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## PRETERM NEUROMATURATION AND KANGAROO MOTHER CARE

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An embryo's genes drive its structural development, including development of the brain. The finite number of genes in the human genome cannot complete brain development without environmental input. Continuous interactions between these genes and the environment constitute the process of becoming who we are. Understanding the functional development of the brain, and the intimate relationship between structural and functional development, is key to understanding the impact of Kangaroo Mother Care (KMC) on the neurodevelopment of preterm and low birthweight infants (LBW, BW below 2500 g).

An embryo's brain begins to function as soon as 2 neurons come together; movement begins as soon as muscles are innervated. Multiple developmental processes are critical for brain structural development: neural induction, neurogenesis, neuroblast migration, programmed cell death, formation of axons and dendrites, energy generation for membrane excitability, transmitter biosynthesis, synaptogenesis, myelination, and refining neural networks. Continuous interactions between genes, the intrauterine, and then the extrauterine environment shape the developing brain. Neuromaturation, the functional development of the brain, is a dynamic process that results from these continuous interactions. Detectable by 6 weeks gestation, fetal movements become more differentiated and fluid with gestational age. Responses to tactile stimuli emerge shortly thereafter: stroking the lip elicits fetal movement at 7.5 weeks; stroking the palm elicits some finger flexion at 10.5 weeks. Fetal heart rates begin to develop a circadian rhythm at 14 to 18 weeks; fetal movement does so shortly after. A fetal-maternal synchrony develops beginning at 20 weeks. By 25 weeks, the spinal monosynaptic stretch reflex, many primitive reflexes, and auditory responses are functional. Preterm infants respond to light at 25 weeks; their visual acuity improves with postmenstrual age.

Neuromaturation proceeds in an orderly sequential manner, during fetal, infant and child development. Fetal and preterm neuromaturation reflect the development of 2 major neural pathways that control movement: 1) the subcorticospinal (or extrapyramidal) system originates in the brainstem and travels down the medial aspect of the spinal cord to the muscles; and 2) the corticospinal (or pyramidal) system that originates in the motor and premotor cortex and travels down the lateral aspect of the spinal cord to the muscles. Myelination of the subcorticospinal (medial) system, from 24 to 34 weeks gestation, is reflected in the caudocephalad pattern of emergence of muscle tone: 1) passive flexor extremity tone, first in the lower then the upper extremities, followed by 2) the development of extensor tone, ascending from the lower extremities upward through the body axis to provide the basis for erect posture against gravity. Myelination of the corticospinal system begins at 34 weeks gestation, providing the ability to modulate motor control needed for stable upright posture and individual finger

movements. Myelination continues after term, as infants master the ability to reach for toys, sit, pick up small objects, stand, walk and turn pages in a book. The rate of myelination slows down after 2 years, but continues to 12 years, as fine motor control becomes more precise.

Neuromaturation of preterm infants proceeds mostly in the same sequence and timing as that of the fetus. Neonatal intensive care has improved survival of infants born at and after 23 weeks gestation, but it is a poor substitute for the womb. We have learned to reduce overwhelming visual and auditory stimuli, pay attention to how preterm infants are positioned, and provide supportive barriers. Kangaroo Mother Care (KMC) is the next step in preterm care: it provides a more human, nurturing environment that can promote preterm neuromaturation. With KMC, the preterm infant snuggles between mother's breasts in a more upright position, is sheltered from bright lights and noises, is generally held with limbs flexed but allowed to move spontaneously, and experiences gentle vestibular-kinesthetic stimuli from maternal movement. Compared to technology based NICU care, the more natural KMC environment provides warmth, soothing sounds of mother's heartbeat, and gentle tactile and kinesthetic sensations while promoting emerging flexor tone, spontaneous movement and upright postural control. With KMC, the infant's position is optimal for visualizing the mother's face, the most potent visual stimulus for infants. KMC is associated with greater physiologic stability, autonomic control, and sleep organization. Many trials have shown a reduction in behavioral distress with painful procedures in preterm infants; KMC is recommended as an effective nonpharmacological method of managing pain in preterm infants from 26 to 36 weeks postmenstrual age.

A 2011 Cochrane review found a statistically significant reduction in mortality, infections, hypothermia, and length of hospitalization with intermittent or continuous KMC. This review and others have found better weight gain and head growth, higher rates and longer duration of breastfeeding, and stronger mother-infant attachment. Promoting and facilitating breastfeeding is a key component of KMC. Mothers' breasts provide olfactory stimulation, non-nutritive sucking, cholostrum, trophic feedings, and opportunity for frequent small feedings. For mothers who cannot provide continuous KMC, KMC for 2 hours or more helps to stimulate breast milk production. Benefits of breast milk include ease of digestion, good nutrition, boosted immunity, and improved cognitive development. KMC's effect on physiological and behavioral stability may also promote growth by reducing the infant's metabolic rate and caloric needs.

Prematurity interrupts pregnancy and separates mother from infant. Physiological instability and severe illness makes some preterm infants untouchable. A NICU is a foreign environment for most parents, and they frequently feel marginalized.

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KMC helps repair the bond between mother and preterm infant. It makes mothers responsible for their infant, thereby promoting feelings of competence. KMC may well re-establish the synchrony between mother and fetus interrupted by preterm birth. Holding, rocking, massaging, watching and talking promotes mothers' connection and sensitivity to her infant's needs, which in turn is associated with providing a more enriched child-oriented home environment. A preterm infant is already processing the sound (or music) of language. When infants begin to associate sounds with meaning at the end of their first year, they have already learned what language sounds like.

The safety of KMC for stable preterm infants is now well established. The use of KMC in low income countries with few or no resources for newborn care is justified by improved survival of preterm infants. In middle income countries, KMC for preterm infants helps conserve limited intensive care resources for the sickest infants. Only a few KMC randomized controlled trials have been in high income countries with ample NICU resources. The potential benefits of KMC highlight the need for more trials in this setting, with neonatal and longterm neurodevelopmental assessments to evaluate if and how KMC influences neuromaturation in preterm and LBW infants.

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