to prescribe intervention for children showing early signs of CP during the period of intervention. To avoid this, a cross-over design, in which all participants are included in both the intervention and the control group and switch places halfway, is commonly used.

The effect of early intervention has been investigated in a range of randomized controlled studies, which have been reviewed in a number of previous reviews.\textsuperscript{54,74–76} An overall conclusion from these reviews has been that there is no convincing evidence to support early intervention. We will only discuss two of the more recent reviews here. In 2005, Blauw-Hospers et al. systematically reviewed 34 studies with a total of 3255 infants to evaluate the effect of early intervention.
on motor development. As a reflection of the problems mentioned in the previous section, the interventions, outcome measures and the age at initiation of intervention were too variable to permit a formal meta-analysis. The authors divided the included studies into groups depending on the onset of intervention and evaluated the quality of the studies according to the level of evidence and internal and external validity. Of the 17 studies initiated after dispatch from the neonatal unit, 12 had a high methodological quality. Only four of these showed a beneficial effect on motor development. Eight of the 12 studies evaluated neurodevelopmental treatment, otherwise referred to as the Bobath concept, which mainly involved passive handling techniques. By and large, these studies found no significant effect on motor development. In contrast, a generally positive effect was found in the remaining high-quality studies, which evaluated interventions that required active participation from the child. Of these, one had an attrition rate of greater than 25%, one investigated children with Down syndrome, one compared conductive education to passive handling and the last study considered a physiotherapeutic intervention. This study by Lekskulchai and Cole is discussed later in this review.

In a recent Cochrane review, Spittle et al. selected a homogenous group of quasi-randomized and randomized controlled trials (RCT) to review the effects of early developmental intervention programmes. The review encompassed 3133 preterm infants who all started some kind of intervention within the first 12 months of life, and at least part of the intervention took place after discharge. The conclusion was that early intervention had moderate effects on cognitive development, but only weak effects were found for motor development and the cognitive improvements did not last into the early school years. Similarly, RCTs not included in the Spittle et al. review have struggled to provide substantial evidence of a positive effect on motor and cognitive development by early interventions.

We find it likely that a key reason for the lack of significant results in these studies is that only very few have investigated the effect of early intervention in children with a high probability of developing CP. According to a meta-analysis of 25 studies, the average prevalence of CP is 14.6% (95% confidence interval [CI] 12.5–17) among preterm infants born at 22 to 27 weeks gestational age, 6.2% (CI 4.9–7.8) at 28–31 weeks, 0.7% (CI 0.6–0.9) at 32 to 36 weeks, and among infants born at term 0.1% (CI 0.093–0.014). Thus, infants born preterm have a higher risk of CP than infants born at term. However, a large number of preterm infants will still develop normally. Therefore, when recruiting infants for a trial, relying solely on preterm birth as a risk factor of CP is somewhat insufficient. The cohort of preterm infants needs to undergo further selection using techniques such as brain ultrasound, MRI or the GMA in order to identify the infants who are in most need of intervention. If this is not done, major effects of early intervention cannot be expected, as a large proportion of the children included in the studies would not require the intervention and, therefore, would dilute the treatment effect in those children who needed it. An early distinction between high-risk infants may help direct the treatment towards infants who are in definite need of the intervention and thereby help ensure stronger evidence of the effect of the intervention. In other words, a more targeted intervention could be pursued. However, it is to be kept in mind that by using targeted intervention there is a risk of excluding infants who may have needed the intervention and, thus, ‘undertreating’ children who do not fit very specific inclusion criteria.

An attempt at this type of early distinction was made almost 30 years ago when 80 preterm infants were divided into ‘normal’, ‘at-risk’ and ‘neurologically impaired’ groups by clinical neurological examination at 3 months corrected age. Subsequently, intervention was offered to randomly selected ‘at-risk’ and ‘normal’ infants, while the most severely affected children in the ‘neurologically impaired’ group were all offered intervention. Unfortunately, the authors do not specify any details of the intervention and it is therefore unclear why they did not gain significant results. However, the notion of focusing on the children who would benefit the most from the intervention is of interest. Along these lines, we have been able to find only three more recent studies in which intervention has been directed specifically towards children with a high risk of CP. Lekskulchai et al. enrolled 111 preterm infants with no congenital abnormalities or serious brain damage. At 40 weeks gestational age the infants were evaluated using the Test of Infant Motor Performance and infants with a score less than 66 were randomly assigned to either intervention or control. The intervention consisted of daily home-based activities, such as assisted kicking and weight bearing on forearms, provided by the primary caregiver, who had been trained by a physiotherapist beforehand and each month new tasks were added. There is no information on the regimen for the control infants. At 4 months corrected age the infants in the intervention group showed significantly better motor development than those in the control group.

Weindling et al. studied 105 preterm infants with major cranial ultrasound abnormalities such as PVL. All infants were included around term age and showed no clinical signs of motor or cognitive disability. The infants were randomized to early physiotherapy or to standard treatment, which was physiotherapy initiated when a paediatrician found it appropriate. Thus, the difference between the groups reflects the effect of the time of onset of physiotherapy rather than the effect of physiotherapy as such. The physiotherapists used neurodevelopmental therapy (a.m. Bobath) where parents of infants in the intervention group were given advice on handling and positioning of their child. A little more than half of the infants developed CP. There was no significant difference between the groups at neither 12 nor 30 months. There may be several reasons for this, including an insufficient difference between the physiotherapy administered for the intervention and control groups respectively, the choice of intervention (the passive manipulation mainly used is likely to
have little effect\textsuperscript{10,86,87}, and that the study included several infants who did not develop CP regardless of intervention.

Hielkema et al.\textsuperscript{68} and Blauw-Hospers et al.\textsuperscript{88} compared an intervention programme, Coping with and Caring for Infants with Special Needs (COPCA), to traditional infant physiotherapy (TIP), mostly based on the principles of neurodevelopmental treatment. At a corrected age of 3 months, 46 infants, who at 10 weeks gestational age had definitely abnormal general movements, were included and randomized to either COPCA or TIP. The COPCA intervention (n=21) was home-based and provided twice-weekly from 3 to 6 months corrected age by specially trained physical therapists. Frequency and location of TIP (n=25) depended on a paediatrician’s advice, the median frequency being once a week. After the intervention period, 36 infants continued receiving physical therapy until 18 months corrected age; 12 infants received COPCA, three had TIP as no COPCA coach was available, and 21 received TIP. All infants were assessed several times using the Infant Motor Profile (IMP), the Pediatric Evaluation of Disability Inventory (PEDI) and other neurodevelopmental examinations. At 18 months, the infants who received COPCA had significantly better functional PEDI skills compared with the infants who received TIP a.m. Bobath. There was no difference between motor outcomes in the two groups; however, some elements of COPCA were associated with a better IMP score. The lack of difference in motor outcome between the intervention and control group is likely to be due to an insufficient difference between the therapies offered to the two groups in combination with a relatively small number of infants.\textsuperscript{68} Additionally, the authors found extensive heterogeneity in the intervention strategies applied within the two groups, especially in the TIP group.\textsuperscript{88}

