Nilsson *Artery Research* (2023) 29:28–33
https://doi.org/10.1007/s44200-023-00031-7

Artery Research

REVIEW

Open Access

Early Life Programming of Vascular Aging and Cardiometabolic Events: The McDonald Lecture 2022

Peter M. Nilsson*

Abstract

The early life programming of adult health and disease (Developmental Origins of Adult Health and Disease; DOHaD) concept has attracted increased attention during recent years. In this review evidence is presented for epidemiological associations between early life factors (birth weight, prematurity) and cardiometabolic traits and risk of disease in adult life. Even if not all studies concur, the evidence in general is supporting such links. This could be due to either nature or nurture. There is evidence to state that genetic markers influencing birth weight could also be of importance for offspring hypertension or risk of coronary heart disease, this supporting the nature argument. On the other hand, several studies, both historical and experimental, have found that the change of maternal dietary intake or famine in pregnancy may cause permanent changes in offspring body composition as well as in hemodynamic regulation. Taken together, this also supports the strategy of preventive maternal and child health care, starting already during the preconception period, for lowering the risk of adult cardiometabolic disease in the affected offspring. Further studies are needed to better understand the mediating mechanisms, for example concerning arterial function, hemodynamic regulation, renal function, and neuroendocrine influences, related to the development of early vascular aging (EVA) and cardiovascular disease manifestations.

Keywords Birth weight, Early life, Epidemiology, Genes, Nature, Nurture

1 Introduction

Two features of human beings are fundamental for understanding of the development of health and disease during the life course, and in particular the development of chronic conditions such as cardiovascular disease (CVD). These features are, firstly that we have all been children, and secondly that we all undergo aging. Thus, there is a strong argument to study both the early life influences on adult health as well as the differences between chronological and biological aging, i.e., differential aging. Some people seem to have a normal aging pattern, going through the different stages of life, while other people may risk an unsuccessful aging with early onset of age-related disease conditions [1], such as CVD and type 2 diabetes (DM2), jointly named cardiometabolic disease manifestations. From an evolutionary perspective it is also a historical fact that humans, like other mammals, are not programmed for long lives in general, but for early survival during infancy and reproduction, even if it is also believed that elderly women may increase reproductive fitness for their daughters and their children if they live longer to provide guidance during critical periods of poor health in childhood of offspring, the so-called grandmother hypothesis [2].

*Correspondence:
Peter M. Nilsson
peter.nilsson@med.lu.se
Department of Clinical Sciences, Lund University, Skane University Hospital, Malmö, Sweden

2 Early Observational Studies

Against this background it makes sense to study different periods of early life exposures for their associations with adult health outcomes (Table 1), as mediated by different mechanisms linked to organ development and physiology, the so-called Developmental Origin of Health and Disease (DOHaD) hypothesis [3]. The initial research work presented by epidemiologists such as Arne Forsdahl, Norway [4], Gerhard Gennser, Sweden [5], and David J Barker, UK [6–8], could show associations between adverse conditions during pregnancy, as mirrored by low birth weight or intrauterine growth retardation, with negative adult health outcomes such as hypertension, DM2, coronary heart disease (CHD), stroke, etc. This initial first phase of research focused on the birth outcomes in relation to gestational age for later follow-up of individuals through national or regional register linkages. A wealth of data has now established these links, especially with hypertension [9], even if there are also studies that could not show the expected associations [10], maybe due to differences in methodology applied or population characteristics. For example, when self-report of birth weight is used, or not adjusted for gestational age, some spurious findings may be expected as compared to other studies based on more solid data derived from searching medical archives (including midwife reports) or national registers including standardized registration of birth data [11].

Table 1 The early life influences on vascular function and cardiometabolic risk

Preconception
Parental genetics
Epigenetic influences on oocytes and sperm
Pre-pregnancy maternal disease or drug treatment
Assisted reproductive technologies (ART)
Pregnancy
Placental function
Gestational age (prematurity)
Intrauterine growth retardation
Birth weight (low, normal, or high)
Organ development and function
Post-natal development
Early feeding patterns
Catch-up growth
Neurocognitive function
Health problems
Congenital malformations
Adolescence
Timing of puberty
Obesity development
Adverse lifestyle (sedentary, alcohol, smoking)
Socio-economic and educational factors

