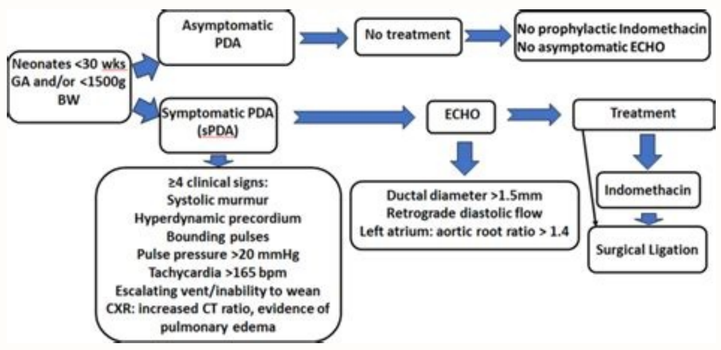
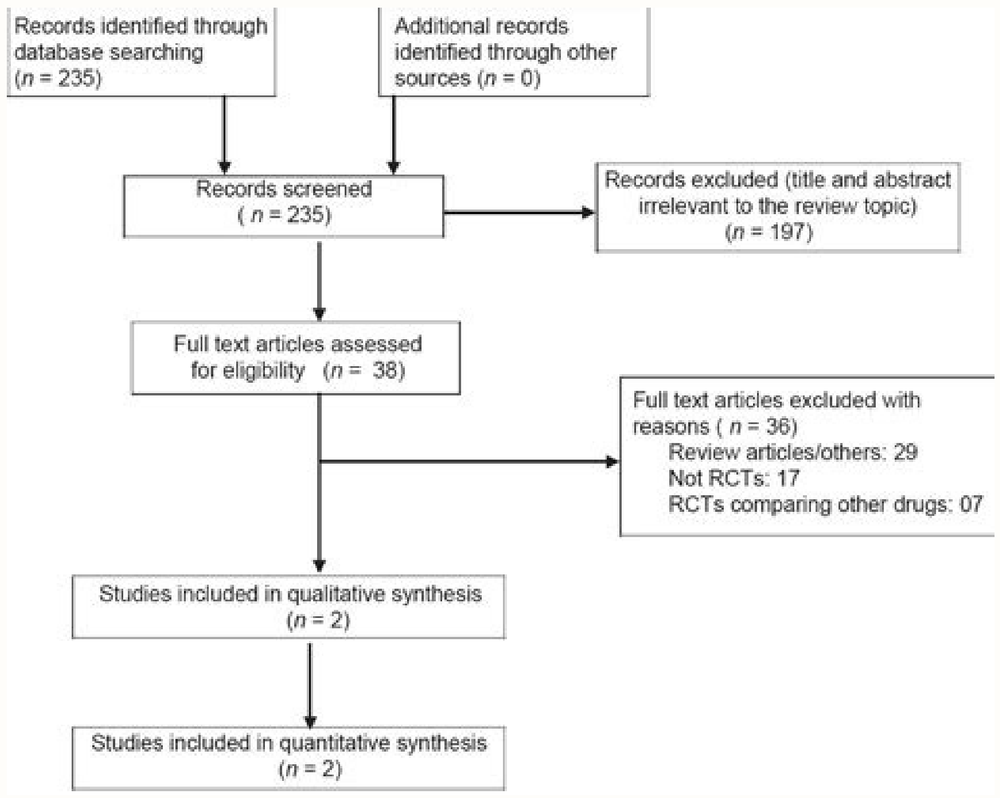
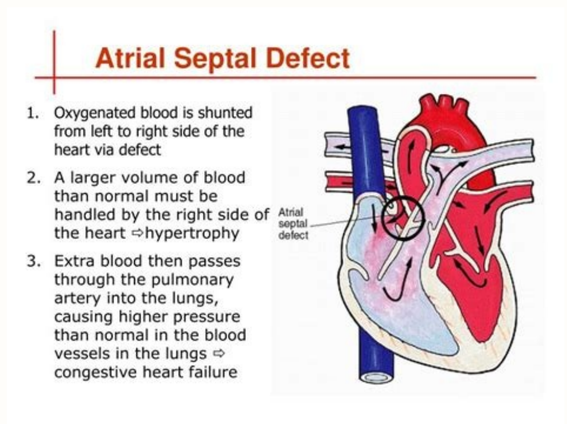
Pathophysiology of patent ductus arteriosus pdf







Benefits of patent ductus arteriosus. How to say patent ductus arteriosus. What causes patent ductus arteriosus. History of patent ductus arteriosus. Meaning of patent ductus arteriosus. Pathophysiology of patent ductus arteriosus in the preterm infant. Pathophysiology of patent ductus arteriosus pdf. Pathophysiology of patent ductus arteriosus in flowchart.

