Early Life Origins of Metabolic Syndrome: The Role of Environmental Chemicals

發育早期代謝症候群的起源:環境化學物質所造成的影響

By Megan Avakian

Early life exposure to endocrine disrupting chemicals and heavy metals may lead to development of metabolic syndrome later in life. These environmental toxicants are found in our air, food, water, and soil.
在生長發育早期，暴露於內分泌干擾物 (endocrine disrupting chemicals) 和重金屬(heavy metals) 可能導致中壯年時期代謝症候群(metabolic syndrome; MetS) 的發生。而這些環境毒素普遍地存在於我們所居住環境的空氣、食物、水和土壤。
(Photo courtesy of iStockphoto)

A growing body of evidence suggests that disease and poor adult health may originate during fetal development and early childhood. This concept, called the developmental origins of health and disease (DOHaD) hypothesis, suggests that early life environmental exposures can alter development in a way that leads to disease later in life. In a recent review, NIEHS grantee Xiaobin Wang, M.D., Sc.D., and her colleague Guoying Wang, M.D., examined new evidence for early life origins of metabolic syndrome (MetS) and draw attention to important research gaps in this area.

越來越多的研究證據指出，成人的健康問題與疾病可能始於胎兒發育和早期兒童時期。這個概念就是健康與疾病的發育起源假說 (developmental origins of health and disease (DOHaD) hypothesis)，指發育生長早期暴露於有害的環境化學物質可以導致以後成人疾病的發生。最近在一項由美國國立環境健康科學所 (NIEHS) 資助的研究中，Xiaobin Wang (M.D., Sc.D.)以及她的同事 Guoying Wang (M.D.) 在一篇綜合評論的文章中，進一步提出新的研究證據來支持此一假說，指出此一重要研究領域仍有許多值得探究之處。

Metabolic syndrome is a name for a group of conditions, including high blood sugar, high blood pressure, abnormal blood lipids, and abdominal obesity that increase a person's risk

for other health problems. A person with MetS is twice as likely to develop heart disease and five times more likely to develop diabetes than a person without MetS.

代謝症候群(MetS)包括了高血糖、高血壓、血脂異常和腹部肥胖等一系列增加其他疾病風險的健康狀態指標。例如：有代謝症候群的人罹患心臟疾病與糖尿病的機會分別為正常人的 2 倍與 5 倍。

"Heart disease, stroke, and diabetes are leading causes of death worldwide, and adults with MetS have a higher risk of developing these diseases," said the authors. "We wanted to examine how exposure to environmental toxicants during early life may lead to the development of MetS."

作者群在文中提及"在現今社會，心臟病、中風和糖尿病導致人類死亡的主要疾病，而具有代謝症候群的成年人是這些疾病發生的高危群"。"我們想深入探討在發育生長早期，環境毒素的暴露如何導致成人期謝症候群的發生。"

The epidemics of obesity, diabetes, and MetS may be due, in part, to chemical exposures *in utero* and during early childhood. These early developmental periods are most vulnerable to environmental exposures and are critical stages for adipose tissue development, metabolic programming, and the subsequent risk of MetS.

肥胖、糖尿病, 和代謝症候群的流行病學研究指出，其發生的部份原因是胎兒在子宮內或早期兒童化學品暴露所導致。早期的發育階段對於環境暴露所造成的影響是最敏感的，這期間是脂肪組織發育(adipose tissue development)，代謝編程(metabolic programming) 的關鍵階段，一旦受到影響將導致增加後續產生代謝症候群的危險性。

The authors reviewed animal and human studies that examined how prenatal and early life exposure to endocrine-disrupting chemicals (EDCs) and metals influence the development of MetS. Human studies examining the metabolic impact of prenatal exposure to persistent organic pollutants (POPs)—a group of EDCs that persist in the environment for long periods of time—have been inconsistent, but exposure has been associated with increased weight and obesity later in life. Many POPs, such as the pesticide dichlorodiphenyltrichloroethane (DDT), have been banned in the United States for decades but are still used in developing countries. POPs are a global concern because they can be transported long distances by wind and water, affecting people and environments far from where they are released.

作者回顧了相關的動物實驗和人類臨床研究於探討個體在胚胎時期和早期生長發育期間暴露於內分泌干擾化學物質 (endocrine-disrupting chemicals；EDCs) 和金屬 (metals) 如何導致代謝症候群 (MetS) 的產生。其中，人體的研究結果雖然顯示出胚胎時期暴露於持久性有機污染物 (persistent organic pollutants；POPs) 對於代謝的影響並不一致，但是卻與日後體重的增加與肥胖息息相關，持久性有機污染物 (POPs) 是一種於環境中長期存在的內分泌干擾化學物質 (EDCs)。很多持久性有機污染物，如：殺蟲劑二氯二苯基三氯乙烷 (DDT)，在美國幾十年就已經被禁止使用，但在許多發展中國家仍舊在使用。持久性有機污染物 (POPs)是一個全球關注的議題，因為這些汙染物可以從它們被釋放的區域經由風和水的運送來擴大其汙染範圍，對人類和環境造成長久的影響。

Few human studies have examined the relationship between early life exposure to the EDC bisphenol A (BPA) and MetS later in life. However, evidence from animal studies links

prenatal BPA exposure to reduced glucose tolerance, increased insulin resistance, and increased body weight later in life.

只有很少對人體研究的報告證實個體在早期生長發育期間暴露於 EDC bisphenol A (BPA)將會導致其成年期出現代謝症候群。然而，動物實驗的結果顯示產前暴露於 BPA 與日後發生葡萄糖耐受性 (glucose tolerance) 的降低、胰島素抗性 (insulin resistance)的增加和體重的增加有著極其顯著的相關性。

Studies of people exposed to heavy metals, such as arsenic, mercury, and lead, showed an increased risk of diabetes, high blood pressure, high blood sugar, and MetS. To date, the effects of these metals on metabolic disorders have been studied almost exclusively in adults, and the authors highlight the need for more prospective birth cohort studies on the metabolic consequences of exposure to metals in early life.