3 The Health Consequences of Post-natal Catch-Up Growth

A *second phase* of this research came when people like Peter Gluckman and Mark Hanson stated that not only the pregnancy period and birth weight are of importance, but also the post-natal development. It has for example been shown that babies born small-for-gestational age (SGA), or with low birth weight (LBW), and later having a rapid catch-up growth pattern over the first few years of life, may be at increased risk of adult cardiometabolic problems [12]. Such a risk has now been documented in several birth cohorts, not only from the UK [13] and Finland [14], but also from Sweden [15]. This puts a focus on early nutrition and growth, not only during pregnancy itself, but also in early infancy, what has been called the important first 1000 days of life [16]. It is therefore of great importance to avoid calorie overfeeding by formula supplementation in premature or SGA babies, if this can be avoided (not always the case), but instead to promote breastfeeding or provide breast milk from external sources in order to avoid too rapid catch-up growth. This is of course based on a compromise with other medical needs in these newborns and often compromised children.

4 More Focus on the Preconception Period

In the current third phase of research dedicated to the importance of early life programming, focus has shifted to the pre- or periconception period, i.e., months to years before the conception or during a time window of about a few weeks around the conception and implantation in the uterine mucosa [17]. Negative influences from maternal obesity, unhealthy lifestyle, chemicals, drugs, infections, dietary deficiencies, and other environmental hazards may not only impact on fertility itself, including defective implantation and loss of fertilized egg cells (about 50% are lost during implantation), but also on the biology of oocytes and sperm through direct or epigenetic changes [18]. This means that lifestyle habits of both the coming mother and father could influence embryonal development which later, after 12 weeks of gestation, continues as the fetal development during the remaining two trimesters of pregnancy. In a recent randomized study from India, it was shown that a multi-facetted health package offered to women during preconception, pregnancy and the immediate post-partum period was beneficial for birth outcomes and early child growth and development, as well as for markers of maternal health [19].

In summary, the influences on health from early life can be studied during all stages, from preconception, over embryonic and fetal development, to birth outcomes and finally according to the growth patterns (trajectories) during the first few years of life. This means that there are different time periods (time windows) when a programming effect can play a role for the further development of the child and function of inner organs.

5 The Influence of Genes or the Environment?

A classical question is also to try to disentangle the influences of nature (genes) versus nurture (environment) on this development and programming effects, i.e., a specific stimulus that during a critical time period might cause permanent changes in the organism. Even if the early researchers emphasized the importance of the environment, for example calorie intake deficiencies in pregnant women and the role of maternal infections and smoking before and during pregnancy, other researchers have focused more on the importance of genetic factors to explain the associations. For example, if maternal genes affecting the risk of hypertension in pregnant women are also transmitted to their offspring and thus increasing the risk of later hypertension, this could explain the association alone, and thus low birth weight could be a secondary effect caused by hypertension in pregnancy influencing placental function [20]. In a similar way, other genetic studies have analyzed several genes associated with birth weight and found that these genes are also of importance for adult hypertension and CHD risk [21].

6 Historical Examples of Environmental Influences on Pregnancy Outcomes and Health

A counterargument to this genetic explanation is that manipulation of the environment, either in animal studies or following historical exposures to famine in pregnant women, could be of importance for both birth outcomes and long-term health risks in offspring. At the intersection between genes and environment influences we find epigenetic changes and imprinting of genes. This could be a more fruitful model to explain how genes and diet, or lifestyle in a wider sense, interact [22]. Historical cohort studies from periods of war and famine, or civil unrest, have repeatedly shown the negative influence on birth outcomes and a worse long-term prognosis for cardiometabolic disease and mortality, in countries as diverse as the Netherlands [23], Nigeria [24], Kenya [25] and China [26]. One exception was a follow-up of the Leningrad siege during WW2 in Soviet Union, when children born or surviving childhood in Leningrad during the famine period 1941 to 1943 were not at higher CVD risk compared to controls from other parts of war-time Soviet Union [27]. This could possibly be explained by the extreme selection pressure for full-time pregnancies and offspring survival during the intense famine period, but also that war-time conditions were very harsh in all parts of the country, a situation that lasted many years after the war with food rationing etc. On the other hand, the Dutch Winter Famine [23] from October 1944 to April 1945 (that occurred only in the northern part of the country) was followed by a far better period according to food supply, also for pregnant women, after the war.