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Prophylactic ibuprofen versus placebo in very premature infants: a randomised, double-blind, placebo-controlled trial. Lancet. 2004;364:1939–1944. et al. [PubMed] [Google Scholar]45. Gournay V, Savagner C, Thirez G. Pulmonary hypertension after ibuprofen prophylaxis in very premature infants. Lancet. 2002;359:1486–1488. et al. [PubMed] [Google Scholar]46. Bellini C, Campone F, Serra G. Pulmonary hypertension following L-lysine ibuprofen therapy in a preterm infant with patent ductus arteriosus. CMAJ. 2006;174:1843–1844. [PMC free article] [PubMed] [Google Scholar]47. Walker PC. Neonatal bilirubin toxicity. A review of kernicterus and the implications of drug-induced bilirubin displacement. Clin Pharmacokinet. 1987;13:26–50. [PubMed] [Google Scholar] The patent ductus arteriosus (PDA) is a vascular structure that connects the proximal descending aorta to the roof of the main pulmonary artery near the origin of the left branch pulmonary artery. This essential fetal structure normally closes spontaneously after birth. After the first few weeks of life, persistence of ductal patency is abnormal. The physiological impact and clinical significance of the PDA depend largely on its size and the underlying cardiovascular status of the patient. The PDA may be “silent” (not evident clinically but diagnosed incidentally by echocardiography done for a different reason), small, moderate, or large. Regardless of the size, complications may arise, and it is important for both pediatric and adult cardiologists to have an understanding of the pathophysiology, clinical implications, and management of PDA.EmbryologyThe ductus arteriosus is a normal and essential fetal structure that becomes abnormal if it remains patent after the neonatal period. In normal cardiovascular development, the proximal portions of the sixth pair of embryonic aortic arches persist as the proximal branch pulmonary arteries, and the distal portion of the left sixth arch persists as the ductus arteriosus, connecting the left pulmonary artery with the left dorsal aorta (Figure 1). Normally, the distal right sixth aortic arch loses its connection to the dorsal aorta and degenerates. This transformation is complete by 8 weeks of fetal life. Figure 1. Schematic of embryonic aortic arch system. The 6 pairs of embryonic aortic arches are demonstrated (left-sided arches are numbered). The portions that normally involute are indicated by broken lines. The distal left sixth embryonic arch normally persists and becomes the PDA, connecting the left pulmonary artery to the proximal descending aorta. The right distal sixth arch normally involutes, as does the eighth segment of the right dorsal aorta (*), which results in a leftward aortic arch. RCA indicates right carotid artery; LCA, left carotid artery; RSCA, right subclavian artery; and LSCA, left subclavian artery.Normal PhysiologyFetal CirculationWhereas ≈65% of the fetal cardiac output is from the right ventricle, only 5% to 10% passes through the lungs.1,2 The preponderance of right ventricular output passes through the ductus arteriosus into the descending aorta. The fetal ductus arteriosus is thus an important structure that is essential for normal fetal development, permitting right ventricular output to be diverted away from the high-resistance pulmonary circulation. Premature constriction or closure may lead to right heart failure, resulting in fetal hydrops.3Histology and Mechanisms of Normal ClosureGrossly, the constitution of the fetal ductus arteriosus appears to be similar to the contiguous main pulmonary artery and descending aorta; there are important histological differences, however.4–9 Whereas the mediae of surrounding aorta and pulmonary artery are composed mainly of circumferentially arranged layers of elastic fibers, the media of the ductus arteriosus is composed of longitudinally and spirally arranged layers of smooth muscle fibers within loose, concentric layers of elastic tissue. The intima of the ductus arteriosus is thickened and irregular, with abundant mucoid material, sometimes referred to as intimal cushions.Fetal patency of the ductus arteriosus is controlled by many factors, the most important of which are relatively low fetal oxygen tension10 and cyclooxygenase-mediated products of arachidonic acid metabolism (primarily prostaglandin [PGE2] and prostacyclin [PGI2]).11 Locally produced and circulating PGE2 and PGI2 in the fetus cause vasodilation of the ductus arteriosus via interaction with ductal prostanoid receptors,12 and circulating PGE2 and PGI2 levels are high in the fetus because of production