Early Human Development – Equity from the Start – Latin America

By Dr. J. Fraser Mustard*

- Abstract: Today we know from studies in social sciences and developmental neurobiology that the environment in the early years of human development sets trajectories for health (physical and mental), learning, and behavior throughout life. We now understand how experience in early life regulates the function of normal genes. Gene functions set in early life are difficult to change. Some societies are beginning to appreciate the importance of early human development for the future quality of their population. Initiatives should be in place that are compatible with the recommendations in chapter 5 of the WHO Commission Report on the Social Determinants of Health. To do this, we must provide equity from the start.

Keywords: Equity from the start, Early human development, Health, learning and behaviour, Experience and early brain development.

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In 1982, he took on the task of creating and establishing a unique Canadian institute, The Canadian Institute for Advanced Research. The Institute’s programs have had a major focus on science, technology, innovation and economic growth and the effect of economic change on the social environment and the health and well-being of individuals and populations.

Dr. Mustard has been a leader in Canada about the socioeconomic determinants of human development and health. A particular emphasis has been on early childhood and the role of communities. He co-chaired a report for the Government of Ontario on early learning with specific community recommendations [The Early Years Study]. Recognition of this has led Dr. Mustard and his colleagues to emphasize to all sectors of society the crucial nature of the early years to provide a healthy and competent population. Dr. Mustard is involved with governments in Canada, Australia, the World Bank, the Inter-American Development Bank, UNICEF and the Aga Khan University in Pakistan in emphasizing the enormous importance to society of early childhood development. Dr. Mustard has received numerous awards for his work including the Companion of the Order of Canada, the Order of Ontario, the Izaak Walton Killam Memorial Prize in Medicine, the Gairdner Foundation International Award for Medical Research, the International Society on Thrombosis and Haemostatis Robert P. Grant Medal. He received the most prestigious Starr Award from the Canadian Medical Association and most recently was inducted into the Canadian Medical Hall of Fame.

Dr. Mustard currently leads The Founders’ Network, which links together 1,000 or more individuals in the private and public sector in Canada and other countries who helped him build CIAR. A number of these individuals are involved with the Founders’ Network in applying the knowledge from the Institute’s programs in their communities. He is Chairman Emeritus of the newly incorporated Council for Early Child Development.

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Desarrollo Humano Temprano – Equidad desde el Principio – América Latina

• Resumen: En la actualidad sabemos, a partir de estudios en ciencias sociales y en neurobiología del desarrollo, que el medio ambiente en los primeros años del desarrollo humano determina el comportamiento de la salud (física y mental), el aprendizaje y el comportamiento del individuo para toda la vida. También entendemos cómo la experiencia regula, durante los primeros años de vida, la función de los genes normales. Las funciones de los genes determinadas en los primeros años de vida son muy difíciles de cambiar. Algunas sociedades están comenzando a valorar la importancia del desarrollo humano temprano para la calidad futura de su población. Las iniciativas deben ser compatibles con las recomendaciones presentes en el Capítulo 5 del Informe de la Comisión de la OMS sobre los Factores Determinantes de la Salud. Para lograrlo, debemos proveer equidad desde el principio.

Palabras clave: Equidad desde el principio, desarrollo humano temprano, salud, aprendizaje y comportamiento; experiencia y el desarrollo temprano del cerebro.

Desenvolvimento Humano na Infância – Eqüidade desde o Principio – America Latina

• Resumo: Hoje em dia, nós sabemos a partir dos estudos nas ciências sociais e na neurobiologia do desenvolvimento que o ambiente dos primeiros anos de desenvolvimento humano determina as trajetórias para a saúde (física e mental), a aprendizagem e o comportamento durante toda a vida. Compreendemos agora como a experiência da infância regula a função dos genes normais. As funções dos genes determinadas na infância são muito difíceis de trocar. Algumas sociedades estão começando a apreciar a importância do desenvolvimento humano na infância na qualidade futura das populações. As iniciativas deveriam ser compatíveis com as recomendações estabelecidas no Capítulo 5 do Relatório da Comissão da OMS sobre os Determinantes Sociais da Saúde. Para fazer isto, devemos fornecer eqüidade desde o principio.

Palavras chave: Eqüidade desde o principio, desenvolvimento humano na infância, saúde, aprendizagem e comportamento, experiência e desenvolvimento do cérebro na infância.

The recent World Health Organization (WHO) report on the social determinants of health, “Closing the Gap in a Generation” (WHO, 2008), has pointed out how experience related to the social environment gets under the skin to affect neurobiological pathways that influence the risk for physical and mental health problems, learning, and behaviour throughout the life cycle (WHO, 2008). In the new review they make the point that the development of the architecture and function of the brain is highly sensitive to the social environment affecting early childhood starting in utero. This is in agreement with other reports. (Barker, 1998; Evans, Barer & Marmor, 1994; Gluckman, 2008) Most recent reports make the point that the goal for early childhood is not just physical survival but also social, emotional, and language and cognitive development. In the WHO report (WHO, 2008) they make the point that the development of young children is influenced by environment across a broad range of sectors including health, nutrition, stimulation, education, water, and sanitation. Because of the linkages between health and early human development, they recommend that WHO and UNICEF set up an interagency mechanism to ensure policy cohesion for early child development such that cross government departments establish a comprehensive whole of government approach to early child development. Other organizations also have an interest in this approach. A number of countries are or are trying to do this (Sweden, Cuba, South Australia) (Skolverket, 2006; Tinajero, in press; Mustard, 2008). This is relevant for government programs for early child development in all Latin American countries. The Commission recommends that governments build universal coverage of a comprehensive package of early child development programs and services for children, mothers, and other caregivers regardless of ability to pay. This is similar to the policies in Nordic countries such as Sweden (Bennett, 2008). Many developed and developing countries are trying to establish a whole of government approach to early child development. This is not an easy goal for societies to achieve.

1. Canadian Institute for Advanced Research – Population Health, Human Development, and Experience-based Brain and Biological Development Programs

My comments on early human development are based on the work of these three programs.