In summary, even if strong arguments exist for the importance of genetic factors regulating birth outcomes and cardiovascular risk in both parents and offspring, there is a strong case for preventive work emphasizing the role of healthy nutrition and vitamin (e.g., folate) supplementation in pregnant women, as well as avoidance of smoking, alcohol overuse, or infections (through immunization) during pregnancy. Finally, it should be remembered that women are selected by evolution to survive many hardships during pregnancy and associated health risks, even if sometimes such mechanisms can back-fire, e.g., in women with APC resistance (to avoid excess bleeding during parturition) being at higher risk of thrombo-embolism [28].

7 The Normal Development of the Vasculature—What Can Go Wrong?

For the normal development of the vasculature, its morphology and function, a normal pregnancy means a fully normal development, with some expected post-natal changes, for example the closure of the *ductus arteriosus* at birth [29]. However, prematurity can cause a less developed capillarization with negative consequences for the microcirculation leading to increased total peripheral resistance during later life, a negative factor for hemodynamic development and control [30]. Correspondingly, a negative influence on fetal growth may deplete the elastin content of the media layer of large elastic arteries [31] that may, at least in theory, cause or influence arterial stiffness during later life, including the Early Vascular Aging (EVA) syndrome [32]. This is because the elastin content of the arterial wall is gradually depleted during the life course and thereby less elasticity will be the consequence, when also the collagen content of the media layer undergoes changes with cross-linkages that will also promote stiffness. Increased arterial stiffness, as measured by pulse wave velocity, is a marker of future risk of not only fatal and non-fatal cardiovascular events, but also of total mortality [33, 34].

Several studies have looked at the relationship between factors acting in early life and different measures of arterial function. Even if the link to hypertension is more

well-established [9], it has been difficult to unequivocally show the early life programming of for example pulse wave velocity (PWV) along the aorta as being the most important marker of arterial stiffness. One study in adolescent from Austria (mean age 16 years) could in fact show that PWV was significantly higher in adolescents with a history of being born small-for-gestational age (SGA) as compared to subject born appropriate for gestational age (AGA) [35]. On the other hand, such an association with birth weight was not possible to show in in a mixed group (SGA, AGA, large for gestational age; LGA) young Finnish children (mean age 6 years) [36]. Not even in extremely premature children, examined at the age of 11 and 19 years in the EpiCure study, UK, it was possible to show any difference in PWV compared to controls born at term [30]. However, these associations have been more widely shown for Augmentation Index (Aix), a complex variable reflecting not only aortic stiffness but also the influence of peripheral vascular resistance (PVR), and several other determinants (heart, the reflex wave, blood pressure levels, and heart rate) [37]. In fact, studies in premature children as well as in more normal children have shown either group differences in Aix compared to controls, or an inverse association with birth weight – the lower the birth weight, the higher the Aix [30, 38–40].

These changes in central hemodynamics in relation to birth weight have also been shown when the mis-match concept has been applied, depicting the catch-up growth pattern seen in people born with a lower birth weight but reaching a higher adult body mass index in adulthood, or at age 20 years, as shown in a study from Sweden [41].

8 Mechanisms of Importance

Some of the potential mechanisms linking early life factors with adverse cardiovascular outcomes have been investigated. These include less developed arterial structure and peripheral microcirculation [42], but also impaired renal function [43] that in turn can impact on blood pressure regulation. In addition, neuroendocrine disturbance [44] and a changed balance of the autonomous nervous system with increased sympathetic nervous activity [45] as well as increased stress susceptibility [46] could be of importance. In the background, factors such as placental dysfunction [47] and chronic inflammation could contribute. Further studies are needed to better understand the interplay between these mechanisms and the development of arterial changes for increased risk of Early Vascular Aging (EVA) and cardiovascular events [32].

9 The Importance for cardiovascular prevention

What could be the clinical implication of these associations? Firstly, they put greater emphasis on preventive maternal and child health care to facilitate a healthy development in early life and thereby a potential also for prevention of cardiovascular disease in adults. This preventive approach can even be further expanded to the pre- and periconceptional period, as recently shown in a randomized study from India with better birth outcomes as well as improved maternal health [19].

Secondly, it might be a good idea to think about an outreach for screening and prevention of cardiovascular risk factors in young adults with a history of being born prematurely [48] or SGA, especially if this is combined with a catch-up weight trajectory pattern in early life up into adolescence.