by the placenta and decreased metabolism in the fetal lungs.After birth, the abrupt increase in oxygen tension inhibits ductal smooth muscle voltage-dependent potassium channels, which results in an influx of calcium and ductal constriction.13 PGE2 and PGI2 levels fall because of metabolism in the now functioning lungs and elimination of the placental source. The medial smooth muscle fibers in the ductus contract, which results in wall thickening, lumen obliteration, and shortening of the ductus arteriosus. Functional complete closure usually occurs within 24 to 48 hours of birth in term neonates. Within the next 2 to 3 weeks, infolding of the endothelium along with subintimal disruption and proliferation result in fibrosis and a permanent seal.14 The resulting fibrous band with no lumen persists as the ligamentum arteriosum.EpidemiologyThe factors responsible for persistent patency of the ductus arteriosus beyond the first 24 to 48 hours of neonatal life are not completely understood. Prematurity clearly increases the incidence of PDA, and this is due to physiological factors related to prematurity rather than inherent abnormality of the ductus.15 In term infants, cases most often appear to occur sporadically, but there is increasing evidence that genetic factors play a role in many patients with patent ductus. In addition, other factors such as prenatal infection appear to play a role in some cases.IncidenceThe reported incidence of PDA varies because of methodological differences related to the population group studied, age of consideration, and method of detection.16 Although the ductus arteriosus usually is functionally closed within 48 hours of birth, some authorities consider the patent ductus to be abnormal only after 3 months of age.17 In children who were born at term, the incidence of PDA has been reported to be ≈1 in 2000 births.18,19 This accounts for ≈5% to 10% of all congenital heart disease. However, if we include children with “silent” patent ductus (those discovered incidentally by echocardiography performed for another purpose), the incidence has been estimated to be as high as 1 in 500.20 The female to male ratio is ≈2:1 in most reports.Genetic FactorsIn contrast to premature infants, in whom PDA generally is due to developmental immaturity, patent ductus in term infants likely results from a significant structural abnormality. PDA occurs with increased frequency in several genetic syndromes, including those with defined chromosomal aberrations (such as trisomy 21 and 4p− syndrome), single-gene mutations (such as Carpenter’s syndrome and Holt-Oram syndrome), and X-linked mutations (such as incontinentia pigmenti). Although most cases of PDA are seemingly sporadic, many are believed to be due to multifactorial inheritance, with the requirement of genetic predisposition and an environmental trigger that occurs at a vulnerable time.21 The genetic mechanism of patent ductus in some patients may be autosomal recessive inheritance with incomplete penetrance.22 In a family having 1 sibling with a PDA, there is an ≈3% chance of a PDA in a subsequent offspring.21The precise mechanisms of how these genetic abnormalities result in persistent patency of the ductus arteriosus are not clear. Genetic studies suggest that the abnormalities in Char syndrome (an inherited disorder with PDA, facial dimorphism, and hand anomalies) result from derangement of neural crest cell derivatives.23,24 There is also evidence of abnormal fibronectin-dependent smooth muscle cell migration as a cause of PDA. Further elucidation of these mechanisms might provide the opportunity for specific targeted genetic or biochemical therapies for PDA and might also provide insight into the development of new strategies to maintain ductal patency in ductal-dependent congenital heart disease.Infection and Environmental FactorsRubella infection during the first trimester of pregnancy, particularly in the first 4 weeks, is associated with a high incidence of PDA.25,26 The histology resembles that of a very immature ductus, and there is an extensive subendothelial elastic lamina that is thought to be incompatible with anatomic sealing.27 PDA has been reported to be associated with other environmental factors, such as in fetal valproate syndrome,28 although the mechanism has not been determined.AnatomyIn the normal heart with a left-sided aortic arch, the ductus arteriosus connects the left pulmonary artery near its origin to the descending aorta just distal to the left subclavian artery. The ductus arteriosus may persist in a wide variety of sizes and configurations. Usually, the aortic end of the patent ductus