Thus, the evidence available regarding early intervention directed specifically at children with a high probability of developing CP is limited. There is clearly a need for additional randomized studies in which early, intensive training is offered to a group of infants showing early signs of CP. Recently, a pilot study on the effects of kicking and stepping exercises in a group of preterm infants with ultrasound-confirmed severe IVH or PVL has provided promising results on motor development.\textsuperscript{89}

**Matching neurodevelopmental evaluation and intervention**

Even if identification of infants with early signs of CP is achieved, the ideal type of early intervention has yet to be found. However, as mentioned earlier, interventions requiring active participation from the infant have shown promising effects. Furthermore, studies on older children with CP and adults with late onset brain damage may be of relevance.\textsuperscript{90,91} These studies also argue that training must involve active participation. In addition, intervention must be of greater intensity and longer duration than what has been used previously\textsuperscript{90} and improvement is more likely if tasks are motivating and practised at home for at least 20 minutes a day.\textsuperscript{91} Thus, we suggest that the early intervention should be performed daily in the child’s home and, considering the importance of the parent-infant relationship, the parents must be trained to administer the intervention. The intervention must stimulate active participation from the child and must, therefore, be both fun and easy to manage to keep parents and children motivated. Ideally, a therapist should be available to support and ensure the quality of the training. However, this will not be possible on a large scale because of costs. This leads us to consider if the vast number of devices available for telecommunication are useful. Professional guidance and encouragement is often necessary to gain sufficient compliance, and online, daily sessions with a physiotherapist may be a financially viable solution.

In conclusion, although systematic reviews of RCTs have struggled to show lasting benefits of early intervention, this evidence is not sufficient to exclude the value of early intervention. The main reasons for this are the lack of precision in identifying infants for intervention studies and insufficient difference between the interventions offered to the two groups in combination with a relatively small number of infants.\textsuperscript{68} Additionally, the authors found extensive heterogeneity in the intervention strategies applied within the two groups, especially in the TIP group.\textsuperscript{88}

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Cerebral Palsy—Don’t Delay

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Cerebral palsy (CP) is the most severe physical disability within the spectrum of developmental delay. CP is an umbrella term describing a group of motor disorders, accompanied by many associated impairments. The disability is a result of injuries to the developing brain occurring any time from the first trimester of pregnancy through to early childhood. However, for the great majority, their full etiological causal pathway remains unclear. It is important to discriminate as early as possible between: (a) mild or nonspecific motor delay, (b) developmental coordination disorder, (c) syndromes, (d) metabolic and progressive conditions, and (e) CP with its various motor types and distributions. The most promising predictive tool for CP is the general movements assessment, which assesses the quality of spontaneous movements of infants in the first 4 months of life. We propose a change in diagnostic practice. We recommend a shift away from referral for intervention following a formal diagnosis to diagnosis of CP, to one of referral for intervention which occurs immediately once an infant is considered “at risk” of CP.

Key words: cerebral palsy; early diagnosis; general movements; perinatal risk factors; neonatal risk factors; brain injury

INTRODUCTION

Global developmental delay is an umbrella term that describes two or more delays in the area of speech and language, social and emotional, cognitive and motor development. Children with cerebral palsy (CP) often fall under the umbrella of global developmental delay, but CP cannot be considered “delay” as children do not “grow out of it.” Health professionals need to understand what clinical features distinguish CP from other motor disorders, so the most effective interventions can be commenced earlier. The American Academy of Pediatrics have developed a policy for the surveillance and screening of developmental disorders (Council on Children with disabilities et al., 2006), however this paper focuses specifically on CP. The objectives of this review are fivefold:

1. Describe the nature of CP and what makes it different to other motor or learning disorders.
2. Outline the prevalence of CP.
3. Determine who is at high risk of CP, what are the predictors and early signs?
4. Identify tools that help clinicians to accurately predict CP.
5. Present an evidence-based algorithmic approach to recognizing CP and developing intervention plans.

In the early months of life, global developmental delay and CP present similarly, if delayed, acquisition of developmental milestones is the only comparator. It is the movement disorders (e.g., spasticity and dystonia), the level of functional impairment, and the associated impairments that set CP apart from other milder motor disorders or learning disorders such as developmental coordination disorder (DCD). DCD is less severe and 25 times more common than CP affecting ~5–6% of the population and current practice is not to diagnose before the age of 5. As a result, the diagnosis of CP is often delayed while the possibility of DCD is explored.

DCD is primarily a learning problem where children can achieve normal movement patterns and skills but have problems with learning and planning the movements. CP conversely is a physical disorder, where children are not able to achieve the normal movement patterns and the primary problem is motoric not learning, although deficits in learning may compound the motor problem.

DCD is used to refer to children who fulfill a certain criteria; poor motor performance which significantly interferes with activities of daily living which are not explained by any medical, neurological, or psychosocial condition. Thus a child with CP whose motor disability is neurological cannot have a diagnosis of DCD [Blank et al., 2011]. The physical disability of CP is life-long whilst DCD is more apparent in the window where the child is learning key motor skills for example, catching a ball, dressing independently, and handwriting.

WHAT IS CEREBRAL PALSY?

CP is an umbrella term which “describes a group of disorders of the development of movement and posture, causing activity limitations, which are attributed to nonprogressive disturbances that occurred in the developing fetal or infant brain.
The motor disorders of CP are often accompanied by disturbances of sensation, cognition, communication, perception, and/or behavior, and/or by a seizure disorder” [Bax et al., 2005]. This most recent definition acknowledges the complexity of the condition and the impact of the associated impairments.

What are the Fundamental Facts We Know About Cerebral Palsy?

Classification of cerebral palsy guides intervention decision making

CP is a heterogeneous condition, and to elucidate prognosis and guide selection of the most appropriate interventions (e.g., constraint induced movement therapy for hemiplegia and selective dorsal rhizotomy for diplegia) three major classifications are applied: motor-type, topography, and function. Clinicians often remark that a child may have two or three different descriptions of their CP within one medical file, evidencing the poor reliability of these traditional classification systems. Tables 1 and 2 outline the traditional motor types and topographies of CP and the proportions of a CP population with each type. In this paper, we refer to the Australian Cerebral Palsy Register (ACPR) when reporting rates and for international comparisons the Swedish Register and a study by Reid et al. [2011a] where registers throughout the world are compared.