Thirdly, these possible effects should also be kept in mind when assisted reproductive technologies (ART) are becoming more and more common. So far there is no indication of increased cardiovascular risk when children born after ART have been screened [49] but of left ventricular diastolic dysfunction [50], but more studies are needed.

10 Conclusions

The study of DOHaD and early life influences on adult cardiometabolic risk offers excellent opportunities for both observational and mechanistic studies, also in new areas such as the influence of epigenetics and gut microbiota patterns [51]. For more focused studies on vascular function and development of arterial stiffness [52–55] we need accurate methods to measure this also in young children, where for example very high-resolution vascular ultrasound (35–55 MHz) has been applied to evaluate carotid function [56]. This methodology is useful to investigate structures close to the skin surface, but not for examination of deeper structures such as the aorta due to technical limitations.

The information described here can be used for risk prediction and early prevention in subjects with a history of adverse conditions in early life, but there is also a link to maternal cardiovascular health. For example, women with a reproductive history of pre-eclampsia [57], other pregnancy complications [58] or multiple SGA births [59] are themselves at increased cardiovascular risk and should be offered a follow-up and preventive services. Thus, health conditions and nutrition in mothers and children should be viewed as interacting [60] and therefore DOHaD perspectives should also include the health of mothers, especially for coming pregnancies if health problems affected the previous pregnancy.

Abbreviations

Aix	Augmentation index
AGA	Appropriate for gestational age
APC	Activated protein C
ART	Assisted reproductive technology
CVD	Cardiovascular disease
DM2	Diabetes type 2
DOHaD	Developmental origins of health and disease
EVA	Early vascular aging
LGA	Large for gestational age
MHz	Megahertz
PVR	Peripheral vascular resistance
PWV	Pulse wave velocity
SGA	Small for gestational age

Acknowledgements
The work behind this review was supported by grants from the Research Council of Sweden and the Heart- and Lung Foundation of Sweden to PMN. I am grateful for fruitful discussions on the topic with Senior Research Associate Carmel McEniery, University of Cambridge, UK.

Author Contributions
Not applicable, only one author.

Funding
Open access funding provided by Lund University. Vetenskapsrådet, 521-2013-2756, Peter M Nilsson, Hjärt-Lungfonden, 20150427, Peter M Nilsson.

Data Availability
Not applicable.

Declarations

Conflict of Interest
None.

Ethical Approval
Not applicable.

Consent to Participants
Not applicable.

Consent for Publications
Not applicable.

Received: 26 December 2022 Accepted: 2 March 2023
Published online: 17 March 2023