is larger than the pulmonary artery end, which results in a somewhat conical configuration. The size, configuration, and relationship to adjacent structures are important with respect to determining resistance to blood flow (an important determinant in the degree of shunting) and also have important implications with regard to interventional closure. Figure 2 demonstrates the wide variability in patent ductus size and configuration using the angiographic classification originally devised to help guide transcatheter closure procedures29 and shows examples of each type. Figure 2. Variations in PDA configuration illustrated with the classification of Krichenko et al.29 The configurations are sketched on the left, and examples of lateral angiograms for each type are on the right. A, Type A (“conical”) ductus, with well-defined aortic ampulla and constriction near the pulmonary artery end. B, Very large type B (“window”) ductus, with very short length. C, Type C (“tubular”) ductus, which is without constrictions. D, Type D (“complex”) ductus, which has multiple constrictions. E, Type

E (“elongated”) ductus, with the constriction remote from the anterior edge of the trachea.PathophysiologyLeft-to-Right ShuntingThe hemodynamic impact of PDA in an otherwise normal cardiovascular system is determined by the magnitude of shunting, which depends largely on the flow resistance of the ductus arteriosus. The length, the narrowest diameter, and the overall shape and configuration of the ductus arteriosus determine resistance. In addition, because flow in the ductus is dynamic and pulsatile, the elasticity of the ductus wall may affect the impedance to blood flow.30The magnitude of shunt flow depends not only on the ductal resistance but also on the pressure gradient between the aorta and the pulmonary artery. This pressure gradient is dynamic, with systolic and diastolic components, and depends largely on pulmonary and systemic vascular resistances and cardiac output. The impact of changes in pulmonary and systemic resistances is greater in larger ductus that have less flow resistance.Left-to-right shunting through the ductus arteriosus results in pulmonary overcirculation and left heart volume overload. Increased pulmonary flow from the ductal shunting leads to increased pulmonary fluid volume, and in patients with moderate or large shunts, this causes decreased lung compliance, which may result in increased work of breathing. Pulmonary edema is uncommon but may occur in older patients with advanced congestive heart failure.Increased flow returning to the left heart results in increased left atrial and left ventricular end-diastolic pressures. The left ventricle compensates by increasing stroke volume and eventually may hypertrophy to normalize wall stress. Neuroendocrine adaptations also occur, with increased sympathetic activity and circulating catecholamines that result in increased contractility and heart rate. The diastolic blood pressure in the aorta decreases owing to diastolic “runoff” through the patent ductus and, coupled with shorter diastolic time due to tachycardia, increased intramyocardial tension from left ventricular dilatation, and increased myocardial oxygen demand, may result in subendocardial ischemia.31Eisenmenger’s SyndromeWith long-standing left-to-right shunting, exposure of the pulmonary artery system to high-pressure and increased flow leads to progressive morphological changes in the pulmonary vasculature. These changes, including arteriolar medial hypertrophy, intimal proliferation and fibrosis, and eventual obliteration of pulmonary arterioles and capillaries, result in a progressive increase in pulmonary vascular resistance. When pulmonary vascular resistance approaches and exceeds systemic vascular resistance, ductal shunting reverses and becomes right to left. The precise pathophysiological mechanisms for this are not completely understood, but there is evidence that microvascular injury stimulates production of growth factors and enzymes that result in intimal proliferation and medial hypertrophy.32 Endothelial dysfunction and platelet activation may also play a role in the obliteration of pulmonary arterioles.33Clinical FeaturesMedical HistoryThe clinical history of patients with PDA varies from those who are completely asymptomatic to those with severe congestive heart failure or Eisenmenger’s syndrome. Many patients present for evaluation of an asymptomatic heart murmur. Others are detected incidentally by an echocardiogram performed for another purpose in patients with no overt clinical manifestations. Some patients may be relatively well but report exercise