AMERICAN ACADEMIC PUBLISHER

INTERNATIONAL JOURNAL OF MEDICAL SCIENCES

ISSN NUMBER: 2692 - 5206 Volume 6. No 05. MAY ,2026

INFLUENCE OF EXTERNAL FACTORS ON THE DEVELOPMENT OF THE AORTA; MAJOR CONGENITAL DEFECTS (COARCTATION)

Termiz iqtisodiyot va servis universiteti Tibbiyot fakulteti o'qituvchisi
Ilmiy rahbar: Kibriyeva Mahfirat Abduraxmonovna
Email:kibriyeva@gmail.com
Termiz iqtisodiyot va servis universiteti Tibbiyot fakulteti
Davolash ishi talim yo'nalish 25- 34 guruh talabasi
Rustamov Abdumannop Chori õg'li
Email: rustamovabdumannop5@gmail.com
Termiz iqtisodiyot va servis universiteti Tibbiyot fakulteti
Davolash ishi talim yo'nalish 25- 34 guruh talabasi
Husan Umbarov Fafzulla o'g'li
Email: HO382844@gmail.com

Annotatsiya: Ushbu maqolada aortaning embrional rivojlanishiga tashqi omillarning ta'siri hamda aortaning asosiy tug'ma nuqsonlari yoritilgan. Homila rivojlanishi davrida ona organizmiga ta'sir qiluvchi infeksiyalar, zararli odatlar, dori vositalari, ekologik omillar va metabolik buzilishlarning aorta shakllanishiga salbiy ta'siri tahlil qilingan. Shuningdek, aorta koarktatsiyasi, aorta stenozi, aorta yoyi anomaliyalari kabi asosiy tug'ma nuqsonlarning etiologiyasi, patogenezi, klinik belgilari va diagnostikasi haqida ma'lumot berilgan. Tug'ma yurak-qon tomir nuqsonlarini erta aniqlash va profilaktikasining ahamiyati yoritib berilgan.

Kalit so'zlar: aorta, embrional taraqqiyot, tashqi omillar, tug'ma nuqsonlar, aorta koarktatsiyasi, aorta stenozi, yurak-qon tomir tizimi, embriogenez, diagnostika, profilaktika.

Аннотация: В данной статье рассмотрено влияние внешних факторов на эмбриональное развитие аорты, а также основные врождённые пороки аорты. Проанализировано отрицательное воздействие инфекций, вредных привычек, лекарственных препаратов, экологических факторов и метаболических нарушений матери на формирование аорты плода. Освещены этиология, патогенез, клинические проявления и диагностика таких врождённых пороков, как коарктация аорты, стеноз аорты и аномалии дуги аорты. Подчёркивается важность ранней диагностики и профилактики врождённых сердечно-сосудистых аномалий.

Ключевые слова: аорта, эмбриональное развитие, внешние факторы, врождённые пороки, коарктация аорты, стеноз аорты, сердечно-сосудистая система, эмбриогенез, диагностика, профилактика.

Abstract: This article discusses the influence of external factors on the embryonic development of the aorta and the main congenital defects of the aorta. The negative effects of maternal infections, harmful habits, medications, environmental factors, and metabolic disorders on fetal aortic formation are analyzed. In addition, the etiology, pathogenesis, clinical manifestations, and diagnostic methods of major congenital anomalies such as aortic coarctation, aortic stenosis, and aortic arch abnormalities are described. The importance of early diagnosis and prevention of congenital cardiovascular defects is emphasized.

Keywords: aorta, embryonic development, external factors, congenital defects, aortic coarctation, aortic stenosis, cardiovascular system, embryogenesis, diagnosis, prevention.