When I finished my term as the Vice-President, Health Sciences at McMaster University, a group of us concerned with the problems of interdisciplinary
research involving health, the biological sciences, and social sciences created a national institution, The Canadian Institute for Advanced Research (CIAR), that could promote interdisciplinary research in complex fields (Brown, 2007). One of the first programs that the Institute established was Population Health to examine how the social environment in which people live affects physical and mental health and what societies could do to improve equity in health. One of the first sets of data this program worked with was the data from England and Wales on mortality by social class (Marmot, 1991). In these studies there are five social classes ranging from professional (category 1) to unskilled (category 5). The standardized mortality ratio for social class 1 was 66, and for social class 5, 166 (Figure 1) (Marmot, 1995). Thus, as one went down the social classes, the mortality rates were higher. Why with a national health care system was there a linear socioeconomic gradient in health? Michael Marmot, who was studying the social determinants of health and the health status of Whitehall civil service in the United Kingdom, became a member of the Population Health program. The data from the study of the Whitehall civil service showed that where you are in the civil service job hierarchy influences your risk of death (Marmot, Bobak & Davey Smith, 1995). Those at the top of the job hierarchy (administrative) have lower mortality rates than the professional executive workers who have lower mortality rates than the clerical staff who have lower mortality rates than those working at lower level tasks in the civil service (Figure 2) (Marmot, 1995). These data are all age and sex adjusted. All the individuals in the U.K. civil service have a salary, are educated, and work in a country with a universal health care system. A key question is why there should be gradients in health as measured by death from a variety of causes in an educated civil service with a national health care system.

Clearly, the inequities in health in the U.K. in the Whitehall civil service were not due to lack of health care. The civil service study of the health gradients as measured by death included both physical and mental health problems. Why in this middle class population (the U.K. civil service) with a national health care program was there inequity in health as measured by death?

At this time there was increasing evidence that early human development including the in utero period set risks for coronary heart disease, blood pressure, and other health problems in adult life (Barker, 1998; Gluckman, 2008). There was some evidence that the function of the stress pathway which is a factor in the risk for cardiovascular disease is influenced by early development. There was increasing evidence that how well individuals cope with their everyday existence was a factor in the risk for coronary heart disease and high blood pressure and that coping skills in later life are influenced during early child development (McEwen, 2002; Mustard, 2006). This led to an increasing interest in the Population Health program about how the development of the neurobiological pathways in early life might be setting
neurobiological pathways that affected risks for physical and mental health problems throughout the life cycle (Daedalus, 1994). This led to the concept of biological embedding in early life. The work of the Population Health program was published in a book, *Why are Some People Healthy and Others Not*, (Evans, Barer & Marmor, 1994).

The members of the Population Health program speculated that if health risks were being influenced by the development of neurobiological pathways in early life, this would also affect learning and behaviour. Recognition of the possible importance of the development of neurobiological pathways in early life on health, led the group to set up a new program to look at the relationship between early development and literacy and behaviour in adult life as well as health. The second program was called Human Development.

The Organization for Economic Co-operation and Development (OECD) had set up a study of literacy in developed countries, which proved to be a valuable resource to look at factors influencing literacy and behaviour throughout the life cycle.

These OECD studies assessed literacy using a scale of 1 (low) to 5 (high) for adults age 16 to 65 (OECD, 2000; OECD, 2001). In Canada, the results of the initial study for Canada were plotted against the socioeconomic status (Canadian) of the families (Figure 3). These data showed as for the health data, that literacy was also a socioeconomic gradient (Willms, 1996). There was a considerable difference between provinces. The data for countries was plotted against the parents’ level of education. Again, literacy was a gradient (Figure 4). Two countries (Sweden and Finland) had high performance, flat gradients, and were above the mean value for all the countries in the study. Canada, Australia, and the United States had more inequity in literacy than Sweden and Finland. In terms of actual performance, Sweden and Finland had a larger portion of their population showing high performance.

A United States study using the OECD format (NALS, 2002) showed that nearly 50% of the population was at Levels 1 and 2. Only 5% were at Level 5 (Figure 5). When they examined the health of the population against the literacy performance, 50% of the population at Level 1 had poor health and less than 1% at Level 5 had poor health (Figure 6). The relationship between health and literacy was also found in the OECD studies. These relationships could mean that health and literacy are all influenced by the development of neurobiological pathways in early life.

There have been no systematic studies about literacy in Latin American countries. However, a few countries have been studied. The results show that the age 16 to 65 population in Chile and Mexico are well behind the literacy levels of the developed countries in the OECD (Table 1). As well as being behind in literacy, Latin American countries also have poorer health as measured by life expectancy. Why? The work of the Human Development program also showed that behaviour of populations also showed a socioeconomic gradient. The work of this program was published as a book, *Developmental Health and the Wealth of Nations*, (Keating & Hertzman, 1999).
The Population Health and the Human Development group concluded that early human development influences health, learning, and behaviour and that this could be related to the development of neurobiological pathways in early life.

2. Developmental Neurobiology

All of this evidence indicates that if one wishes to improve the health and competence of populations, there has to be increased investment in early human development. Since the neurobiological pathways are important in how the brain affects health, learning, and behaviour, it is clearly important to understand how brain development in the early years affects health (McEwen, 2007; Mustard, 2006; Shonkoff & Phillips, 2000; McCain, Mustard & Shanker, 2007), learning, and behaviour throughout life. The conclusion from the assessment of the social determinants of health and learning has led to the conclusion that brain development in the early years of life can set neurobiological trajectories that affect health, well-being, and competence for life. Recognizing these relationships, The Canadian Institute for Advanced Research has set up a third program to follow Population Health, and Human Development, called Experience-based Brain and Biological Development (Canadian Institute for Advanced Research, 2009).

In one sense we are the neurons in our brain, which affects health, learning, and behaviour. We now know that the architecture and function of the brain is not just produced by your genes. The development of the architecture and function of the brain is sculpted by a lifetime of experience. Experience both pre and post-natally as well as the later stages of life, has a significant effect on neuron development and function. The most important period for the development of the neurobiological pathways is in the first few years of life. Experience that affects brain development in the early years includes sound, touch, vision, smell, food, thought, drugs, injury, and disease.