intolerance or have the diagnosis of reactive airways disease. Although most patients with PDA compensate well even with a moderate left-to-right shunt and remain asymptomatic during childhood, many years of chronic volume overload may lead to symptoms of congestive heart failure in adulthood. Symptoms may begin with onset of atrial fibrillation that results from chronic and gradually progressive left atrial enlargement. A previously well-tolerated PDA may become clinically significant when its effects are combined with acquired conditions such as ischemic heart disease or calcific aortic stenosis.Physical ExaminationThe physical examination findings vary as much as the medical history. Patients with tiny, incidentally discovered patent ductus have no abnormal physical findings. The hallmark physical finding is a continuous murmur, located at the upper left sternal border, often referred to as a “machinery” murmur. The murmur often radiates down the left side of the sternum and into the back, and a thrill may be present. Occasionally a diastolic rumble is audible at the cardiac apex in patients with moderate or large ductal shunts. If the shunt is moderate or large, the left ventricular impulse will be prominent, and the pulse pressure will be increased. The peripheral pulses may be prominent or bounding. Except in older patients with congestive heart failure, rales are uncommon even with a large shunt.Patients with Eisenmenger’s syndrome are cyanotic and may have differential cyanosis (cyanosis and clubbing of the toes but not the fingers because the right-to-left ductal shunting is distal to the subclavian arteries). Cyanosis may be more profound when systemic vascular resistance is decreased, such as in hot weather or after exercise. There may be no murmur during systole or diastole, because shunting may be minimal. Auscultation may reveal a high-frequency diastolic decrescendo murmur of pulmonary regurgitation and/or a holosystolic murmur from tricuspid valve regurgitation. The intensity of the pulmonic component of the second heart sound may be increased. Peripheral edema may be present late in the course of disease when right ventricular dysfunction is present.Chest RadiographDepending on the amount of ductal shunting, the chest radiograph may be completely normal or it may demonstrate cardiomegaly (specifically with signs of left atrial and left ventricular enlargement) with increased pulmonary vascular markings. The main pulmonary artery is frequently enlarged, and particularly in older adults with pulmonary hypertension, calcification of the ductus may be evident.ElectrocardiogramThe ECG may demonstrate sinus tachycardia or atrial fibrillation, left ventricular hypertrophy, and left atrial enlargement in patients with moderate or large ductus shunts. In patients with smaller ductal shunts, the ECG is often completely normal. In the patient with a large ductus arteriosus and elevated pulmonary artery pressure, signs of right atrial enlargement and biventricular hypertrophy are frequently present.EchocardiogramThe echocardiogram is the procedure of choice to confirm the diagnosis and to characterize a PDA (Figure 3). In conjunction with the clinical information, the echocardiogram is often useful in classifying the PDA as silent, small, moderate, or large. In addition to evaluating the ductus arteriosus, the echocardiogram is used to identify and evaluate other associated cardiac defects. Figure 3. Echocardiogram study demonstrating PDA. A, Two-dimensional image of a PDA as seen in a high parasternal short-axis view. DAO indicates descending aorta; MPA, main pulmonary artery. B, Color Doppler image in a similar view shows left-to-right shunting through the ductus. C, Spectral Doppler profile of continuous left-to-right ductal flow.M-mode echocardiography is used to measure the cardiac chamber sizes and quantitate left ventricular systolic function. In a patient with a small ductus arteriosus, chamber sizes are usually normal, although mild left atrial and/or left ventricular enlargement may be present. In a patient with a moderate or large patent ductus, the left atrium and left ventricle are enlarged. Two-dimensional imaging demonstrates the geometry of the ductus. Color Doppler is a very sensitive modality in detecting the presence of a PDA and is frequently used to estimate the degree of ductal shunting. Even an extremely tiny patent ductus can be detected by a color flow signal entering the pulmonary artery near the origin of the left pulmonary artery. In patients with high pulmonary vascular resistance and PDA, with low velocity or right-to-left flow, the ductus