References

1. Aviv A, Levy D, Mangel M. Growth, telomere dynamics and successful and unsuccessful human aging. Mech Ageing Dev. 2003;124(7):829–37.
2. Hawkes K, Coxworth JE. Grandmothers and the evolution of human longevity: a review of findings and future directions. Evol Anthropol. 2013;22(6):294–302.
3. Arima Y, Fukuoka H. Developmental origins of health and disease theory in cardiology. J Cardiol. 2020;76(1):14–7.
4. Forsdahl A. Are poor living conditions in childhood and adolescence an important risk factor for arteriosclerotic heart disease? Br J Prev Soc Med. 1977;31(2):91–5.
5. Gennser G, Rymark P, Isberg PE. Low birth weight and risk of high blood pressure in adulthood. Br Med J (Clin Res Ed). 1988;296(6635):1498–500.
6. Barker DJ, Osmond C. Low birth weight and hypertension. BMJ. 1988;297(6641):134–5.
7. Barker DJ. The developmental origins of adult disease. J Am Coll Nutr. 2004;23(6 Suppl):588S-595S.
8. Syddall HE, Sayer AA, Simmonds SJ, Osmond C, Cox V, Dennison EM, Barker DJ, Cooper C. Birth weight, infant weight gain, and cause-specific mortality: the hertfordshire cohort study. Am J Epidemiol. 2005;161(11):1074–80.
9. Mu M, Wang SF, Sheng J, Zhao Y, Li HZ, Hu CL, Tao FB. Birth weight and subsequent blood pressure: a meta-analysis. Arch Cardiovasc Dis. 2012;105(2):99–113.
10. Fan J, Shi X, Jia X, Wang Y, Zhao Y, Bao J, Zhang H, Yang Y. Birth weight, childhood obesity and risk of hypertension: a Mendelian randomization study. J Hypertens. 2021;39(9):1876–83.
11. Nilsson PM, Ostergren PO, Nyberg P, Söderström M, Allebeck P. Low birth weight is associated with elevated systolic blood pressure in adolescence: a prospective study of a birth cohort of 149378 Swedish boys. J Hypertens. 1997;15(12 Pt 2):1627–31.
12. Gluckman PD, Hanson MA, Cooper C, Thornburg KL. Effect of in utero and early-life conditions on adult health and disease. N Engl J Med. 2008;359(1):61–73.
13. Ni Y, Beckmann J, Hurst JR, Morris JK, Marlow N. Size at birth, growth trajectory in early life, and cardiovascular and metabolic risks in early adulthood: EPICure study. Arch Dis Child Fetal Neonatal Ed. 2021;106(2):149–55.
14. Eriksson JG, Forsén T, Tuomilehto J, Winter PD, Osmond C, Barker DJ. Catch-up growth in childhood and death from coronary heart disease: longitudinal study. BMJ. 1999;318(7181):427–31.
15. Fagerberg B, Bondjers L, Nilsson P. Low birth weight in combination with catch-up growth predicts the occurrence of the metabolic syndrome in men at late middle age: the atherosclerosis and insulin resistance study. J Intern Med. 2004;256(3):254–9.
16. Mameli C, Mazzantini S, Zuccotti GV. Nutrition in the first 1000 days: the origin of childhood obesity. Int J Environ Res Public Health. 2016;13(9):838.
17. Fleming TP, Watkins AJ, Velazquez MA, Mathers JC, Prentice AM, Stephenson J, Barker M, Saffery R, Yajnik CS, Eckert JJ, Hanson MA, Forrester T, Gluckman PD, Godfrey KM. Origins of lifetime health around the time of conception: causes and consequences. Lancet. 2018;391(10132):1842–52.
18. Hieronimus B, Ensenauer R. Influence of maternal and paternal pre-conception overweight/obesity on offspring outcomes and strategies for prevention. Eur J Clin Nutr. 2021;75(12):1735–44.
19. WINGS Study Group, Taneja S, Chowdhury R, Dhabhai N, Upadhyay RP, Mazumder S, Sharma S, Bhatia K, Chellani H, Dewan R, Mittal P, Bhan MK, Bahl R, Bhandari N. Impact of a package of health, nutrition, psychosocial support, and WaSH interventions delivered during preconception, pregnancy, and early childhood periods on birth outcomes and on linear growth at 24 months of age: factorial, individually randomised controlled trial. BMJ. 2022;379:e072046.
20. Warrington NM, Beaumont RN, Horikoshi M, Day FR, Helgeland Ø, Laurin C, et al. Maternal and fetal genetic effects on birth weight and their relevance to cardio-metabolic risk factors. Nat Genet. 2019;51(5):804–14.
21. Horikoshi M, Beaumont RN, Day FR, Warrington NM, Kooijman MN, Fernandez-Tajes J, et al. Genome-wide associations for birth weight and correlations with adult disease. Nature. 2016;538(7624):248–52.
22. Cutfield WS, Hofman PL, Mitchell M, Morison IM. Could epigenetics play a role in the developmental origins of health and disease? Pediatr Res. 2007;61(5 Pt 2):68R-75R.
23. Kyle UG, Pichard C. The Dutch Famine of 1944–1945: a pathophysiological model of long-term consequences of wasting disease. Curr Opin Clin Nutr Metab Care. 2006;9(4):388–94.
24. Hult M, Tornhammar P, Ueda P, Chima C, Bonamy AK, Ozumba B, Norman M. Hypertension, diabetes and overweight: looming legacies of the Biafran famine. PLoS ONE. 2010;5(10): e13582.
25. Dybjer E, Linvik J, Nilsson PM. Civil unrest linked to intrauterine growth restriction in western Kenya. J Dev Orig Health Dis. 2014;5(5):370–3.
26. Chen C, Nie Z, Wang J, Ou Y, Cai A, Huang Y, Yang Q, Liu S, Li J, Feng Y. Prenatal exposure to the Chinese famine of 1959–62 and risk of cardiovascular diseases in adulthood: findings from the China PEACE million persons project. Eur J Prev Cardiol. 2022;29(16):2111–9.
27. Stanner SA, Bulmer K, Andrès C, Lantseva OE, Borodina V, Poteen VV, Yudkin JS. Does malnutrition in utero determine diabetes and coronary heart disease in adulthood? Results from the Leningrad siege study, a cross sectional study. BMJ. 1997;315(7119):1342–8.
28. Lindqvist PG, Svensson PJ, Dahlbäck B, Marsál K. Factor V Q506 mutation (activated protein C resistance) associated with reduced intrapartum