A critical question in human development is does experience have the same effects on brain development at different times in life? The answer is, no. There are qualitative differences at different stages of life. There is something fundamentally different pre-natally versus infancy versus the juvenile period versus adult life. A key factor is gene expression. Experience can alter the response and function of normal genes in neurons leading to differences in phenotype in identical twins who have the same genotype (Caspi, Moffitt, Morgan, Rutter, Taylor, Arseneault, et al., 2004). Each neuron has a nucleus with DNA that is involved in protein synthesis that is important in the function of neurons. Since all of the brain cells in an individual’s head have the same DNA composition, there have to be biological pathways by which specific DNA functions in each neuron can be switched on. This process is referred to as epigenetic, which regulates the function of normal DNA in nerve cells.

Experience is an important factor in switching on the different functions of
DNA in neurons. The neurons, through their axons and dendrites, connect with each other to form neural networks. The strength of the connections between axons and dendrites is also influenced by experience. If neural pathways are underused, the connections are lost. This complex process is often referred to as the wiring and sculpting of the brain.

Detailed studies of the nerve connections that form from birth to adult life have been carried out (Huttenlocher, 2002; Sternberg, 2000). Although the number of neurons does not change significantly after birth, the connections that form the neural pathways grow. By age 6, the neural pathways are extensive. At this stage, weak pathways tend to be cut out so that by the age of 14, a more limited set of neural pathways, as judged by synapse formation, have developed.

Understanding of these processes has led to increased interest in experience and the formation of brain circuits and their functions. High levels of brain circuits depend on precise or reliable information from lower levels in order to accomplish their function (Knudsen, 2004). Sensitive periods for the development of lower-level circuits tend to end early in life. Higher-level circuits remain plastic for a longer period. The implication of this knowledge is that the development of the architecture and function of the brain in the early years has a major effect on subsequent development. Studies of brain development have shown that the sensing pathways for vision, hearing, touch, and other pathways begin before birth and are largely finished within four years after birth.

Language is very dependent upon the development of the critical sensing pathways. The basic capability for language is largely set by four years of age (Pugh, 2008). Higher cognitive functions, which is where education programs have a major effect, are built upon the neural pathways that are started early in life. Chuck Nelson prepared a diagram (Figure 7), which was in From Neurons to Neighborhoods, (Shonkoff, 2000) showing how language pathways begin to develop after sensing pathways. This illustrates how early brain development begets later learning and skill development. Thus, experience dependent shaping of high level circuits depends on the quality of information provided by the lower level circuits. The high level circuits cannot be completed until the feed from the lower level circuits are stable and reliable. The sensitive periods for high level circuits can remain plastic for a longer period than low level circuits. This may be one of the reasons why with proper treatment of individuals with dyslexia, normal brain pathways can be established.

One of the important new observations about sound particularly in relation to language is that the plasticity of the neurons for sound is very good during infancy (first seven months of life) (Kuhl, 1992). Thus, infants exposed to two languages (e.g. English and Japanese) in this period can develop fluency in both languages with no accent (Werker, 2008). If you do develop capability in two languages in early life, it may be easier to learn other languages later in development.
The differentiation of neurons for sound or language in the early years is affected by the degree of language exposure in the first three to four years. Figure 8 shows the exposure of three groups of children to words in the first three years of life (Hart & Risley, 1995). During the first three years exposure to language, children in low socioeconomic circumstances are not exposed to the same number of words as children in the higher socioeconomic circumstances. Vocabulary growth of children during the first three years is highest in the top socioeconomic group that has the most language exposure (Figure 9) (Hart & Risley, 1995). The children in the lowest socioeconomic group show on average the lowest vocabulary growth and they have least language exposure during the first three years. The children with the best verbal skills at age three do best in language and literacy in the school system. Those with low verbal skills do poorly in language and literacy in the school system. All of this evidence is in keeping with the increasing evidence that experience in the early years of life has a major effect on the differentiation and function of neurons and neural pathways that are involved in literacy and language.

Health and behaviour are profoundly influenced by what is often referred to as the hypothalamic pituitary adrenal gland pathway or stress pathway. McEwen (2007), in attempting to get better understanding of how this pathway affects how we function each day, has proposed that it should be called allostatic pathway and the load of this pathway each day called the allostatic load. This implies that stress can be normal, excessive, or low depending on the allostatic load. Excessive stress tends to be damaging to biological systems (McEwen, 2002). Emotional stimuli coming in through the sensing pathways can stimulate the amygdala, which can stimulate the prefrontal cortex and the hypothalamus. The hypothalamus can stimulate the sympathetic division of the autonomic nervous system to release adrenaline from the adrenal gland. This is often referred to as the fast response stress pathway. The hypothalamus can also stimulate the anterior pituitary gland to release hormones (ACTH, TSH, FSH, LH, GH, and prolactin). ACTH stimulates the adrenal gland on the kidney to release cortisol. The response of this pathway affects the cortisol (sterol) levels in the blood every day. Cortisol affects the cells and tissues throughout the body including the brain. This is often referred to as the slow reactive stress pathway. Cortisol can enhance the effects of stimuli on the amygdala.

Cortisol levels are in part regulated by the hippocampus in the brain, which has cortisol receptors that can bring the stress response into equilibrium. Excess stimulation of the stress pathway can lead to overproduction of cortisol with effects on behaviour (ADHD), violence, mental health problems like depression, type II diabetes, malnutrition, cardiovascular disease (myocardial infarction and blood pressure), memory loss, problems with immune systems, and drug and alcohol addiction (McEwen, 2007). It is also possible to have under-production of cortisol, which is associated with chronic fatigue,
fibromyalgia, immune system (autoimmune disorders), rheumatoid arthritis, allergies, and asthma (McEwen, 2002; McEwen, 2007). This brain pathway has major effects on how individuals respond to events every day, which in poor environments can lead to excess stimulation. As well as its effect on health (physical and mental), this pathway can affect behaviour, memory and learning. In a recent review, McEwen (2007) summarizes the importance of this pathway.