arteriosus may be very difficult to demonstrate with color flow Doppler, even if it is large. Findings such as septal flattening, unexplained right ventricular hypertrophy, and high-velocity pulmonary regurgitation should prompt a thorough investigation for a PDA. Contrast echocardiography may be helpful in this setting; intravenous injection of agitated saline leads to microbubbles in the descending aorta (from ductal right-to-left shunting) but not in the ascending aorta.A complete pulmonary artery pressure curve can be generated from the spectral Doppler signal of ductal flow.34 The right ventricular pressure can be estimated from the peak velocity of the tricuspid regurgitation jet, if present. The Doppler velocity of the pulmonary regurgitation flow, if present, can be used to estimate the pulmonary artery diastolic pressure. With the outflow tract cross-sectional areas and Doppler-derived mean flow velocities, the degree of left-to-right shunt can be calculated.Magnetic Resonance Imaging and Computed TomographyIn the adult with PDA, computed tomography can assess the degree of calcification,35 which may be important if surgical therapy is considered. Magnetic resonance imaging and computed tomography may be useful in defining the anatomy in patients with unusual PDA geometry and in patients with associated abnormalities of the aortic arch.36 One example is the patient with ductus arteriosus aneurysm, which may present as a chest mass.37,38 Other examples include PDA associated with vascular ring, with right aortic arch, and with cervical arch.Cardiac CatheterizationTherapeutic catheterization is currently the treatment of choice at most centers for most children and adults with patent ductus. Complete diagnostic assessment of hemodynamics before transcatheter closure is particularly important in adults with patent ductus, in whom it is imperative to fully evaluate the pulmonary vascular resistance and degree of shunting before intervention. In patients with elevated pulmonary artery pressure, assessment of pulmonary vascular resistance and its response to vasodilating agents such as oxygen, nifedipine, prostacyclin, sildenafil, and nitric oxide may be helpful in determining advisability of ductus closure. Assessment of hemodynamics during temporary test occlusion with a balloon catheter may also provide important information regarding advisability of closure.Angiography defines the anatomy of the ductus arteriosus. Detailed assessment of the ductal anatomy is essential before transcatheter closure so that the proper device and device size can be chosen for the intervention. Important features include the minimum diameter, the largest diameter (usually at the aortic ampulla), the length, and the relationship of the ductus to the anterior border of the tracheal shadow, which helps guide device positioning.Natural History and ComplicationsThe natural history of PDA depends largely on the size and magnitude of the shunt and the status of the pulmonary vasculature. Many patients with small ductus arteriosus never have signs of significant hemodynamic impairment and, other than the risk of endarteritis, have a normal prognosis. Those patients with significant left heart volume overload, however, are at risk of congestive heart failure or irreversible pulmonary vascular disease, even if asymptomatic or minimally symptomatic during childhood.Congestive Heart FailureChildren and adults with moderate to large patent ductus frequently develop symptoms of congestive heart failure due to pulmonary overcirculation and left heart volume overload. If the ductus is large and offers minimal resistance to flow (nonrestrictive), the degree of shunting depends on the status of the pulmonary vascular resistance. In many children with moderate or large patent ductus, pulmonary vascular resistance remains modestly elevated, which limits the shunting sufficiently to lessen the physiological impact and permit survival and growth. Although patients with small to moderate ductus often remain asymptomatic during infancy and childhood, and some may never develop symptoms, those with significant chronic volume overload of the left heart may develop congestive heart failure in adulthood, starting in the third decade.39 In the adult, heart failure is frequently associated with atrial flutter or fibrillation.40Hypertensive Pulmonary Vascular DiseasePatients with large nonrestrictive or minimally restrictive patent ductus are likely to eventually develop irreversible pulmonary vascular disease.41 Some cases appear to be secondary to long-standing pressure and volume overload in the pulmonary circulation, although