blood loss–a possible evolutionary selection mechanism. Thromb Haemost. 1998;79(1):69–73.
29. Conrad C, Newberry D. Understanding the pathophysiology, implications, and treatment options of patent ductus arteriosus in the neonatal population. Adv Neonatal Care. 2019;19(3):179–87.
30. Hurst JR, Beckmann J, Ni Y, Bolton CE, McEniery CM, Cockcroft JR, Marlow N. Respiratory and cardiovascular outcomes in survivors of extremely preterm birth at 19 years. Am J Respir Crit Care Med. 2020;202(3):422–32.
31. Martyn CN, Greenwald SE. Impaired synthesis of elastin in walls of aorta and large conduit arteries during early development as an initiating event in pathogenesis of systemic hypertension. Lancet. 1997;350(9082):953–5.
32. Nilsson PM, Lurbe E, Laurent S. The early life origins of vascular ageing and cardiovascular risk: the EVA syndrome. J Hypertens. 2008;26(6):1049–57.
33. Vlachopoulos C, Aznaouridis K, Stefanadis C. Prediction of cardiovascular events and all-cause mortality with arterial stiffness: a systematic review and meta-analysis. J Am Coll Cardiol. 2010;55(13):1318–27.
34. Ben-Shlomo Y, Spears M, Boustred C, May M, Anderson SG, Benjamin EJ, et al. Aortic pulse wave velocity improves cardiovascular event prediction: an individual participant meta-analysis of prospective observational data from 17,635 subjects. J Am Coll Cardiol. 2014;63(7):636–46.
35. Early Vascular Aging (EVA) Study Group, Stock K, Schmid A, Griesmaier E, Gande N, Hochmayr C, Knoflach M, Kiechl-Kohlendorfer U. The impact of being born preterm or small for gestational age on early vascular aging in adolescents. J Pediatr. 2018;201:49–54.
36. Olander RFW, Sundholm JKM, Suonsyrjä S, Sarkola T. Arterial health during early childhood following abnormal fetal growth. BMC Pediatr. 2022;22(1):40.
37. Wilkinson IB, Cockcroft JR, Webb DJ. Pulse wave analysis and arterial stiffness. J Cardiovasc Pharmacol. 1998;32(Suppl 3):S33–7.
38. Lurbe E, Torro MI, Carvajal E, Alvarez V, Redón J. Birth weight impacts on wave reflections in children and adolescents. Hypertension. 2003;41(3 Pt 2):646–50.
39. Enigma Study investigators, Miles KL, McDonnell BJ, Maki-Petaja KM, Yasmin Cockcroft JR, Wilkinson IB, McEniery CM. The impact of birth weight on blood pressure and arterial stiffness in later life: the Enigma Study. J Hypertens. 2011;29(12):2324–31.
40. Sperling J, Nilsson PM. Does early life programming influence arterial stiffness and central hemodynamics in adulthood? J Hypertens. 2020;38(3):481–8.
41. Sperling J, Sharma S, Nilsson PM. Birth weight in relation to post-natal growth patterns as predictor of arterial stiffness and central hemodynamics in young adults from a population-based study. Artery Res. 2021;27:112–20.
42. Visentin S, Grumolato F, Nardelli GB, Di Camillo B, Grisan E, Cosmi E. Early origins of adult disease: low birth weight and vascular remodeling. Atherosclerosis. 2014;237(2):391–9.
43. Laucyte-Cibulskiene A, Sharma S, Christensson A, Nilsson PM. Early life factors in relation to albuminuria and estimated glomerular filtration rate based on cystatin C and creatinine in adults from a Swedish population-based cohort study. J Nephrol. 2022;35(3):889–900.
44. Phillips DI, Walker BR, Reynolds RM, Flanagan DE, Wood PJ, Osmond C, Barker DJ, Whorwood CB. Low birth weight predicts elevated plasma cortisol concentrations in adults from 3 populations. Hypertension. 2000;35(6):1301–6.
45. Boguszewski MC, Johannsson G, Fortes LC, Sverrisdóttir YB. Low birth size and final height predict high sympathetic nerve activity in adulthood. J Hypertens. 2004;22(6):1157–63.