AMERICAN ACADEMIC PUBLISHER
INTERNATIONAL JOURNAL OF MEDICAL SCIENCES
ISSN NUMBER: 2692 - 5206 Volume 6. No 05. MAY ,2026

Introduction

The cardiovascular system is of particular importance in human embryogenesis as the first system to form and function. The aorta is the largest artery in the body, originating from the heart and supplying the entire body with oxygen and nutrients. Its normal ontogenesis will depend on the complex morphogenesis processes of the embryo, genetic programming, and environmental (environmental) influences. Congenital aortic defects, particularly aortic coarctation (CoA), in combination with other cardiac defects, cause severe hemodynamic disturbances, heart failure, and long-term complications in the neonatal and postnatal periods. This article is devoted to the analysis of the main mechanisms of aortic embryological development, the pathogenic effects of external factors, and the epidemiological and pathophysiological aspects of the main congenital anomalies.The embryological formation of the aorta occurs between the 3rd and 8th weeks of gestation and involves complex cellular and molecular processes. The initial cardiac tube forms paired dorsal aorta, which later fuse to create a single descending aorta. The aortic arch (arch), on the other hand, is formed from six pairs of aortic arches; Some of these arches undergo regression, while others develop into the brachiocephalic, carotid, and subclavian arteries. Neural crest cell migration, epithelial-mesenchymal transition (EMT), hemodynamic stresses (blood flow), and matrix components play crucial roles in this process. Any disorder — genetic mutations, hemodynamic changes, or external teratogenic effects-can cause hypoplasia, narrowing (coarctation) of the aorta, interrupted aortic arch, or other conotruncal abnormalities.1b000e

Aortic coarctation (CoA) is a narrowing of the aorta, usually in the isthmus part where the ductus arteriosus is located, accounting for about 5-8% of all congenital heart defects, and occurs in one in every 1,700 — 2,500 live births. This defect is observed twice as often in men as in women. Coarctation is often not an isolated condition, but is accompanied by other defects (bicuspid aortic valve, aortic stenosis, hypoplastic left heart syndrome). There are two main theories in pathogenesis: the hemodynamic theory (a decrease in blood flow to the intrauterine left ventricular exit slows the development of the aortal isthmus) and the ductal tissue theory (smooth muscle cells of the ductus arteriosus migrate to the aorta to form narrowing). With postnatal ductus closure, the narrowing increases, causing a difference in arterial pressure in the upper and lower extremities. The etiology of congenital aortic defects is multifactoral. Although genetic factors (e.g., Turner syndrome, which has a dramatically increased risk of CoA with a 45,X karyotype) are important, in most cases, external (environmental) factors play a decisive role in the background of genetic predisposition. In the first trimester of pregnancy, during organogenesis, due to rapid cell division and differentiation, external influences significantly affect the development of the cardiovascular system.

Nutrient deficiencies and other factors: Folic acid deficiency, maternal age (40+), stress, occupational exposures, and socioeconomic factors indirectly increase the risk.a5fc6dou factors cause aortic and left ventricular output defects by disrupting neuronal crest cell migration, EMT process, NOTCH, VEGF and other signaling pathways, epigenetic modifications (methylation, acetylation). As a result, clinically severe neonatal heart failure, arterial hypertension, aneurysm, heart failure, and other long-term complications develop. In modern medicine, controlling external factors is an important strategic direction in preventing congenital heart defects. Folic acid supplementation, protection from infections, avoidance of harmful substances, strict control of diabetes, and avoidance of environmental hazards can have significant preventive effects in pregnant women. In addition, genetic counseling, prenatal screening (ultrasound,

AMERICAN ACADEMIC PUBLISHER
INTERNATIONAL JOURNAL OF MEDICAL SCIENCES
ISSN NUMBER: 2692 - 5206 Volume 6. No 05. MAY ,2026

NIPT, echocardiography), and molecular diagnostic capabilities are expanding. This review provides scientifically based data to medical professionals, embryologists and genetic researchers through an in-depth analysis of the delicate molecular and cellular mechanisms of aortic development, the pathogenic effects of external factors and the clinical-epidemiological significance of major birth defects. Further research into the interaction between genetic and environmental factors (gene-environment interaction) will help reduce the global burden of congenital heart defects.