many cases appear to be related to coincident primary pulmonary vascular disease rather than occurring as a result of the ductus.42 Some infants and children with a large patent ductus do not experience the normal postnatal fall in pulmonary vascular resistance, and even after closure of the ductus, pulmonary vascular disease may progress and eventually prove fatal.42,43EndarteritisThe incidence of infective arteritis associated with PDA has decreased dramatically since the early natural history studies before the era of routine surgical closure and use of antibiotics, when the incidence of infective arteritis was reported to be 1% per year.39,44–47 The reasons for this decline are probably many and include the improved availability of health care, including dental care; widespread use of antibiotics, including use for infective endocarditis prophylaxis; and importantly, the fact that routine closure of PDA over the past few decades has markedly decreased the substrate. In countries with limited health resources and access to health care, infective endarteritis associated with ductus arteriosus remains a significant health issue.48 Vegetations usually occur on the pulmonary artery end of the ductus, and embolic events are usually of the lung rather than the systemic circulation.Aneurysm of Ductus ArteriosusAneurysm of the ductus arteriosus is an entity with a reported incidence as high as 8%.49 The true incidence is unclear because the definition of ductus arteriosus aneurysm is not precise and because many incidentally discovered ductus arteriosus aneurysms detected by fetal or neonatal echocardiography resolve spontaneously with ductal closure and thrombosis, without clinically apparent sequelae.50 Ductal aneurysm most commonly presents in infancy49–51 but has also been reported in adults52 and may develop after infective endarteritis, surgical closure, or transcatheter coil occlusion.53–55 In approximately one fourth of patients, an underlying disorder such as trisomy 21, trisomy 13, Smith-Lemli-Opitz syndrome, type IV Ehlers-Danlos syndrome, or Marfan’s syndrome is present.51Rarely, the ductus arteriosus aneurysm may present with symptoms of a thoracic mass, including hoarseness due to left vocal chord paralysis from recurrent left laryngeal nerve impingement56 and left bronchial obstruction.57 Although many have a benign course, surgical resection is indicated if there is functional compromise of adjacent structures, persistent patency of the ductus, thrombus that extends into adjacent vessels, evidence of thromboembolic events, or underlying connective tissue disease.51 The role of percutaneous occlusion with aneurysm obliteration has not been established for ductus arteriosus aneurysm, but one potentially promising technique is placement of a covered stent in the aorta to simultaneously exclude the aneurysm and occlude the ductus arteriosus.58Other ComplicationsPDA, particularly in association with pulmonary hypertension, may lead to recurrent laryngeal nerve paralysis even without aneurysm, due to impingement of the nerve as it courses through the triangle formed by the aortic arch, enlarged pulmonary artery, and ductus arteriosus.59 Dissection and/or spontaneous rupture of an aneurysmally dilated pulmonary artery due to PDA with pulmonary hypertension may occur.60–62 In addition, acute aortic dissection may also occur.63 These complications are rare.Medical ManagementSymptomatic patients with PDA usually improve with a medical regimen of diuretics and digoxin. Afterload reduction, such as with angiotensin-converting enzyme inhibition, may also affect clinical improvement, although definitive studies in this setting are not available. Antidysrhythmia medications may be useful in patients with atrial fibrillation or flutter, and although some patients may be successfully cardioverted and maintained in sinus rhythm after closure of the ductus, adults with atrial fibrillation may require therapy indefinitely, including anticoagulation. Observance of infective endocarditis prophylaxis precautions is recommended for all patients with PDA, including those with silent PDA, until 6 months after closure. Medical therapy for congestive heart failure due to PDA may be short-term, until definitive surgical or transcatheter closure is performed, but may also be required long-term in patients with cardiomegaly and persistent symptoms.Patients with PDA and pulmonary vascular disease who are considered unacceptable candidates for definitive closure may be managed with pulmonary vasodilating agents such as chronic oxygen, PGI2, calcium channel blockers, endothelin antagonists, and phosphodiesterase