46. Nilsson PM, Nyberg P, Ostergren PO. Increased susceptibility to stress at a psychological assessment of stress tolerance is associated with impaired fetal growth. Int J Epidemiol. 2001;30(1):75–80.
47. Thornburg KL, O'Tierney PF, Louey S. Review: the placenta is a programming agent for cardiovascular disease. Placenta. 2010;31(Suppl):S54–9.
48. Liefke J, Steding-Ehrenborg K, Sjöberg P, Ryd D, Morsing E, Arheden H, Ley D, Hedström E. Higher blood pressure in adolescent boys after very preterm birth and fetal growth restriction. Pediatr Res. 2022. https://doi.org/10.1038/s41390-022-02367-3. (**Epub ahead of print PMID: 36344695**).
49. Yeung EH, Mendola P, Sundaram R, Lin TC, Broadney MM, Putnick DL, Robinson SL, Polinski KJ, Wactawski-Wende J, Ghassabian A, O'Connor TG, Gore-Langton RE, Stern JE, Bell E. Conception by fertility treatment and cardiometabolic risk in middle childhood. Fertil Steril. 2022;118(2):349–59.
50. Sciuk F, Vilsmaier T, Kramer M, Langer M, Kolbinger B, Li P, Jakob A, Rogenhofer N, Dalla-Pozza R, Thaler C, Haas NA, Oberhoffer FS. Left ventricular diastolic function in subjects conceived through assisted reproductive technologies. J Clin Med. 2022;11(23):7128.
51. Lurbe E, Ingelfinger J. Developmental and early life origins of cardiometabolic risk factors: novel findings and implications. Hypertension. 2021;77(2):308–18.
52. Crisafulli A, Bassareo PP, Kelleher S, Calcaterra G, Mercuro G. Factors predisposing to hypertension in subjects formerly born preterm: renal impairment, arterial stiffness, endothelial dysfunction or something else? Curr Hypertens Rev. 2020;16(2):82–90.
53. Mora-Urda AI, Acevedo P, Montero López MP. Relationship between prenatal and postnatal conditions and accelerated postnatal growth. Impact on the rigidity of the arterial wall and obesity in childhood. J Dev Orig Health Dis. 2019;10(4):436–46.
54. Sehgal A, Allison BJ, Gwini SM, Menahem S, Miller SL, Polglase GR. Vascular aging and cardiac maladaptation in growth-restricted preterm infants. J Perinatol. 2018;38(1):92–7.
55. Oliveira RS, Wehrmeister FC, Oliveira IO, Gonçalves H, Menezes AMB. Ideal cardiovascular health, inflammation, and arterial stiffness in the transition to adulthood. Int J Cardiol. 2022;15(355):45–51.
56. Sundholm JK, Olander RF, Ojala TH, Andersson S, Sarkola T. Feasibility and precision of transcutaneous very-high resolution ultrasound for quantification of arterial structures in human neonates - comparison with conventional high resolution vascular ultrasound imaging. Atherosclerosis. 2015;239(2):523–7.
57. Okoth K, Chandan JS, Marshall T, Thangaratinam S, Thomas GN, Nirantharakumar K, Adderley NJ. Association between the reproductive health of young women and cardiovascular disease in later life: umbrella review. BMJ. 2020;7(371): m3502.
58. Cho GJ, Um JS, Kim SJ, Han SW, Lee SB, Oh MJ, Shin JE. Prior pregnancy complications and maternal cardiovascular disease in young Korean women within 10 years after pregnancy. BMC Pregnancy Childbirth. 2022;22(1):229.
59. Nilsson PM, Li X, Sundquist J, Sundquist K. Maternal cardiovascular disease risk in relation to the number of offspring born small for gestational age: national, multi-generational study of 2.7 million births. Acta Paediatr. 2009;98(6):985–9.
60. Keats EC, Das JK, Salam RA, Lassi ZS, Imdad A, Black RE, Bhutta ZA. Effective interventions to address maternal and child malnutrition: an update of the evidence. Lancet Child Adolesc Health. 2021;5(5):367–84.