To solve the problem of low inter-rater (and sometimes intra-rater) reliability when identifying topographical subtype, the Surveillance of Cerebral Palsy Europe [SCPE, 2000] has recommended that traditional topographies be combined into two easily definable topographies: Unilateral (one side of the body), Bilateral (both sides of the body). The ACPR instead applies a limb by limb coding using the Australian Spasticity Assessment Scale (ASAS) [Love, 2007]. The ASAS scores the muscles’ response to rapid passive movement without the subjectivity and wording ambiguities of the modified Tar-dieu and Ashworth scales [Mutlu et al., 2008]. Nonspastic motor types are also coded, resulting in a “stick figure diagram” of motor impairment, which provides an objective picture of the CP.

The gold standard tool for reliably describing motor function in CP is the GMFCS [Palisano et al., 1997]. GMFCS provides a common language that conjures up a “picture” of a child with CP. GMFCS is a five level classification system of gross motor function in people with CP. The classification is based on the person’s ability to self initiate movement with a focus on sitting, transferring, and mobilizing [Palisano et al., 1997]. Different classification descriptions exist at different age groups. Table 3 summarizes the system for 2–4-year olds, to coincide with the most common time of recognition and the proportion in a CP population with each level of GMFCS.

It should be noted that whilst the GMFCS classification can be applied to infants, about 40% change classification levels by age 2. After 2 years, the classification system is stable and thus GMFCS reassessment is recommended after age 2 [Gorter et al., 2008]. This is clinically and diagnostically very important, because parents are anxious to learn early about the severity of their child’s condition for future planning but in reality the most accurate description of function and severity can only be given at 2 years.

The presence of associated impairments and functional limitations affects the child’s outcome

For many children with CP, it is not just a physical disability. When seeking to prognosticate the severity of

<table>
<thead>
<tr>
<th>Table 2. Classification by Topography</th>
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<tr>
<td><strong>ACPR</strong></td>
</tr>
<tr>
<td>Hemiplegia:</td>
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<tr>
<td>Diplegia:</td>
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<tr>
<td>Quadriplegia</td>
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*Australian Cerebral Palsy Register.
Table 3. Classification by Gross Motor Function at 2-4 Years

<table>
<thead>
<tr>
<th>Level</th>
<th>Description</th>
<th>ACPR*</th>
</tr>
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<tbody>
<tr>
<td>I</td>
<td>Floor sits independently, hands-free. Walks without assistive devices.</td>
<td>32%</td>
</tr>
<tr>
<td>II</td>
<td>Floor sits independently, hands-free with balance affected. Walks using an assistive mobility device.</td>
<td>27%</td>
</tr>
<tr>
<td>III</td>
<td>Floor sits using w-sitting. Walks short distances indoors using a hand-held mobility device with assistance.</td>
<td>12%</td>
</tr>
<tr>
<td>IV</td>
<td>Floor sits when placed, uses hands for balance. Rolls, creeps or crawls for short distances.</td>
<td>14%</td>
</tr>
<tr>
<td>V</td>
<td>Unable to sit independently. No form of independent mobility.</td>
<td>15%</td>
</tr>
</tbody>
</table>

*Proportion in Australia with each level of GMFCS.

CP and determine intervention plans, assessment of associated impairments must also occur. The likelihood and severity of associated impairments increase with the severity of motor impairment [Himmelmann et al., 2006; Odding et al., 2006]. Some have reported that associated impairments impact more on function and quality of life than the motor impairment [Himmelmann and Uvebrant, 2011]. A meta-analysis of CP registers calculated the overall rates of associated impairments and functional limitations in the CP population to be: three in four are in pain; one in two have an intellectual disability; one in three cannot walk; one in three have a hip displacement; one in four cannot talk; one in four have epilepsy; one in four have a behavior disorder; one in four have bladder control problems; one in five have a sleep disorder; one in five have a hip displacement; one in 10 are blind; 1 in 15 are tube fed; and 1 in 25 are deaf [Novak et al., in press]. Many will have a number of these impairments, and the presence of these impairments complicates therapy, decreases health status and quality of life for the individual and their family, and increases costs for the family and to society. The associated impairments of CP will now be discussed briefly.

Epilepsy. Epilepsy can potentially severely limit the quality of life for the person with CP and their family, and adults with CP and epilepsy are less likely to find employment [Michelsen et al., 2005]. Epilepsy occurs in 30% of individuals with CP [Arnaud et al., 2008; ACPR Group, 2009]. In 2% of individuals with CP, their epilepsy will be resolved by the time they turn 5 years of age [ACPR Group, 2009]. For those whose seizures are not resolved, epilepsy is a lifelong condition. Rates of epilepsy are higher in those with: spasticity born at term (48%) compared with preterm (28%); bilateral CP (34–87%) compared with unilateral (23%); and those with intellectual impairment (61%) compared with no intellectual impairment (19%) [Carlsson et al., 2003; Wichers et al., 2005; Himmelmann et al., 2006]. Intellectual impairment. Intellectual impairment can be defined by low general intellectual functioning as measured by IQ scores, in combination with difficulties with adaptive behavior, all manifesting before the age of 18. Practically, this means that people with an intellectual impairment have memory deficits, difficulty reasoning, learning new skills, attending and organizing information. 50% of individuals with CP have an intellectual impairment and between 20 and 30% [Jarvis et al., 2005; McManus et al., 2006] have a severe intellectual impairment. Formal assessment of intellect is essential (but at times difficult) for an individual with CP.

Communication. Communication disability can have a major impact on the individual with CP and their family. Impairment in this domain can impact on both understanding of language and expression. For individuals who have severe communication impairment, social isolation and poor self-esteem can result. Between 20 and 30% of people with CP are nonverbal which means that systems to support other forms of communication are required [Arnaud et al., 2008; ACPR Group, 2009; Andersen et al., 2010; Parkes et al., 2010]. They are more likely to be nonverbal if they are non-ambulatory (GMFCS IV–V, 57%) compared to those who are able to walk (GMFCS I–III, 4%) [Shevell et al., 2009]. Augmentative and alternative communication (AAC) systems, which can range from low/light technology systems such as signing or use of alphabet charts to high technology systems such as speech generating devices, may be used to communicate. It is a fundamental human right to have the opportunity to communicate; however, high technology AAC systems are expensive, requiring wait listing and for some individuals will mean that they are unable to access systems that would support them to communicate.

Vision. Vision impairments can range from mild requiring glasses, to functionally blind. About 5–12% of individuals with CP have a severe impairment, or are functionally blind [McManus et al., 2006; ACPR Group, 2009]. Another 30% will have a mild to moderate vision impairment.

Hearing. Hearing impairments can also range from a mild impairment to bilateral deafness. Bilateral deafness occurs in 2% of people with CP while other hearing impairments occur in a further 10% [Surman et al., 2006; ACPR Group, 2009]. Assessment of vision and hearing in children with CP should be thorough and done early, as it can impact greatly on their ability to learn and achieve milestones.

