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## Various Influence for Nutritional Status by the Developmental Origins of Health and Disease (DOHaD) Theory

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### Abstract

Among various problems for diet and nutrition worldwide, important concept has been Developmental Origins of Health and Disease (DOHaD) theory or Fetal origins of Adult Disease (FOAD). DOHaD means that predisposition to adult diseases has been formed in the interrelationship between genes and the environment during fertilization, embryonic, fetal, infancy, and adult periods. Related diseases include Atherosclerotic Cardiovascular Disease (ASCVD), Diabetes Mellitus (DM), Chronic Kidney Disease (CKD), and others. Low Birth Weight (LBW) babies have higher risk of disadvantage states for disability, metabolic diseases and low educational achievement later. Recognizing DOHaD in advance enables reduction of the predicting risks.

**Keywords:** Epigenetic Shift, Circadian Clock Genes.

**Abbreviations:** DOHaD- Developmental Origins of Health and Disease, FOAD- Fetal origins of Adult Disease, LBW - Low Birth Weight, SGA –Small for Gestational Age, NCD- Non-Communicable Diseases, ASCVD- Atherosclerotic Cardiovascular Disease.

For decades, various problems have been continued for diet and nutrition worldwide. Furthermore, lifestyle-related diseases and Non-Communicable Diseases (NCDs) have been important for adequate management. Recent international trend includes declining birthrate and increasing elderly population especially in developed countries. Proper discussion from medical and social points of view is required from fetus to centenarian period. In fact, there has been an important concept, which is Developmental Origins of Health and Disease (DOHaD) theory [1]. Another term can be used as Fetal Origins of Adult Disease (FOAD) [2].

DOHaD or FOAD has been recently in focus [3]. It was proposed by David Barker in 1986 [4]. The original perspective meant that predisposition to adult diseases has been formed in the interrelationship between genes and the environment during fertilization, embryonic, fetal, infancy periods and adults with a negative lifestyle load after birth. Various diseases may develop through certain mechanisms, which includes predisposition with epigenetic shift and trans-generational effect [5]. Some topics related to these will be described in this article.

As to general perspective of DOHaD, birth weight has been inversely related with the incidence of later lifestyle-related diseases for adult life. Especially, several diseases have been found such as Atherosclerotic Cardiovascular Disease (ASCVD), Diabetes Mellitus (DM), Chronic Kidney Disease (CKD) and so on [6]. Lower Birth Weight (LBW) may be occurred due to various undesired intrauterine environments, including stress, malnutrition, alcohol drinking and smoking.

DOHaD theory has been known to originate from fertilization to neonatal period that interacts between human genes and some environments such as stress, nutrition and environmental chemicals. Historically, the related episodes of DOHaD and Dutch Hunger Winter (1944-1945) and Great Leap Forward in China (1959-1961) were observed [7].

Several diseases have been known which showed increased risk from LBW [8]. They include hypertension, cardiovascular disease, impaired glucose tolerance, Type 2 Diabetes (T2D), metabolic syndrome, osteoporosis, dyslipidemia, psychoneurological abnormalities, Chronic Obstructive Pulmonary Disease (COPD), early menopause, short stature due to Small-for-Gestational Age (SGA), pregnancy complications and others. LBW babies have higher risk of disadvantage states for disability, metabolic diseases and low educational achievement in the future than normal birth weight babies. As to a retrospective study, 4224 babies followed up at university hospital for 6 years were analyzed [9]. The ratio of LBW was 1028 cases (24%), and 231 out of 1028 were born from multiple pregnancies. Among 797 singleton cases, 518 (65%) was born in preterm situation.

For LBW infants, higher risk in later life has been observed for developing increased insulin resistance and related comorbidities. In the light of DOHaD concept, intrauterine and postnatal environments may indicate an important role for elevating these risks. LBW infants, however, show additional characteristics, in which they are not necessarily obese or overweight during their life [10]. There may be inconsistency to show thrifty phenotype that is related to lower lean

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body mass and impaired growth course. Regarding LBW infants, detail investigation was conducted by socio-economic survey [11]. The results included as follows:

- i) Poor grades and performances in school age: Generally, total score of English and mathematics was 25% or more lower in the O-level test.
- ii) Social development: They showed lower scores of intellectual development and also social development score.
- iii) Wages for working in adult: Their wages for working during adult period are low, and the unemployed rate at the age of 33 is higher.

The emaciation status of young female will bring a variety of problems from medical, social and economic points of view. They include the following.

- i. Her life for long years: Various diseases will increase from young to elderly period [12]. They include decreased ovarian function, irregular menstruation, amenorrhea (1st and 2nd), decreased Quality Of Life (QOL), and decreased neuropsychiatric disfunction in older age, and increased risk of diseases and impaired states.
- ii. Disadvantageous impact on the next generation: Epigenetics changes due to under nutrition in the fetus [13]. Therefore, the predisposition to disease is transmitted across the generations. Furthermore, the risk of some illness in the next generation will increase and the QOL/ADL due to illness will be affected associated with elevated medical expenses.
- iii. Unbeneficial influences on society: This kind of future problem seems to be more serious than simply imbalance of the population with decreasing birthrate and increasing elderly [14]. In other words, several crucial impacts will be found such as productivity declines, socio-economic stagnation, increased medical costs, and changes in disease structure.

By recognizing the DOHaD theory in advance, it is possible to reduce the predicting risks during bringing up the child. For continuing DOHaD research, to develop preferable situation will be expected where some kinds of intervention can be performed. The possible trials are as follows:

- i) Breastfeeding and physical contact: physical contact (skinship) has been important even if the mother is unable to breastfeed.
- ii) Regular lifestyle: Establish a habit of early going to bed, rising and breakfast from childhood. Always think about the existence and effects of circadian clock genes in human [15].
- iii) Exercise habits: Get the joyous feeling of moving the body from younger period and continuing sports for the rest of your life.
- iv) Weight gain in the first half year: Changes in body weight, especially for 0-6 months are important. For this period, use the growth/development chart and consult with a specialist including a pediatrician.
- v) Treatment method: Currently, some medical agents have been under research and development.

People who had malnutrition in earlier life show higher risk for ASCVD [16]. A study was conducted whether improved nutrition can predict cardio metabolic function. Subjects were 1027 cases, and 22.9% were provided improved nutrition in the first 1000 days from pregnancy to 2-year birthday [17]. The protocol included a mixed-component meal tolerance challenge with post-prandial response of glucose, insulin and others. The results showed more favorable glucose response in the group of early exposure of improved nutrition.

In summary, the topic of DOHaD theory was described. Developmental physiology has 3 categories, including promoting conceptual advances, demonstrating broad relevance and improving experimental approaches [18]. These fields will develop challenge and great opportunity in the future.

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