“The intent of this review has been not only to summarize salient facts pertaining to the central role of the brain in the effects of stress on brain-body interactions over the life course, and the protective and damaging paradox of these interactions, but also to provide a conceptual framework for future studies that will infuse physiology and neuroscience into the better mechanistic understanding of complex stress-related social problems and their solution by every means available: biological, behavioral, sociological, and political.” (McEwen, 2007).

“Events early in life affect how the brain responds to stressors throughout adult life and influences the aging process as well as susceptibility to the diseases of modern life, such as cardiovascular disease, diabetes, and depression. This connection occurs in part because the nervous system regulates and responds to systemic processes via the neuroendocrine, autonomic, and immune systems. Social factors, along with physical activity, have a powerful impact on brain development, structure, and function throughout the life course and thereby affect the health of the body as well. Therefore, manipulations of the social environment via policies of government and the private sector, along with promoting increased physical activity, healthy life-style, and social support at an individual level, can help encourage individual behaviour change, that, in turn, is an effective way of counteracting the deleterious effects of chronic stress as an adjunct and, in some cases, alternative to pharmaceutical therapy.” (McEwen, 2007).

In studies of rats, monkeys, and humans, touch appears to be one of the experiences in early life that affects the function of the stress pathway. In rats, it has been shown that touch can alter through epigenetic expression of the neurons in the stress pathways (Meaney, 2001).

The work of Meaney and his colleagues (McGowan, Meaney & Szyf, 2009) has shown in rats that the adult offspring of mothers that have had strong pup licking/grooming (i.e., high licking and grooming mothers) over the first week of life show increased hippocampus expression of the glucocorticoid receptor. Enhanced glucocorticoid feedback sensitivity decreases hypothalamic corticotrophin releasing (CRF) expression. This leads to more modest HPA stress response compared to animals reared by low licking and grooming.
mothers that do not have adequate glucocorticoid receptors. Cross-fostering studies suggest direct effects of maternal care on both gene expression and stress responses. These studies support an epigenetic mechanism since the fostering mother and not the biological genetic mother defined the stress response of the offspring. They have demonstrated that the GR exon I, promoter is programmed differently in the hippocampus of offspring of the High and Low LG maternal care and that differences which emerge between day 1 and 6 after birth remains stable thereafter. These differences include histone acetylation and DNA methylation of the glucocorticoid receptor gene. This is one of the first demonstrations about how the function of genes can be influenced by experience in early life. (Meaney, 2001; Meaney & Szyf, 2005; Szyf, McGowan & Meaney, 2008). The rat pups that are poorly licked will show excess response to stress with increased blood glucocorticoid levels, behaviour problems, memory loss, and addiction to alcohol.

Caspi and colleagues (Caspi, Moffitt, Morgan, Rutter, Taylor & Arseneault, 2004) have examined in the Dunedin birth cohort the relationship between the structure of the serotonin transporter gene and experience in early life. In this population, they had three groups of people: those who had two short alleles (from the father and mother); those who had a short allele and a long allele; and those that had two long alleles. The children with the short alleles subject to neglect and abuse when young had an increased risk of depression at age 26. Those with the long alleles, subject to neglect and abuse, did not show an increased risk for depression. All three gene groups brought up in supportive non-abusive households did not show an increased risk for depression. Similar results have been found in studies of rhesus macaque monkeys. Thus, neglect and abuse in monkeys and humans when young can lead to effects on the serotonin transporter gene function. If those with the short gene structure are well nurtured when young, their risk for depression is the same as for those with the long alleles brought up in normal or abnormal circumstances. Individuals with the long alleles are resilient to the effects of poor nurturing (Figure 10). This and other studies demonstrate that there are gene environment interaction in which epigenetics is important. We also know that microRNAs can affect gene function (Chuang & Jones, 2007). Experience also affects the function of microRNAs.

Although monozygotic twins because they have identical genes will have the same genotype, they will not all have had the same experience in early life and thus there will be differences in gene expression (phenotype) among identical twins (Caspi, 2002; Fraga, 2005). Although the twins will have the same genotype they can have as adults different phenotypes. The processes which regulate normal gene function includes epigenetics and microRNAs. Thus, the nature nurture debate requires that integration of genetics and epigenetics to better understand experience and neuron development. Experience can change gene function.

Fetal growth in utero has a significant effect on future health and cognition
and probably involves epigenetics and microRNAs (Barker, 1992; Gluckman, Hanson, Cooper & Thornburg, 2008). A smaller size and relative thinness at birth is associated with increased rates of coronary heart disease, type II diabetes, blood pressure, obesity, and probably is a factor in causing the metabolic syndrome. Prematurity itself, independent of size for gestational age, has been associated with insulin resistance and glucose intolerance in young children. In studies of the 1958 U.K. birth cohort (Jefferis, Power & Hertzman, 2002), the researchers found that low birthweight infants did poorly in mathematics at ages 7 and 14. They found that low birthweight children in the upper social classes improved their performance in mathematics in the school system (but did not equal the performance of children of normal birthweight), while those in the lower social class deteriorated in performance. This evidence is compatible with the concept that later experience may not overcome a poor start even if it begins in utero.

It is now clear that early life has a significant effect on brain architecture and function in adult health, learning, and behaviour. Early experience affects:
2. Shapes emotion, regulates temperament and social development.
3. Shapes perceptual and cognitive ability.
4. Shapes physical and mental health and behaviour in adult life.
5. Shapes physical activity (e.g. skiing, swimming, etc).

3. Early Brain Development and Health, Learning, and Behaviour

Our increased understanding of how early experience affects the architecture and function of the brain, with major effects on health, learning, and behaviour, has provided evidence about how poor early development can affect literacy, cognition, and health throughout the life cycle. In medicine, conditions which share some common pathways are usually listed as “co-morbidity”. In terms of the function of the brain, this concept now needs to be extended. The biological pathway involved in physical and mental health, learning, cognition, and behaviour can lead to problems because of poor early development in all these sectors, often manifested in the same individual. For example, individuals with myocardial infarction often suffer from depression.