Other. Other impairments strongly associated with CP are hip dislocation (8%), displacement (27–35%) [Hagglund et al., 2005; Soo et al., 2006] and spine deformities, sleep disorders (23%) [Newman et al., 2006], pain (70%) [Jahnsen et al., 2004; Arnaud et al., 2008], eating (8% tube fed) [Shevell et al., 2009; Sigurdardottir and Vik, 2011], excessive drooling (22%) [Parkes et al., 2010], bladder and bowel control complaints (24%) [Roijen et al., 2001], and behavior difficulties (26%) [Parkes et al., 2008]. These less well-understood impairments are more likely to occur with bilateral CP and intellectual impairment.

CP is the most common physical disability in childhood with prevalence unchanged for 60 years.

The overall prevalence of CP is ~0.2% of the population (i.e., 1 in 500) in developed countries. As can be seen by a projected age distribution of one state in Australia (Fig. 2), even though the injury responsible for CP occurs in the developing brain, it is a lifelong condition, with most patients having a normal life expectancy. In reality, CP is not just a condition of childhood.

The true incidence of CP cannot be estimated as there are a proportion of infants who die in the intrapartum, neonatal and infant period, who had brain lesions that may or may not have met
the criteria for CP. It has been suggested therefore that the closest rate to incidence (for CP) is prevalence of neonatal survivors (NNS). Western Australia (WA) is one register that reports in this manner, and is also one of the longest running CP Registers in the world. CP is mandatorily reported in WA, therefore it is assumed that this register has as close to a total population cohort as is possible. WA’s CP rates reported in 2006 are 2.78/1,000 NNS increasing to 3.9/1,000 when post-neonatal CP is taken into account [Blair and Watson, 2006; Watson et al., 2006]. NNS are important when rates are reported by gestational age stratum. The lower the gestational age stratum, the more rates differ between NNS and live births. It is particularly important for those at the youngest gestational ages. When reporting rates in the birth years 2005 and 2006 for those born between 20 and 27 weeks in WA, the rate per 1,000 NNS was 72 (95% CI 32–110) compared to live births 51 (95% CI 24–79) [Watson, 2012, personal communication]. If neonatal deaths are not taken into account, live births give a misleading lower rate. In term births (37+ weeks), where the rate of intrapartum/neonatal death is proportionally much less, the difference between NNS 1.7 (95% CI 1.4–2.1) and live births 1.7 (95% CI 1.4–2.0) becomes inconsequential. Despite this denominator being the most accurate, for comparison live births are the most widely used denominator.

Estimates of prevalence throughout the world vary depending on the methodology of “count,” percentage ascertained and variations in selection criteria. CP Registers have identified rates ranging between 1.4 and 2.77/1,000 live births; surveillance programs range between 2.1 and 3.6/1,000 live births; and cross-sectional surveys range between 1.05 and 4.1/1,000 live births. The two largest data sets, the ACPR and the SCPE both have an overall birth prevalence of 2/1,000 live births. In developing countries, it is thought that incidence is higher as the public health measures that help prevent some CP cases are not freely available in developing countries [Blair and Watson, 2006]. All data sets across the world agree there is a higher proportion of boys diagnosed with CP. Although CP is found across all socio-economic classes, there is a clear association between low birth weight and low socio-economic status, and in normal birth weight ranges, rates of CP are 2.42/1,000 live births for those in the lowest socio-economic groups, compared to 1.29/1,000 for the most affluent groups.

The overall rate of 2/1,000 has been fairly stable over the last 60 years in contrast to the dramatic falls in perinatal mortality rates. However, there have been some trends in gestational age stratum, shown in Figure 3. Rates in the extremely and very low
gestational groups rose during the 1980s, but are now trending down. Moderately premature infants’ rates have decreased slightly, while in term infants the rates are unchanged [Blair et al., 2001; Watson et al., 2006]. Because the majority (>73%) of infants are born over 32 weeks gestational age, the increases and decreases in the extremely and very preterm groups have made little difference to the overall rate.

Identification of infants “at-risk of cerebral palsy” is possible; assessment and screening should follow

Since there are no identifiable biomarkers to accurately predict CP, and clinical risk factors only identify subpopulations of infants at risk [McAdams and Juul, 2011], understanding the term “causal pathways” is important. CP atiologies are described in terms of causal pathways, as there is very rarely one specific cause of brain damage severe enough to cause CP. Much research has been published that attempts to discern the risk factors that lie on one or more causal pathways to CP. What researchers are beginning to realize is how little is known about how these risk factors interact on causal pathways. Risk factors can be described according to when they occur or when they are identified. The following examples have been identified for CP:

- Prior to conception: Previous gynecological history of stillbirths/multiple miscarriages/neonatal death/premature birth, family history of CP and other genetic predispositions, maternal diagnoses, for example, intellectual impairment, epilepsy and low socioeconomic status.
- Early pregnancy: Infection, birth defects, multiple births, male gender, and other genetic predispositions.
- During pregnancy: Maternal disease, for example, thyroid disorders, pregnancy complications, for example, preclampsia and bleeds in the second and third trimester, infection and inflammation, intrauterine growth restriction (IUGR), placental abnormalities and other precursors to premature birth.
- Around the time of birth and the neonatal period: An acute intrapartum hypoxic event, stroke, seizures, hypoglycemia, jaundice, and infection.
- Postnatal period: Infections, accidental and nonaccidental injuries, stroke both spontaneous and following surgery.

The rate of CP in neonatal survivors varies significantly with level of risk at birth. To describe the risk of developing CP, infants have been separated into three distinct groups shown in Figure 4: (1) premature infants (30–40% of all CP); (2) term born infants who shortly after birth have neonatal encephalopathy (NE), a clinically defined syndrome of disordered neonatal brain function (15–20% of all CP); and (3) term born “healthy” infants, who do not require special care in the neonatal period (40–50% of all CP) and do not appear to have identifiable risk factors at birth [Badawi et al., 2005; Wu et al., 2006; McIntyre et al., 2011].

Premature infants. When considering which babies are at risk of CP, preterm infants commonly come to mind. The risk of CP increases as gestational age
decreases, therefore babies born at 36 weeks' gestation are at much lower risk than those born at 24 weeks. As a result, rates in premature infants range between 3 and 80/1,000 neonatal survivors, reflecting the wide variation in levels of risk across premature gestations. Premature infants constitute up to 40% of infants who develop CP [Kirby et al., 2011]. So why are premature infants at increased risk of CP, and which ones are at the highest risk?