Main part

In human embryogenesis, the cardiovascular system begins to form as early as the third week of pregnancy and completes its basic structure by the eighth week. The aorta, as the largest elastic artery in the body, is formed by the fusion of the paired dorsal aortae and the complex transformation of the six pairs of aortic arches (branchial arch arteries). The primitive heart tube forms the ventral and dorsal aortas, with the dorsal aortas later fusing to form the descending aorta. The aortic arch is formed from six pairs of aortic arches, which phylogenetically correspond to the ancient gill arch arteries. The first and second arches undergo regression, the third arch forms the carotid arteries, the fourth arch forms the main part of the aortic arch and the subclavian arteries, and the sixth arch forms the ductus arteriosus and the pulmonary arteries. Cardiac neural crest cells play an important role in this process: they migrate and provide the smooth muscle layer of the aortic arches and septation. Epithelial-to-mesenchymal transition (EMT), NOTCH, VEGF, TGF-β, Wnt, and BMP signaling pathways, as well as hemodynamic forces (shear stress and blood flow), control normal development. Any disruption—delayed cell migration, altered apoptosis, or hemodynamic disruption—leads to conotruncal and aortic anomalies. For example, interrupted aortic arch or coarctation can occur when there is insufficient migration of neural crest cells.

Coarctation of the aorta (coarctation of the aorta – CoA) is a narrowing of the aorta, usually in the isthmus section following the left subclavian artery exit (in the area where the ductus arteriosus is located), accounting for 5-8 percent of all congenital heart defects. Epidemiological data suggest that it occurs in approximately 1 in 1,700–2,500 live births and is 1.5–2 times more common in males than in females. There are two main pathogenetic theories. The first is hemodynamic theory (Rudolph's theory), in which left ventricular outlet obstruction (e.g. bicuspid aortal valve or subaortal stenosis) in the intrauterine period reduces blood flow to the aortal isthmus and leads to its hypoplasia. The second is the ductal tissue theory (Skoda theory), which states that smooth muscle cells of the ductus arteriosus migrate aberrantly into the aorta, causing a constriction. The constriction increases with postnatal ductus closure. Coarctation is often not in isolation but is accompanied by other abnormalities, notably bicuspid aortal valve (50-85% of cases), ventricular septal defect (VSD), atrial septal defect (ASD), and hypoplastic left heart syndrome. In severe cases, heart failure, shock, and metabolic acidosis develop in the neonatal period. In older children, arterial hypertension in the upper extremities, hypotension in the lower extremities, weakening of the femoral pulse, radial-femoral delay, systolic murmur, and rib notching on radiography are observed. Long-term complications include heart failure, aortic aneurysm and dissection, intracranial hemorrhage, renal failure, and premature death. Other important congenital aortic defects include interrupted aortic arch (IAA), aortic arch anomalies (vascular rings and slings), aortic hypoplasia, and hypoplastic left heart syndrome (HLHS). Interrupted aortic arch is a complete interruption of the aortic arch and accounts for approximately 1.5 percent of congenital heart defects. There are three types: Type

AMERICAN ACADEMIC PUBLISHER
INTERNATIONAL JOURNAL OF MEDICAL SCIENCES
ISSN NUMBER: 2692 - 5206 Volume 6. No 05. MAY ,2026