Another example of this relationship between early development, learning, and health is the correlation found in the OECD studies of literacy between life expectancy and literacy capability (OECD, 2000). A variety of explanations can be given for this relationship, but in light of the new evidence from our understanding of the development of neurobiological pathways and their effects on physical and mental health, cognition, and behaviour brings out the importance of understanding experience and the development of the function of the brain and the gradients in health and literacy.
A Swedish study found that children, who have poor verbal skills at the age of 2, tend to do poorly in literacy as teenagers in the Swedish education system. About 25% of the male children in this group of teenagers engaged in behaviour that brought them into the criminal justice system. We now know that the conditions of very early life influence the neuronal pathways that affect behaviour and language and literacy and are profoundly influenced by stimulation including touch in very early life. Children with poor verbal skills at age 2 (Stattin & Klackenberg-Larsson, 1993) are unlikely to have had adequate stimulation (including touch) with a caregiver and language. Thus, they could be deficient in the extent of touch and verbal exposure they were exposed to when they were very young which, of course, will affect the stress pathway with its effect on behaviour as well as literacy and language development.

3.1 Health

Another condition that we know is influenced by the in utero period and infancy is the risk for developing coronary artery disease and high blood pressure. The relationship between coronary artery disease and depression (Anda, Williamson & Jones, 1993; Carney, Blumenthal & Stein, 2001; Grippo & Johanson, 2002) can probably be related back to early development and the effects on the neural pathways that affect coronary artery disease and the HPA pathway and depression. Another example of early development and cognitive development is the relationship between birthweight and cognitive outcomes at age 33 (Jefferis, Power & Hertzman, 2002). Since birthweight reflects the prenatal period, this evidence shows, as does the evidence of Barker and others that development prenatally affects later development with effects on cognition, behaviour, and health in adult life.

The studies of population health have shown that early development affects adult health and health inequities in adult life (Barker, 1998; Gluckman & Hanson, 2004). Most of the socioeconomic gradients in health have been dependent upon the studies of adult populations. Recent studies have shown that using more sensitive measures of health, gradients in health can appear within the first three years of life (Case, Lubotsky & Paxson, 2002) (Figure 11). Birthweight is a predictor of health, behaviour, and learning in later life (Power, Hertzman, Matthews & Manor, 1997). Malnutrition also contributes to gradients in health.

A Swedish longitudinal study of early child development and adult health found that the more adverse the early child development environment, the greater the risk of poor physical and mental health in adult life (Stattin & Klackenberg-Larsson, 1993). Children brought up in the most adverse circumstances had a substantially increased risk of cardiovascular disorders. This study did not take into account the conditions of pregnancy which we now know increase the risk for cardiovascular disorders in later life. In this
study they also found that adverse early circumstances substantially increase the risk of mental health problems such as depression in adult life.

Donald Acheson’s study (Acheson, 1998) of inequalities in health in the United Kingdom came to the following conclusion: “Follow-up through life of successive samples of birth has pointed to the crucial influence of early life on subsequent mental and physical health and development.”

In studies of early human development, inadequate attention is paid to how early development in utero and in the first years of life sets risks for chronic health problems in adult life as well as learning and behaviour.

### 3.2 Behaviour

A Swedish study (Stattin & Klackenberg-Larsson, 1993) looking at early learning and criminal behaviour found a significant correlation with registered criminality and language development at 6, 18, and 24 months. As explained in the section on developmental neuroscience, language exposure in the early period has a significant on subsequent language and literacy development in the school system. A major factor in developing language capability in the early years is the extent of language exposure which involves reading and talking to infants and toddlers. This will require holding the young child (touch) with its effects on the HPA pathway.

Another striking feature of development in the early years and the neurobiological pathways is the relationship between poor early developmental environments and addiction to drugs and alcohol. In the Adverse Childhood Experiences (ACE) study (Kaiser Permanente) (Felitti, Anda, Nordenberg, Williamson, Spitz & Edwards, 1998), it was found in a retrospective study of adults with drug and alcohol addiction, that the degree of neglect and abuse when they were young correlated with the risk of drug and alcohol addiction. Teicher (2002), in a detailed study of early development and brain development, came to the conclusion that maltreatment at an early age can have a negative effect on a child’s development and function. He came to the conclusion that the aftermath of poor early development can appear as depression, anxiety, suicidal thoughts, or post-traumatic stress or as aggression, impulsiveness, delinquency, hyperactivity, or substance abuse. This co-morbidity is not surprising since the neural pathways that influence these conditions share some common pathways and are all influenced by poor early development, in part through effects on gene expression (epigenetics) in the HPA pathway and related structures such as the amygdala and the prefrontal cortex.

### 3.3 Literacy and Cognition

It is generally accepted that in today’s complex world with the exponential growth in knowledge and technologies that the literacy and cognitive capability of populations is very important for societies. The OECD has been doing
studies of developed countries and found that there is considerable variation in terms of the literacy performance of these countries. In doing this work on populations aged 16 to 65, the OECD (2000) uses five levels of literacy competence. Level 1 indicates persons with very poor skills. Level 5 means competence in sophisticated reading tasks, ability to integrate knowledge from different fields, and critical thinking skills. They considered Level 3 as the minimum for coping with the demands of everyday life and work in today’s world with exponential growth in new knowledge and technologies.

In this work, they have plotted the literacy scores for populations aged 16 to 65 against the parents’ level of education. The data for developed countries shows that literacy is a socioeconomic gradient using parents’ level of education (Figure 4). In this assessment, the literacy gradient for Sweden and Finland is above the mean for developed countries. Canada and Australia have a significant portion of their population below the mean for developed countries as does the United States. Chile, which is one of the better Latin American countries, has a gradient below the mean for developed countries. The OECD has done studies comparing developed countries like Sweden, Canada, US with Chile and Mexico. In this study more than 80% of the population aged 16 to 65 in Chile and Mexico had low levels of literacy (levels 1 and 2) (Table 1). Less than 3% of their populations were at levels 4 and 5. This data implies that Latin American countries need to substantially invest in early human development (including the in utero period) if they wish to have more equity in literacy, health, and the competence of their future populations.