The group of preterm infants can be separated according to gestational age, with the first subgroup being extreme prematurity, generally considered less than 28 weeks' gestation. There is much data in the literature which depicts the outcomes of extremely premature infants and much research has been conducted in this age group [Hoon and Fara, 2010; Reid et al., 2011]. In the 1970s and 1980s, the frequency of CP in this gestational age group increased. This was attributed to the increasing survival of extremely preterm infants and their predilection to germinal matrix hemorrhage and periventricular leukomalacia (PVL) [Stanley and Watson, 1992; Hagberg et al., 1996]. Evidence from population-based samples in Europe, Australia and the United States, and analyses from CP Registers in Australia and Europe describing trends in prevalence, subtypes, and severity, suggest that this rise in frequency of CP in extremely preterm infants has reached its peak and is now decreasing [SCPE, 2000; Reid et al., 2011; Watson, 2012, personal communication]. Up to 10% of extremely preterm infants (variations in reports exist from as low as 3–10%) and up to 5% of infants between 28 and 31 weeks gestation will be described as having CP [Himpens et al., 2008; Watson, 2012, personal communication]. Up to 6% of extremely preterm infants (variations in reports exist from as low as 3–10%) and up to 5% of infants between 28 and 31 weeks gestation will be described as having CP [Himpens et al., 2008; Watson, 2012, personal communication].

Practice point. Mothers whose labor is imminent (and prior to 30 weeks gestation) should now be offered magnesium sulphate for neuroprotection of their child. Meta analyses have shown that CP can be reduced by 30% for infants under 30 weeks gestation [Crowther et al., 2010]. A number of premature infants can be separated according to gestational age, with the first subgroup being extreme prematurity, generally considered less than 28 weeks' gestation. There is much data in the literature which depicts the outcomes of extremely premature infants and much research has been conducted in this age group [Hoon and Fara, 2010; Reid et al., 2011]. In the 1970s and 1980s, the frequency of CP in this gestational age group increased. This was attributed to the increasing survival of extremely preterm infants and their predilection to germinal matrix hemorrhage and periventricular leukomalacia (PVL) [Stanley and Watson, 1992; Hagberg et al., 1996]. Evidence from population-based samples in Europe, Australia and the United States, and analyses from CP Registers in Australia and Europe describing trends in prevalence, subtypes, and severity, suggest that this rise in frequency of CP in extremely preterm infants has reached its peak and is now decreasing [SCPE, 2000; Reid et al., 2011; Watson, 2012, personal communication]. Up to 10% of extremely preterm infants (variations in reports exist from as low as 3–10%) and up to 5% of infants between 28 and 31 weeks gestation will be described as having CP [Himpens et al., 2008; Watson, 2012, personal communication]. Up to 6% of extremely preterm infants (variations in reports exist from as low as 3–10%) and up to 5% of infants between 28 and 31 weeks gestation will be described as having CP [Himpens et al., 2008; Watson, 2012, personal communication].

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adjunct therapies to help those that do not respond to cooling alone are currently in animal model and phase 1 neonatal studies, for example, erythropoietin, melatonin, xenon, and topiramate [Gonzalez and Ferriero, 2009].

In term infants with moderate to severe NE, imaging showing basal ganglia/thalamus injury has a positive predictive value for CP of 88% [de Vries et al., 2011]. In a study of 173 term infants with NE, the basal ganglia/thalamus pattern of injury was associated with the most severe motor and cognitive outcomes at 30 months [Miller et al., 2005].

Practice point. Term infants with moderate to severe NE and a basal ganglia/thalamus injury should be automatically described as “At high risk,” and go straight to Pathway B (Figure 5). They should receive a GMs Assessment, be referred to active surveillance and early intervention when they leave the hospital.

The remaining infants with NE that go on to be described as having CP have antenatal risks such as IUGR, intrauterine infection, metabolic abnormalities, syndromes, and birth defects [Badawi et al., 1998; Kurinczuk et al., 2010]. Perinatal arterial stroke occurs in ~1.7/100,000 live births. In the newborn period, it can also result in NE, but the majority of these infants present after the immediate neonatal period with seizures or hemiparesis. Mothers with preeclampsia and infants who have IUGR are at risk of perinatal arterial stroke [Shankaran, 2008]. Stroke with abnormalities involving the cerebral peduncle are also highly predictive of CP PPV 78% [de Vries et al., 2011].

Practice point. Infants with a cerebral birth defect, or stroke with involvement of the cerebral peduncle should be identified as “at risk” of CP and should join Pathway B (Figure 5) at “assessment for CP.”

The risk of developing CP in term infants who have received routine care at birth, the third group of infants who go on to develop CP, is ~1/1,000 neonatal survivors and these infants are at the lowest risk. However, they represent 45% of all infants with CP and numerically comprise the largest group (Fig. 4). Why do these apparently “neurologically normal” children at birth develop CP, and can we identify them earlier so they can have access to active surveillance and early intervention?

From a total population case control study in Western Australia, McIntyre et al. [2011] compared the clinical descriptions of 295 term infants with CP with 442 term control infants none of which required special care. They identified six independent predictors of CP in the neonatal period: abnormal fontanelle OR 4.4 (95% CI 0.8–23); abnormal tone OR 7.3 (95% CI 2–26.8); birth defects identifiable in the newborn period OR 5.2 (95% CI 2.4–10); ventilatory assistance restricted to the labor room only OR 2.9 (95% CI 2–26.8); abnormal consciousness referred to irritability and lethargy, but none were comatose OR 3.7 (95% CI 2–7); and in the small group with abnormal temperature regulation temperature was down or fluctuating, not high OR 4.1 (95% CI 1.2–14). A number of these predictors are reminiscent of criteria for mild NE, and the presence of two or more of these factors yielded a high specificity (99%), but low sensitivity (14%) for CP. This is not surprising considering the unknown etiology of this group of infants. Of this low risk group who had CP, 58% did not have any of these neonatal factors, yet 60% of these infants had moderate to severe CP.

This is not the first time a finding like this has been reported. The National Collaborative Perinatal Project reported that most children with CP did not derive from groups at high risk (low Apgar scores, or the presence of neonatal signs). About 43% were examined and classified as “neurologically normal” in the neonatal period and concluded that a large proportion of CP cases remain unexplained [Nelson and Ellenberg, 1986; Ellenberg and Nelson, 1988]. Earlier still, in 1970, Eva Alberman attempted to model what were at that time the three most important risks around birth: (1) parity >4; (2) abnormal method of delivery—breech, face or shoulder delivery, internal version, or delivery by an untrained person; and (3) neonatal illness in the 1st week of life—convulsions, cyanotic attacks, cerebral signs, hypothermia, jaundice, Rh incompatibility, or serious illness. Infants were at the highest risk of disability when all three of these risks were apparent. They were only a small group (0.1% of total births), but more importantly only 0.2% of those with a disability. When any combination of these three risks were used, 13.2% of all live births were classified as at risk, and this identified 26.3% of all those with a disability. A striking finding was that 74% of all those with CP, severe mental handicap, hearing, and sight impairments could not be identified using this model.