A (after the left subclavian artery), Type B (between the left carotid and subclavian — the most common and strongly associated with 22q11.2 deletion), and Type C (proximal). This defect is often associated with VSD, truncus arteriosus, and other conotruncal defects. The pathogenesis involves a disruption in the migration of neural crest cells, and the prognosis is poor without timely surgical intervention in the neonatal period. Aortic arch anomalies (right aortic arch, double aortic arch, aberrant subclavian artery) compress the trachea and esophagus, causing difficulty breathing and swallowing. Bicuspid aortic valve is the most common defect associated with CoA and significantly increases the risk of subsequent aortopathy and aneurysm. The etiology of congenital aortic defects is multifactorial in nature, and external factors are decisive against the background of genetic predisposition (mutations in the genes NOTCH1, TBX1, GATA4, NKX2-5, Turner syndrome — 45,x karyotype). During organogenesis (weeks 3–8 of pregnancy), due to rapid cell division and differentiation, external influences determine a very high sensitivity of the cardiovascular system. Major teratogenic factors include maternal infections (rubella, cytomegalovirus, parvovirus B19, toxoplasma), metabolic disorders (pregestative and gestational diabetes, obesity), drugs (retinoic acid, valproate, carbamazepine, ibuprofen, SSRI), harmful habits (alcohol, smoking, drugs), environmental pollution (PM2.5 metals, heavy metals, pesticides, endocrine disruptors), and nutrient deficiencies (folate, vitamin D). These factors are affected by cytokine storm, oxidative stress, hypoxia, disruption of the EMT process, inhibition of signaling pathways (NOTCH, Wnt, VEGF), and epigenetic modifications (DNA methylation, histone acetylation, miRNA). An example of gene-environment interaction is that maternal diabetes or air pollution may increase the penetrance and severity of the defect in the background of NOTCH pathway mutations. In terms of diagnostics, fetal echocardiography (18–22 weeks), NIPT, and genetic testing play an important role in the prenatal period. In postnatal diagnosis, ECG, transthoracic and transesophageal echocardiography, MRI or CT angiography, and pressure gradient measurement are used. Treatment involves infusion of prostaglandin E1 (open ductus storage), surgical correction (resection with end-to-end anastomosis, subclavian flap aortoplasty, patch aortoplasty) in neonatal severe cases, or balloon angioplasty and stenting via catheter in adults. Long-term follow-up is necessary to detect complications such as reocclusion, aneurysm, and hypertension early. Controlling external factors is strategically important in preventing congenital heart defects. Periconseptive folate supplmentation in pregnant women, infection protection (vaccine), strict diabetes control, total withdrawal from harmful habits, environmental risk avoidance, and genetic counseling in high risk groups as well as screening programs can have significant preventive effect. A deeper understanding of these factors will not only serve to improve modern surgical and interventional techniques, but also to reduce the global burden of congenital heart defects. It is expected that future molecular genetics, epigenetics, and population studies will further elucidate gene-environment interactions.

Diagnosis, treatment, and disease course

Timely detection, proper treatment and follow-up of aortic coarctation and other aortic birth defects are some of the most important issues. The severity of these defects varies. In some, the condition develops immediately after the birth of the baby, while in others it gradually manifests itself over the years. Therefore, diagnosis is carried out in several stages. The possibility of prenatal diagnosis during pregnancy is great. Around weeks 18-22, doctors can see the narrowed area of the aorta, the position of the left ventricle, and the disruption of blood flow through fetal echocardiography. However, mild coarctation is difficult to detect in the fetal period because the ductus arteriosus is still open and no pressure difference is created.

AMERICAN ACADEMIC PUBLISHER
INTERNATIONAL JOURNAL OF MEDICAL SCIENCES
ISSN NUMBER: 2692 - 5206 Volume 6. No 05. MAY ,2026

Genetic tests, such as NIPT or other tests, can also help identify genetic problems such as Turner syndrome or 22q11.2 deletion. After birth, or in the postnatal period, diagnosis becomes even more important. Coarctation of the aorta becomes apparent when the ductus arteriosus begins to close in the newborn. In the child, the pulse in the lower extremities weakens or is not felt at all, and a large difference appears between the arterial pressure in the arms and legs (more than 20 mm Hg). The child breathes rapidly, the heart rate increases, the liver enlarges, and sometimes a state of shock occurs. In older children, high blood pressure, cold feet, fatigue when running, and radial-femoral delay (difference in pulse between the arm and leg) are the main symptoms. The doctor may hear a murmur in the back. Among the main instrumental investigations, echocardiography (EchoKG) is the first. It clearly shows the narrowing site, pressure gradient, bicuspid aortal cap and other concomitant defects. A chest X-ray may show an enlarged heart, changes in the aorta, or a "notching" sign on the ribs. Magnetic resonance imaging (MRI) and computed tomography (CT angiography) provide a complete picture of the aorta, especially in older children and are very useful in assessing postoperative status. Cardiac catheterization allows for direct pressure measurement and angiography. An ECG may show signs of left ventricular hypertrophy. Treatment is determined by the severity of the defect and the age of the child. In the most severe neonatal cases, a prostaglandin E1 drug is given intravenously. This medication keeps the ductus arteriosus open, improving blood supply to the lower body. At the same time, measures are taken to restore Heart Support drugs, artificial respiration and metabolic balance.