UNESCO has done two studies of language and mathematics in Latin American schools. The first study shows that Cuba has a mean value in language scores in grade 3 and grade 4 (UNESCO, 1998) that was two standard deviations better than the mean value for the other Latin American countries (Figure 12). This is a substantial difference. In this study they found that the language scores for the populations based on the parents’ level of education was a gradient (Willms, 2002) (Figure 13). The gradient for Cuba is much higher and flatter than the gradient for the other Latin American countries. Cuba had more equity in language capability of the grade 3 and grade 4 students.

In the second UNESCO study reported in 2008 (UNESCO, 2008), in grade 3 and grade 6 reading and mathematics scores, the performance of the Cuban children was again substantially better than for the children in other Latin American countries. However, the performance was not as good as in the first study. It is possible the Cubans changed aspects of their early child development programs or that there was improvement in the many Latin American countries. The Cubans in the late 1970s introduced a program to help pregnant mothers and mothers with young children. This polyclinic approach was well staffed with well-trained health professionals including family physicians and pediatricians (Alfredo Tinajero, personal communication). This program
involved extensive home visits during pregnancy and after the baby was born. The program provided health prevention, nutrition, and stimulation. In view of what we now know about child development in the early period, it is possible that the polyclinic approach had a significant effect on child development in all parts of Cuban society (rural and urban). The Cuban mathematics and literacy performance in grade 3 and grade 6 in rural areas is nearly as good as in the urban areas (UNESCO, 2008). In 1993, the Cubans introduced a program, Educa a tu Hijo, to pick up families with young children that did not go into their Circulos Infantiles program, although they took part in the polyclinic program started in the 1970s (Alfredo Tinajero, personal communication). The results of the first UNESCO study (1998), that sampled children at age 8-9, are probably related to the effect of the health polyclinic program since the early child development program was not started until 1992-1993 (Educa a tu Hijo). From what we now know from developmental neuroscience, the largest effects on literacy performance are in the first three years of life. Thus, the children in the first UNESCO study would have had the full polyclinic program, which provided good health, nutrition, and stimulation and would not have benefited from the Educa a tu Hijo program in the early years which was started in 1992-1993. The results of the 2008 study may have been affected by the changes in the polyclinic program and the move to the new program. 

There has been reduced participation by physicians because of the large number of Cuban health professionals working overseas. We do know that the Cuban early child development programs, polyclinics, and education involve at least 99% of all families with young children. The other Latin American countries do not have universal population-based programs for early development that are similar to Cuba.

### 4. Outcome Measures for Early Brain and Human Development

One measurement that is now increasingly used to examine early development and the stress pathway is to measure salivary cortisol, which is a measure of the blood levels. There is increasing evidence that children who have a poor early development have abnormal cortisol levels in their blood (Hill, Waldfoe & Brooks-Gunn, 2002). Another set of measures that relate to brain development and function are the conditions of pregnancy and the effects on the size and birthweight of a newborn child. Because the early period of development can have a long reach affecting later development, there are attempts to build an assessment of early child development at 18 months. This is difficult to do on a population basis in my country because the first time that we can capture all the children after birth is when they come into the school system. It is at this time of school entry that we can assess the first five years of development. We have developed the Early Development Instrument (EDI) to assess children at the time they enter kindergarten (Janus & Offord, 2000). The EDI is a crude macro measure of early brain
development. It examines physical health, activity and well-being, social knowledge and competence, emotional health and maturity, language and cognitive development, communication skills, and general knowledge. These are all measures that relate to brain and biological pathway development in the early years.

In the application of this technique in Canada we have arbitrarily adopted the concept that children who score in the bottom 10% of any of the assessments can be considered as vulnerable (Kershaw, Irwin, Trafford & Hertzman, 2005); that is, they will not progress well in the school system. In our assessment of children age 5-6 years at the time of school entry, about 32% of the children in families with a low income are vulnerable, while about 13% of children in the families in the higher income group are vulnerable. Like health, the vulnerable children plotted against socioeconomic measures (family income) show a gradient. Thus, the EDI is picking up the effects of the social environment on the early years on development and it is, like health, a socioeconomic gradient. This technique has been used in Australia and they too found a gradient in vulnerable children in relation to family income (Mustard, 2008).

In Canada we have examined school performance against the EDI results. In the case of reading, 13% of the children in Vancouver without an EDI vulnerability failed to pass grade 4 test (Hertzman, 2004). Children with 4-5 vulnerabilities, 48% failed to pass the grade 4 test. A problem with school-based tests is that a number of children will not come to school to do the exams. Therefore, the percent not passing grade 4 (including those not doing the test) with zero vulnerabilities was 17%, and the percent not passing grade 4 vulnerable in 4 or 5 of these assessments was 68%. Similar results were found for the numeracy tests.

One of the advantages of doing the EDI by district is that districts with a number of vulnerable children can take steps to improve performance. In Western Australia they took two districts with close to 50% vulnerable children and put in an early development program for the children and within three years dropped the percentage of vulnerable children to less than 15% (Sally Brinkman personal communication).

The EDI is a simple measure to assess early child development in communities and provides information that is relevant to performance in the school system and also provides a benchmark against which one can measure the effect of early child development programs to reduce the number of vulnerable children.

5. Cendi, Mexico, and Cuba

CENDI in Monterrey Mexico has adapted aspects of the Cuban programs for children in a poor district of Monterrey Mexico. This program begins with pregnancy. We have applied the EDI to these children (Magdalena
Janus and María Guadalupe Rodríguez Martínez, personal communication). This assessment measured at the time children enter the formal school system physical health activity and well-being, social knowledge and competence, emotional health/maturity, language and cognitive development, communication, and general skills. Children who score in the bottom 10% on any of the assessments are considered vulnerable. In Canada where there has been extensive use of the EDI, it was found that children in Vancouver who are vulnerable in four out of five of these assessments had a high failure rate for grade 4 reading tests. Eighteen percent of the children in the poor district of Monterrey in the CENDI program were vulnerable at the time of school entry on the EDI assessment, whereas 38% of the children in the district that did not have the CENDI program were vulnerable on the EDI test. We found that the CENDI children, compared to a Canadian normative sample, outperformed the Canadians in all but the fourth category. Canada does not have a CENDI program but our comparison of middle class children, who go to a variety of early childhood programs in Canada, with poor children in Monterrey in the CENDI program indicates that the Mexican children are doing much better on the EDI than the Canadian sample of middle class children (Alfredo Tinajero and Magdalena Janus personal communication).