Very little has changed for those born at term without any noticeable signs during the neonatal period since the first studies of these cohorts in the 1950s. For these infants, failure to reach major motor milestones, such as rolling, sitting or standing, have often been the catalyst for the commencement of developmental assessments and interventions. Given that the window for milestone attainment in typically developing children is quite broad [WHO Multicenter Growth Reference Study Group, 2006], this usually leads to a “wait and see” approach where infants receive no intervention during their period of rapid neural development. In view of the fact that every second child with CP will be born at term and requires no special care in the neonatal period, it is imperative that frontline health professionals such as pediatricians, general practitioners and allied health practitioners have a best practice pathway to follow when a parent...
presents with a child who falls into this category.

**Practice point.** When parents bring their term-born child (3 months to 3 years of age) that did not require special care when born to a health professional with concerns regarding motor development or abnormal posturing they should go straight to Pathway B at “screen for CP.” We propose that a tiered approach as developed by Rosenbaum et al. [2009] should be adopted. They recommend using the ages and stages questionnaire + three extra questions for parents. Consideration should also be given to risk factors during pregnancy and signs of mild NE in the neonatal period. When an abnormal result is derived, Pathway B (Figure 5) should be followed to “assessment for CP” through standardized motor assessments.

**The description of cerebral palsy is traditionally given late but can be given earlier**

This review is timely as “it is now universally accepted that the earliest possible diagnosis and treatment (of CP) are essential to prevent, or at least minimize, the handicapping effects of a disability and to make the most of the assets a child possesses” [Alberman and Goldstein, 1970]. Yet, paradoxically, 40 years later families are not automatically receiving early intervention while they “wait and see” whether their child will “catch up” from simply a slower motor developmental trajectory or if their child actually has CP or DCD or an intellectual impairment with associated motor difficulties.
CP registers indicate the average age for a description of CP to be given is 19 months, but the range is wide. For those with severe motor impairment the description of CP can be given as early as 1 week but may take up to 3 years, and less surprisingly for those with mild or moderate motor impairment the description of CP is given anywhere between 1 week and 5 years of age [Watson et al., 2006]. The burgeoning body of recent neuroplasticity literature suggests that intensive, repetitive, task-specific intervention for CP ought to commence very early while the brain is most plastic (i.e., in the first 2 years of life), which is almost never the case when the family is taking part in “wait and see” monitoring prior to description.

Good evidence shows that earlier detection of CP is both possible and accurate and, more importantly, diagnostic-specific early intervention is therefore possible. Rather than waiting for a formal description of CP to be given, infants should be identified as “at high risk of CP” when they are high risk, and therefore commence diagnostic-specific early intervention straight away. For those who are not at high risk but have early signs, they should be regularly comprehensively assessed to ensure access to the most appropriate early intervention.

Why is Cerebral Palsy Missed and Why is the Description so Difficult for Doctors to Make?

Health professionals hesitate to use the terminology CP early for a number of reasons, but importantly the condition is not a diagnosis; it is a “clinical description.” There are no biological markers or definitive tests for CP. The
term does not infer etiology, and it has no prognostic value as severity and associated impairments are incredibly variable. However, 86% of parents know something is wrong with their child before a description of CP is given [Baird et al., 2000]. Leading up to this point in time, most parents experience being told by their medical team that the plan is to “wait and see.” When health professionals use the term “wait and see,” the intention is to use this time to rule out other diagnoses, delay the delivery of bad news or provide time for the child to grow out of it.

**Rule out other diagnoses**

Doctors first rule out other diagnoses that may explain the symptoms. This is an important step as there are other conditions that mimic the early signs of CP which can have important treatment implications, such as: neurodegenerative conditions (e.g., Ataxia Telangiectasia); metabolic syndromes (e.g., Glutaric acidemia); and genetic conditions (e.g., Trisomy 18, Angelman Syndrome, Cornelia de Lange syndrome) [Badawi et al., 1998].

**Delay the delivery of bad news**

Doctors sometimes delay the delivery of bad news while exploring the possibility of a less severe, more common disorder such as DCD. Differential diagnosis is critical as it informs the selection of intervention strategies suited to the specific condition. For example, effective intervention for
DCD involves cognitive approaches best suited to school-aged children, whereas CP intervention uses a variety of pharmacological, motor, social and cognitive intervention approaches that can commence early in life. It is therefore important that children with CP are differentiated earlier in order to get the right interventions early.

Provide opportunity to grow out of it

Doctors sometimes delay the delivery of bad news to provide enough time for the possibility that the child may “grow out of it.” However for those few whose motor signs resolve, commonly they transpire to have an intellectual impairment or behavioral problems [Nelson and Ellenberg, 1981].

The brain injury responsible for CP may be suspected or even confirmed in the neonatal period, but the diagnosis for many does not occur until the motor impairments and activity limitations inherent in the definition are observable. This lag time is not useful to families or to the child.

...I am very worried about my son, he is 5 months old, and over the last month I have noticed he seems to go into strange positions, I especially notice it each time I pick him up. I went to the GP, who agreed and thought I should see a pediatrician. I went to the pediatrician who agreed they were unusual and said let us see how he is when he is 10 months old. That is too long to wait! So I went to another pediatrician who agreed again, it was abnormal, so now I am booked to go to a physiotherapist for further tests, and after that they will decide what to do” but I do not know what to do now...” (Personal communication, February 4, 2012, parent discussion with first author over the phone).

System barriers to description are also potentially at work. For example, for any mother and her newborn, obstetricians hold vital information about maternal-fetal health. If the baby is premature or ill, care is immediately transferred to neonatal specialists, where the primary patient is now the infant, not the mother, and some of the relevant preconception and pregnancy history about risk factors for CP may not be passed on. When the infant is well and discharged from hospital, care is likely to be transferred to a community based general practitioner or pediatrician who may lack access to the relevant maternal-fetal and/or neonatal medical history. The pediatrician may then be assessing a healthy baby that may just appear slightly “delayed,” and it is not until later in infancy that the gravity of the problem may be evident, precipitating a late diagnosis.

What are the Most Important Things that can be Done in Clinical Practice to Describe Cerebral Palsy Earlier?

We propose a new clinical pathway that is designed to circumvent the existing screening and diagnostic barriers by tying together the relevant evidence needed to make an earlier diagnosis and commence earlier intervention (see Pathways A and B). These pathways have been developed using GRADE level evidence [Guyatt et al., 2008] and “traffic lights” to signify the effectiveness of the interventions [Novak and McIntyre, 2010]. Green equals “go,” (high quality evidence to support the use of the intervention, therefore use this approach); Yellow equals “measure” (low quality or conflicting evidence supporting the effectiveness of the intervention). Red equals “stop” (high quality evidence indicating ineffective interventions) [Novak and McIntyre, 2010].