Conclusion

Aortic development is a complex embryological process, and its normal formation depends on the interaction of genetic programs and environmental factors. Congenital aortic defects, particularly coarctation of the aorta (CoA), interrupted aortic arch (IAA), bicuspid aortic valve, and hypoplastic left heart syndrome, are the result of disruptions that occur during embryogenesis between weeks 3 and 8. Migration of neural crest cells, epithelial-to-mesenchymal transition (EMT), hemodynamic factors, and normal functioning of signaling pathways (NOTCH, VEGF, Wnt) are key conditions for aortic development.

Studies show that in most cases of congenital heart defects, external factors play a decisive role against the background of a genetic predisposition. Maternal infections (rubella, CMV), pregestative and gestational diabetes, obesity, teratogenic drugs (retinoic acid, valproate), harmful habits (alcohol, smoking), environmental pollution (PM2.5, heavy metals) and nutrient deficiency (folate) significantly increase the risk of aortic and left ventricular outflow defects. These factors act through oxidative stress, epigenetic changes, and impaired cell migration. . This article provides useful information to medical professionals and researchers by analyzing the molecular and cellular mechanisms of aortic development, the pathogenic effects of external factors, and the clinical aspects of major congenital defects. Further research into gene-environment interactions and improvements in prevention programs will be important contributions to reducing the global burden of congenital heart defects.

AMERICAN ACADEMIC PUBLISHER
INTERNATIONAL JOURNAL OF MEDICAL SCIENCES
ISSN NUMBER: 2692 - 5206 Volume 6. No 05. MAY ,2026

List of literature used

1. Law MA, et al. Coarctation of the Aorta. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024. Available from: https://www.ncbi.nlm.nih.gov/books/NBK430913/
2. Tikkanen J, Heinonen OP. Risk factors for coarctation of the aorta. Teratology. 1993;47(6):565-572. doi:10.1002/tera.1420470608
3. Zhang TN, et al. Environmental Risk Factors and Congenital Heart Disease: An Umbrella Review of 165 Systematic Reviews and Meta-Analyses. Front Cardiovasc Med. 2021;8:640729. doi:10.3389/fcvm.2021.640729
4. Familiari A, et al. Risk Factors for Coarctation of the Aorta on Prenatal Ultrasound: A Systematic Review and Meta-Analysis. Circulation. 2017;135(8):772-785.
5. Lynch TA, Abel DE. Teratogens and Congenital Heart Disease. Journal of Diagnostic Medical Sonography. 2015;31(5):301-313.
6. Centers for Disease Control and Prevention (CDC). Coarctation of the Aorta. Available from: https://www.cdc.gov/heart-defects/about/coarctation-of-the-aorta.htm
7. Greene CL, et al. Origins of Aortic Coarctation: A Vascular Smooth Muscle Cell Perspective. PMC, 2025.
8. Yokoyama U, et al. Pathology and molecular mechanisms of coarctation of the aorta. Pediatrics International. 2017.
9. Ceuppens AS, et al. Aorta pathology and pregnancy-related risks in adult congenital heart disease. PMC, 2023.
10. do Amaral Lopes SAV, et al. Risk factors for critical and complex congenital heart defects. Seminars in Fetal and Neonatal Medicine. 2023.