6. The need for Early Child Development Programs involving parents

One of the questions that is raised about early child development programs is when the programs should begin. The Cuban and CENDI (Mexico) data suggests that you should begin at least during pregnancy. Grantham-McGregor (1991); Walker and Grantham-McGregor (2005) studied the effect of improved nutrition for undersized children at birth (low height for age) (Figure 14). She found that 24 months of improved nutrition improved the development of these stunted children. Stimulation (experience) also improved mental development of these children. The combination of stimulation and nutrition in this early period of life brought the undersized children close to the performance of children with normal height. This demonstrates the importance of nutrition in the early years and stimulation on development. It is interesting that in this study, the benefits of stimulation were still present at age 11. Another study that has looked at the importance of early development is the study of children in the Romanian orphanages (Le Mare, 2005; Rutter & O’Connor, 2004; Ames, 1997). Following the collapse of Communism, the studies found that children adopted into middle class homes after eight months in the orphanages, show at 11 years of age, in contrast to the children adopted within four months of birth, abnormal brain development (small brain, low metabolic activity, abnormal EEGs), social and cognitive problems (low IQ), high vulnerability to behaviour problems (ADHD, aggression, and quasi-autism). In a more recent study (Nelson, 2007), they randomized the children in the orphanages into foster parenting homes and kept the others
in the orphanage. They found in this study that the cognitive outcome of children who remained in the orphanages was markedly below that of non-orphanage children in Romania and children taken out of the orphanage and placed in specially trained foster care programs. The earlier the children were placed in foster care, the better the outcome.

Another study which examined the effect of early development programs on reading and numeracy is the Abecedarian study (Campbell & Ramey, 2002; Ramey, Campbell, Burchinal, Skinner, Gardner & Ramey, 2000). In this study the children in a poor Black community in North Carolina were randomized at 4 months of age into an intense preschool program with home visits or left with whatever community support the families could find (Figure 15). At the time of school entry, the two groups were then split randomly so that one group went into a special 3-year education program and the other remained in the standard school system. At the time of school entry, the children that had been in the preschool program and placed in the standard school system showed improvement in reading and numeracy which was present at age 21. The children from the preschool program randomized into the special 3-year program showed the best performance in reading and numeracy at the age of 21. The children not given the preschool program or the special 3-year program had the poorest performance in reading and mathematics.

In a New Zealand education study, they found that children who were in the highest quartile of performance at the time of school entry on a developmental assessment performed well in mathematics and reading up to age 14 in the school system. The majority of those in the lowest quartile, 80-90%, performed poorly up to age 14 (Wylie, 2004). All of this evidence is in keeping with the argument that early child development affects performance in the school system.

Ludwig and Sawhill (2006) at the Brookings Institution in reviewing all the evidence argued for the need to establish early child development and parenting centres linked to the primary school system. These programs should begin with parents when a child is born. The programs based on what we now know about experience and early brain development should start early, with continuing participation for families with young children in a group structure with quality staff and effective programs.

The weight of the evidence from studies in developmental neurobiology and studies of child development in different countries indicates that countries should establish early child development and parenting centres for families with young children. They should if possible be available from pregnancy to primary school. They should provide support for parents and non-parental care. They should provide home visits. It is important that they be integrated with the primary schools. Several countries have placed early child development in their ministries of education (Sweden, Cuba, and South Australia). Because of the effect of early child development on health, such centres should also be linked with public health.
The Scandinavian countries tend to have early development programs available for all families with young children. These are not compulsory programs but more than 85% of families with young children take part. This is probably one of the reasons why these countries tend to outperform other developed countries.

The cost in Canada of poor early child development in respect to crime and violence in the population is over $120 Billion per year (Mustard, 2009). The cost to individuals and society of mental health, behaviour, and drug use is at least $100 Billion per year (Mustard, 2009; Gnam, Sarnocinska-Hart, Mustard, Rush & Lin, 2006). In Canada a universal early child development and parenting program properly staffed and funded for 2.1 million children with an 80% uptake by families with young children would cost about $18 to $20 Billion per year. The economic and social benefit to societies if they can put these early child development programs in place is huge. Jim Heckman, a University of Chicago economist (Heckman, 2000) has shown that the return for dollar invested in preschool programs is greater than per dollar in school programs. He has concluded (Heckman, 2000), “We cannot afford to postpone investing in children until they become adults nor can we wait until they reach school – a time when it may be too late to intervene.”

The Latin American countries should consider adopting the recommendation in chapter 5 of Marmot’s WHO report (2008) – Equity From the Start: “Governments build universal coverage of a comprehensive package of quality early child development programs and services for children, mothers, and other caregivers regardless of ability to pay.” The Economist magazine writing about early child development in 1998 stated that because of the importance of early child development and “the principle of free education for school age children is already entrenched throughout the rich world, there would be nothing incongruous about extending it further down the age range.” (The Economist, 1998).

7. Socioeconomic Considerations and policy

The cost of universal early child development and parenting programs in Canada would be between $18 to $20 Billion per year. That would be about 1.5% of our gross domestic product (GDP). The present expenditure in Canada is about 0.25% of GDP. In an assessment of public spending and cash benefits for families with young children as a percentage of the GDP, Sweden’s figure is 22.9%; Canada’s expenditure is 3.41% (Lynch, 2006). The Swedish expenditure for children age 1 to 6 years in their universal programs is $15,000 per year per child (Mustard, 2009). This is significantly higher than the cost for their regular school system of $10,500 per year per child. The Swedes provide good maternal and parental leave policies with income support.

In this report we have referred to a rich developed country that gives a
high priority to early child development (Sweden) and a relatively poor Latin American country (Cuba) that does the same thing. In both these countries the investment in early childhood is a priority has a profound effect on equity in health (physical and mental), literacy, and language competence. This reinforces Jim Heckman’s conclusion when he looked at the return to human development investment: “We cannot afford to postpone investing in children until they become adults nor can we wait until they reach school - a time when it may be too late to intervene.” (Heckman, 2000) The challenge to Latin American countries if they wish to improve the quality of their populations for the future is to start investing in high quality early child development programs now. It will take at least a generation before the benefits will extend to all the population.