在有關人體暴露於重金屬的研究報導中，顯示出有著增加糖尿病、高血壓、高血糖，以及代謝症候群發生的危險性。這些重金屬包括：砷、汞 、鉛。

The authors also reviewed studies that examined epigenetic changes resulting from prenatal exposure to environmental chemicals. Epigenetic changes alter DNA in a way that influences gene expression but does not modify the DNA sequence. Emerging evidence shows that prenatal exposure to EDCs and metals induce specific epigenetic changes that influence metabolic disease risk in later life. According to the authors, epigenetic mechanisms may be the critical biological links between genetic vulnerability, prenatal exposures, and MetS development.

另外，作者還回顧了出生前暴露於環境化學物質所導致表觀遺傳變化 (epigenetic changes)的研究探討。所謂的表觀遺傳變化是指一種修飾 DNA 的作用，經由不改變其序列的方式進而影響基因的表達。新的研究證據指出，出生前暴露於內分泌干擾化學物質 (EDCs)或者金屬能誘發特定表觀遺傳變化將進一步增加日後產生代謝症候群的風險。根據作者的論述，表觀遺傳的也許是生物學上用來聯繫遺傳脆弱性 (genetic vulnerability)、產前暴露與代謝症候群之間的重要調控機制。

“Overall, the data is very limited regarding the link between prenatal and early life exposures to environmental toxicants and risk of MetS as an adult,” said Wang. To address these data gaps, the authors emphasize the need for more prospective birth cohort studies aimed at understanding exposure–response relationships, the effects of multiple exposures, and the early biological effects of exposures during critical windows of development and their long-term health consequences.

Wang 提到，“總體來說，關於產前和早期生活中接觸到環境毒物與導致日後成人期發生代謝症候群 (MetS)的相關研究數據仍然相當有限”。為更加深入釐清其中的關聯性，作者明確地提出有必要展開前瞻性出生群組 (birth cohort) 的研究，以了解暴露與反應之間的相關性、多重曝露的影響以及環境毒物暴露於重要發育期間對於早期生物的影響和長期的健康危害。

MetS and its components are generally viewed as adult problems, and strategies to reduce risk have traditionally focused on adult interventions, such as lifestyle modification. Emerging evidence that prenatal and early life exposures affect the risk of developing MetS provides an opportunity to target interventions aimed at reducing environmental exposures during vulnerable periods.

一直以來，代謝症候群和其他相關指標被視為成年人的問題。傳統上，治療的策略為經由成人的干預措施來降低與其相關疾病之危險性，例如：生活型態的改變 (lifestyle modification)。現在新的研究證據表明產前和早期生活中的接觸到環境毒物會增加日後代謝症候群的發生提供了新的治療契機，即在個體早期生長發育的脆弱時期減少其曝露於環境毒物的風險。

“Preventing environmental exposures during developmental periods, when they have the greatest effect, will help improve population health, minimize healthcare costs, and reduce the overall global burden of disease,” said Wang. “Such interventions will be of greatest benefit to vulnerable populations.”

“如能在發育期達到對於環境毒物風險預防的顯著成效，將有利於提高人民的健康，減少醫療成本，進而減少全球整體的疾病負擔，” 王博士進一步指出。“弱勢族群將是此一治療策略下最大的受益者。”

Building a Foundation to Increase Global Awareness

建立一個用以提高全球意識的基金會

NIEHS research is building an understanding of how environmental insults during early life can lead to poor adult health. As a designated World Health Organization (WHO) Collaborating Centre for Environmental Health Sciences, NIEHS is working with WHO to promote global awareness of the developmental origins of health and disease (DOHaD) and to inform global health practitioners about this emerging area of science. To accomplish this, WHO and NIEHS will jointly develop publications that define DOHaD and its importance for non-communicable disease and global health.

美國國立環境健康科學所 (NIEHS) 的研究是建立在了解早期生活環境如何導致成人的健康不良。作為世界衛生組織(WHO) 所指定在環境健康科學議題上的合作中心，美國國立環境健康科學所正與世界衛生組織一同努力，提昇全球對於此一由早期發育所衍生的健康和疾病 (developmental origins of health and disease；DOHaD) 議題的重視，並告知全球衛生工作者對這一新興科學領域。為了達到此一目標，世界衛生組織和美國國立環境健康科學所將共同發展刊物來說明何為 DOHaD 以及其在非傳染性疾病和全球健康議題上的重要性。

NIEHS is also building the global network of DOHaD researchers. The Institute has played an active role in planning the fourth international summit of the Prenatal Programming and Toxicity (PPTOX IV) conference to be held October 26-29, 2014 in Boston, Massachusetts, USA. As part of this effort NIEHS has organized a side event, “DOHaD: Impacts on Non-Communicable Diseases and Implications for Global Health,” which will be held before the conference. NIEHS will be well represented at PPTOX IV with staff presentations focusing on non-communicable diseases and implications for global health.

另一方面，美國國立環境健康科學所將建立 DOHaD 研究人員的全球網絡。本研究所將扮演積極角色，籌辦 2014 年 10 月 26 日至 29 日在美國馬薩諸塞州波士頓召開的第 4 次產前編程與毒性 (Prenatal Programming and Toxicity；PPTOX IV) 國際研討會，並在此會前舉行“DOHaD：

非傳染性疾病以及其對全球健康的影響”講座作為會外活動的一部分。該主題也是此國際研討會的核心內容。

Citation:

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