The serious nature of these standard care limitations has led us to conclude that “waiting and seeing” is potentially harmful to children with CP and their families. We therefore have identified solutions to three of the major problems relating to the late diagnosis of CP, which are timely and possible for the health system to redress:

New clinical diagnostic and intervention pathways

When the system fails to recognize a child with CP very early due to using the “wait and see” monitoring mode, this decision essentially ensures that infants receive limited or no diagnostic-specific intervention within the critical window of brain development. The window of brain development, where the brain is actively sprouting and pruning in response to activity, is often misspent in children with CP. In Pathways A and B, we review the evidence for early intervention possibilities in CP. The evidence tells us quite clearly that general early intervention and parent interventions, designed to enhance in-home care characterized by positive interactions, categorically improve a child’s cognition with the
best effect seen in children of low socio-economic status. However, more recent neuroplasticity evidence suggests that a skill-based, high-intensity practice approach to early intervention is required to impact on motor outcomes, as is the case in most adult brain injuries. These newer types of motor learning approaches, which are effective in older children with CP, require urgent study within the CP infant population. It is therefore the responsibility of the health professional who observes major risk factors or a motor delay to investigate further, diagnose “at risk of CP” early, and refer to early intervention at a minimum to optimize their cognitive function. We outline a way to do this via systematic use of risk factor history taking, neurobehavioral predictive tools, in addition to MRI (Pathways A and B).

**Promotion of a climate for new research that will improve outcomes**

Late description of CP is creating a major problem for recruitment of infants to promising early rehabilitative and potentially curative studies. Lack of diagnosis is impeding the advancement of regenerative medicine, early intervention and other well-recognized treatments for CP yet to be tested in the earlier years, for example, medical interventions for tone management, reflux, and epilepsy. When a health professional identifies an infant at high risk for CP, coupled with referral to early intervention trials, it will help to accelerate future discoveries for these children and change the landscape of the diagnosis and prognosis.

**Promotion of good family mental health and resilience for the long-term**

If late description is not helping infants or research, are we helping parents by sheltering them from bad news? A population study conducted in Britain found that parental dissatisfaction with delayed diagnosis of CP is associated with higher rates of parental depression [Baird et al., 2000]. So it would appear that sparing parents from bad news is unhelpful. Therefore early recognition and provision of early preventive mental health support for families may help parents manage the inevitable stress, which could help improve family outcomes long-term.

The concept of “at risk” is not a new one. During the 1960s in the United Kingdom, there were “at risk” registers, with the usual accompanying debate over their value and cost effectiveness. It was deemed not practicable to have universal screening of all children, but it was felt essential that all children at risk be monitored. In a letter to the Lancet in 1967 defending the concept, Dr. Ronald Mac Keith and colleagues wrote, “by the criterion of identifying handicaps which are in some cases undoubtedly, and in other cases probably, benefitted by having treatment started without delay, developmental and neurological assessment from the age of 5 months is neither difficult nor inefficient” [Mac Keith et al., 1967]. The concept itself was deemed by most to be a sound one. The problem at this time was the “at risk” criteria used was identifying up to 60% of all live births in an area. The goal of these programs was to screen 10–20% of all births to identify the majority of the invisible handicaps that is, those that would otherwise not be identified until the 4th and 5th years of life. We recommend that the “wait and see” period is reframed to the “wait and be” period, where children are diagnosed “at risk of CP” early and are immediately referred to diagnostic-specific early intervention.

**What Tools can be Used to Accurately Predict and Identify Early Signs of Cerebral Palsy?**

**Imaging**

**Practice point.** All children with a presumed or suspected brain injury should have magnetic resonance imaging (MRI).

Neuroimaging is used as an integral part of the diagnostic process [Krageloh-Mann and Horber, 2007]. MRI is the gold-standard neuroimaging technique for elucidating the pathogenesis of CP: white matter damage of immaturity (WMDI) including PVL, lesions of the deep grey matter, malformations, focal infarcts, and cortical and subcortical lesions [Bax et al., 2006]. Cranial ultrasound (CUS) is a safe and inexpensive alternative used in the neonatal intensive care unit (NICU) to detect structural changes in the newborn brain. However, MRI has higher sensitivity and specificity than CUS as a predictor of CP in very low birth weight (VLBW) infants [Mirrnan et al., 2004]. Despite strong correlations between clinical findings and MRI, 12–14% of children with CP will have normal MRIs [Bax, 2006; Krageloh-Mann and Horber, 2007] and therefore MRI should not be used in isolation for making the description of CP.

Newer techniques and technologies are being developed which are likely to advance the role of imaging in the diagnostic process and treatment selection process. Advanced neuroimaging techniques such as diffusion weighted imaging (DWI) and diffusion tensor imaging (DTI) have been utilized to more specifically identify diffuse or subtle white matter injuries [Hoon and Faria, 2010]. Magnetic resonance spectroscopy (MRS), provides measures of brain biochemistry and is proving an effective tool in understanding prognosis in NE and preterm infants [Ancora et al., 2010; Van Kooij et al., 2012]. Large deformation diffeomorphic metric mapping (LDDMM), where a 3D atlas of the brain is produced, shows great promise for illuminating the structural brain abnormalities that occur in CP with the potential for informing selection, design, and measurement of rehabilitation interventions [Faria et al., 2011].

**General neuromotor and developmental assessments**

Many neuromotor and developmental assessments with sound psychometric properties exist for infants and young children. For diagnostic purposes, tools with predictive properties are the most worthwhile. However, there has been a historical preference by pediatricians and neonatal follow-up teams to use discriminative tools that assess a combination of: abnormal muscle tone of the trunk and extremities; the presence of primitive reflexes; the quality and quantity of voluntary movement (e.g., milestone acquisition); and the presence of involuntary movement. The problem with this persistent practice is that these tools are only useful for discriminating between infants who are developing typically from those who are not. Determining who is typically developing and who is not is even more complicated in premature infants because they have their own developmental trajectory [Heinemann and Hadders-Algra, 2008; Spittle et al., 2008a]. Routinely used neuro observational and standardized developmental tests were not designed to specifically detect the presence of CP and thus further compound the complexity of the CP diagnostic process. They may be helpful to some diagnosticians but will lack adequate specificity for most.

Ideally the aim of monitoring ought to be to differentiate why some children are not developing normally, to enable diagnostic-appropriate best-
available evidence-based intervention to be provided. This paper will now focus on the evidence for the best available tools for predicting and recognizing CP, distinct from tools better suited to suspecting global developmental delay (GDD). Clinometric reviews indicate that different tools need to be used at different ages to describe and detect CP and that a combination of tools is best practice [Heinemann and Hadders-Algra, 2008; Spittle et al., 2008a].

**Practice point.** A combination of risk factor history taking, neurological examination that includes assessment of quality of movement, volitional movement and neuroimaging are required. A health professional with clinical expertise and experience in motor development should interpret and evaluate the findings generated by these assessments (Figure 6).