Implementing a comprehensive approach to early child development, as recommended by the WHO (2008) and other reports, would provide a healthy start for all children in Latin American countries. The goal of equity from the start as set out in the WHO report should be the policy for all Latin American countries as well as Canada and the United States.

References


Henry Press.


Figure 2 - Age Adjusted Mortality Rates (percentage) by Grade of Employment for Whitehall civil servants age 40-64. First ten years of study.


Figure 4 – This figure shows the population (ages 16 to 65) plotted against parents’ level of education. Adapted from *Literacy in the Information Age: Final Report of the International Adult Literacy Survey*. 2000. OECD and Statistics Canada.
Figure 5 - National Adult Literacy Survey (NALS). (2002). Adult literacy in America. National Center for Education Statistics. U.S. Department of Education.
Figure 6 - National Adult Literacy Survey (NALS). (2002).
Figure 7 - Prepared by Chuck Nelson, this shows that the development of the sensing pathways for vision, hearing, touch and other pathways, begins before birth and is largely finished by the time a child is four years old. The development of these sensing pathways is important for the development of language which starts after the sensing pathways for sound and vision get established. It is of interest that the basic capability for language is largely set by four years of age. Higher cognitive functions, which is where education programs have their major affect, are built upon the neural pathways that are started earlier.
Figure 8 - When the children of this study of Hart and Risley were tested for their vocabulary over the first three years of life it was apparent that the children in the high SES group exposed to extensive vocabulary, had the most vocabulary growth, while children in the low SES group with less language exposure showed a much smaller vocabulary growth. In this study the children were followed into the school system, and those that had the greatest language exposure had the best performance in language and literacy in the school system at age 9.
Figure 9 - This slide shows that the children in the group with the highest vocabulary score had the greatest exposure to language. This is obviously related to talking and reading to the child. This is a demonstration of what can be called the “dose” effect, that is, the degree of interaction or stimulation with the child at this stage of development is important and influences outcomes in later life.
Figure 10 - We now better understand the dynamics between genes, experience and gene expression (epigenetics). This slide shows the evidence concerning the serotonin transporter gene function, the hippocampus prefrontal brain interaction, and the risk for depression in adult life. These data by Caspi and colleagues are from the longitudinal study of the Dunedin birth cohort in New Zealand. Similar observations have also been provided from studies of rhesus macaque monkeys. Neglect and abuse of monkeys or humans when they are young can lead to effects on the serotonin transporter gene function. Those with the short allele for the serotonin transporter gene, if they are neglected and maltreated when they are young, their serotonin pathway in adult life is altered (inadequate serotonin levels) and their risk of depression as adults is greatly increased. If they are well nurtured when they are young, their risk for depression in adult
life is the same as those with the long alleles. Individuals with the long alleles are resilient to the effects of poor nurturing. This is evidence from humans and monkeys about the effects of early experience on brain function and mental problems in adult life and how the interaction between experience and gene function is probably related to epigenetic effects. Since mental health problems such as depression are a significant cost to society, it is quite clear that investment to improve early child development in our society should be an important public health measure. The costs of treating individuals with depression and its social costs are probably greater than the costs of improving the conditions for quality early child development.
Figure 11 – Health and income for children from the National Health Interview Survey (NHIS) (1986-1995) and Panel Study of Income Dynamics.
Figure 12 - One test of the effectiveness of the Cuban program, carried out by UNESCO, showing that the mean value for Cuba in terms of language scores in grade 3, is two standard deviations better than the value for other Latin American countries. We believe that this difference is largely related to the quality of the ECD program provided for families with young children in Cuba. There has been no direct comparison of these results for Cuba with the results from developed countries. From a practical standpoint, Canadians who run significant businesses in Cuba, find that the young Cubans are the best educated workforce in all developing countries. We have been exploring using the Canadian Early Development Instrument (EDI), how the early child development as measured by the EDI compares between Canada and the program based on the Cuban program in Monterrey, Mexico. This figure is adapted from the 1998 UNESCO study. The solid black vertical line is the mean.
Figure 13 – This shows the results from 1998 UNESCO study. Cuba’s result is outstandingly better than other Latin American countries. Adapted from Willms, 2000. In: From early child development to human development. M.E. Young (ed.). The World Bank.
Figure 14 – From Grantham-McGregor et al. 1991. Mean development scores of stunted groups adjusted for initial age and score compared with a non-stunted group adjusted for age only, using Griffiths Mental Development Scales modified for Jamaica.
The Abecedarian study was a randomized trial of African American children in North Carolina at four months of age. The children were split into two groups. One group was placed in an early child development group involving home visits for 12 months for each year. The other group was supported by whatever family and community support was available for them. At school entry, the groups were split into two groups: one attending school with a special education program for the first three years and the other half went to existing three-year education programs. At age 21, the children in the four groups were assessed in terms of numeracy and literacy. The three groups which had been given the preschool programs and or the three-year special education program were compared in literacy and numeracy to the group that had neither the preschool program or the preschool program. The special three-year education program improved the reading and numeracy scores at age 21. The effect was gradually lost. The children given the preschool program followed by the standard education program did better but again the initial effect diminished. The children given the preschool program plus the special three-year program did very well and the effect was very apparent at age 21.
<table>
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<tr>
<th>Country</th>
<th>Level 1 and 2</th>
<th>Level 4 and 5</th>
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<tr>
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<td>34%</td>
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<tr>
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<td>42%</td>
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<td>Australia</td>
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<tr>
<td>Chile</td>
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<td>3%</td>
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<tr>
<td>Mexico</td>
<td>84%</td>
<td>1.7%</td>
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Table 1 – Adapted from Literacy in the information age. 2000. OECD. Level 1 is low; Level 5 is high.
EDI Vulnerability and Failing to Meet Grade 4 Foundation Skills Assessments - BC

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<td>27.3</td>
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<tr>
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<td>48.4</td>
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