**Tools predictive of cerebral palsy**

**Qualitative assessment of general movements [Einspieler et al., 2004].** Of all the tools available to predict CP, GMs is consistently the most predictive, with specificity and sensitivity rates higher than MRI [Burger and Louw, 2009].

The GMs assessment measures the quality of spontaneous movements with the infant lying supine. Scoring is done by trained assessors via observation of video footage and can be used from the preterm period until 20 weeks post term age (PTA). Two distinct time periods for assessment exist; the writhing period (up to 9 weeks PTA) and the fidgety period (from 9 to 20 weeks PTA). In both periods, the infant is scored with “normal” or “abnormal” GMs. Abnormal GMs are then further classified. In the writhing period, abnormal GMs known as “cramped synchronized” have been shown to be highly predictive of CP (sensitivity = 100%; specificity = 84%; PPV = 9.4%; NPV = 100%) [Spittle et al., 2009].

When correlated with MRI findings, namely white matter injury, the GMs assessment (specifically “absent fidgety”) has been shown to accurately predict CP 100% of the time in very preterm infants [Spittle et al., 2008a]. Evidence of the predictive value of GMs in full term infants with hypoxic ischemic encephalopathy (HIE) has also been demonstrated [Prechtl et al., 1993]. Importantly, the GMs assessment has good clinical utility because it is quick, inexpensive, and noninvasive. Rater training is provided by the GMs trust. The Hammersmith infant neurological assessment [Haataja et al., 1999]. The Hammersmith assessment is based on the Dubowitz and Dubowitz [1981] assessment of the newborn and is a simple method of examining infants between 2 and 24 months of age. There are three parts to the examination: neurologic signs, developmental milestones, and behavior. In the first section, the neurologic exam, an optimality score is obtained from the assessment of cranial nerve function, posture, quality and quantity of movement, tone, and reflexes and reactions. The second and third sections do not form part of the overall score but give important additional information regarding developmental progress. Recent studies have demonstrated the predictive value of the Hammersmith infant neurological assessment (HINE) for CP. A large study by Pizzarelli et al., 2008 of 658 infants who were either preterm or term with NE were prospectively studied from birth until 12 months corrected age. ROC curve analysis was used to test the predictive power of the HINE. Global HINE scores showed high prediction of CP at all ages (ROC curve areas above 0.9), but most importantly movement quality and quantity test items had even higher predictive power.

A retrospective study of 70 infants diagnosed at 2 years with CP observed a strong (r = −0.82) negative correlation between HINE scores at 3–6 months of age and levels of GMFCS [Romeo et al., 2008a]. Infants in GMFCS levels 3–5 scored below 40, whereas those in levels 1–2 scored between 40 and 60. Combined use of the HINE and GMs at 3 months PTA can be used to describe an infant as at “high risk” of CP [Romeo et al., 2008b].

**Practice point.** Routine follow-up for preterm and sick infants should be scheduled at three-months and six-months corrected, not the conventional four-months, to enable medical teams to use the best predictive tools to help make the description of CP earlier.

**Practice point.** When examining infants, do not discount CP when spasticity or dyskinesia is not identified. A period of time lapses between the original damage to the developing brain, whether in utero or during early infancy/childhood, and the appearance of impairments. It is well known that the brain, which begins development in utero, continues to develop during childhood. Thus a child’s neural development is “age-specific,” so brain dysfunction will manifest according to the brain’s development at that age [Hadders-Algra, 2004]. Compared with a mature brain which responds to injury with specific and localized signs, a young infant may present with generalized and nonspecific signs (e.g., hypotonia) [Kuban and Leviton, 1994; Hadders-Algra, 2004]. It is proposed that further brain development in an infant, including myelination of axons and maturation of basal ganglia neurons, must occur before spasticity and dyskinesia can manifest [Kuban and Leviton, 1994]. The infant with hypotonia may thus “develop” spasticity and dyskinesia by the age of 1 or 2 years, as the complexity of neural functions increases [Kuban and Leviton, 1994; Hadders-Algra, 2004].

**Movement assessment of infants [Chandler et al., 1980].** The movement assessment of infants (MAI) is a criterion-referenced scale that evaluates neuromotor dysfunction in high risk infants at 4, 6, 8, and 12 months of age. The assessment is carried out by a therapist and takes 30–60 min to complete, requiring a manual but no specialized equipment. The MAI assesses tone, primitive reflexes, equilibrium reactions, and volitional movement. The test has been shown to be twice as sensitive as the Bayley scales of infant development in detecting early signs of CP [Harris, 1987]. Studies of predictive values at 4 and 8 months of age report sensitivity rates ranging from 73.5 to 96.0 and specificity of 62.7–78.2 [Spittle et al., 2008b]. A recent investigation of the predictive validity of the MAI at 6 months of age demonstrated a significant correlation between MAI scores and Bayley scales of infant development at 12 months, although sensitivity and specificity for CP were not reported [Metgud et al., 2011].

**Other useful assessments.** Several other neuromotor assessments, such as the test
of infant motor performance (TIMP) [Campbell, 2005]. The neuro-sensory motor development assessment (NSMDA) [Burns et al., 1989], and the Alberta infant motor scale (AIMS) [Piper and Darrah, 1994], are appropriately used to discriminate infants with abnormal motor function from those typically developing. All have sound psychometrics. Of these tools, the TIMP has been shown to be sensitive to change in response to intervention [Campbell et al., 1995].

Assessment summary.

- High risk infants should be routinely assessed using the GMs preferably three times; during early admission, around term corrected (if preterm) and at 9–14 weeks (corrected for gestational age).
- “High risk of CP” designation should be given to infants at 9–14 weeks (corrected) with a combination of absent fidgety GMs and white matter injury on MRI.
- After 20 weeks (corrected), use the HINE or MAI.
- MRI is the best imaging tool to elucidate the pathogenesis of CP and should be offered to all infants who have abnormal findings.
- Use the CP description form to describe motor type and severity to inform intervention planning.

CONCLUSION

Until recently, CP was considered unpreventable, incurable, and almost untreatable. However, preventive efforts including: rubella vaccination, iodine supplementation in areas of severe iron deficiency, anti-D vaccination, preventing methyl-mercury contamination, reducing the number of embryos transferred in invitro fertilization (IVF) (in Australia), and enforcing laws for seat belts and fencing around swimming pools have been successful prevention strategies. Recently, magnesium sulfate and hypothermic intervention have also started to prevent a small proportion of CP. Both of these interventions occur very early and require health professionals to be mindful of CP as a potential pathway which make recognizing “at high risk” of CP easier for health professionals. We propose a change in diagnostic practice, a shift away from referral for intervention following a formal (most often late) description to one of referral when an infant is “at high risk” of CP. This will provide the opportunity for targeted research in early intervention, thus providing optimal outcomes for children with CP.

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