type V inhibitors. One strategy in such patients is to accomplish partial closure of the ductus by surgery or transcatheter techniques, to make it “restrictive” but not completely closed, followed by long-term therapy with pulmonary vasodilating agents. If in follow-up, the pulmonary vascular resistance decreases, then complete closure may be considered. Systematic study of the benefits of pulmonary vasodilating agents in the setting of PDA and high pulmonary vascular resistance are not available, however, and such treatment strategies are unproved and results anecdotal at the present time.Definitive Therapy: Closure of PDAHistorical PerspectiveTechniques for closure of PDA have evolved since the first report of surgical ligation by Gross and Hubbard in 1939.64 Transcatheter methods, to avoid thoracotomy, were pioneered by Portsmann et al,65 who reported use of a conical Ivalon plug in 1967, and by Rashkind and Cuaso,66 who reported initial results of an umbrella-type device in 1979. These devices were rather large and cumbersome to use, requiring large introducer sheaths and frequently leaving residual shunting. After Cambier et al67 in 1992 reported the use of Gianturco coils for transcatheter closure of PDA, transcatheter coil occlusion quickly became a widely used technique for closure of the small to moderate patent ductus. Subsequently, newer devices and techniques have been developed such that moderate and large patent ductus are usually amenable to occlusion by transcatheter techniques. In addition, the development of less invasive surgical techniques has paralleled the development of transcatheter techniques.Indications for Closure of PDADuctus closure is clearly indicated for any child or adult who is symptomatic from significant left-to-right shunting through the PDA. In asymptomatic patients with significant left-to-right shunting that results in left heart enlargement, closure is indicated to minimize the risk of complications in the future.68 In adults with PDA, reported outcomes after PDA closure have been very good, including for those with modest elevation in pulmonary vascular resistance and even some with Eisenmenger’s syndrome.69 Elimination of the shunt reduces pulmonary blood flow, and therefore pulmonary artery pressure, even if the pulmonary vascular resistance remains elevated.70In patients with pulmonary vascular resistance >8 U/m2, lung biopsy has been recommended to determine candidacy for closure.71 Such patients may be hemodynamically worse after ductal closure because of loss of the avenue for right-to-left shunting, which leads to suprasystemic pulmonary artery pressure, low cardiac output, and right ventricular failure. Unfortunately, lung biopsy may not be sufficiently predictive to justify the risk. Pulmonary vascular disease characterized by histological changes consistent with severe, irreversible pulmonary vascular disease may completely resolve after closure of the PDA.72 Reactivity of the pulmonary vascular bed to pulmonary vasodilating agents and/or significant reduction of pulmonary artery pressure and resistance during test occlusion may offer reassurance with regard to reversibility, but the absence of such evidence does not exclude the possibility of reversibility in the long term.The indications for closure of patent ductus with small shunts, including those that are tiny and incidentally discovered (“silent”), are less certain, particularly in older adults. Endarteritis of clinically silent PDA has been reported.73,74 Although the incidence of ductus arteriosus endarteritis has decreased dramatically over the past several decades, the risk has not disappeared completely. Because closure methods are effective and safe and are associated with minimal morbidity, a strategy advocating routine closure of any PDA in children and young adults appears most reasonable.Transcatheter ClosureTranscatheter occlusion has become the treatment of choice for most patent ductus in children and adults. In cases of calcified ductus arteriosus with increased pulmonary vascular resistance, transcatheter closure offers considerable advantages over surgical closure, which frequently involves cardiopulmonary bypass with an anterior approach through a median sternotomy.The basic technique is to advance a catheter or delivery sheath across the ductus arteriosus from either the pulmonary artery or the aorta and position a closure device in the ductus to occlude it. Since the initial experience with standard, nondetachable Gianturco coils, which occasionally migrated or assumed unacceptable positions, several techniques were developed to stabilize the coils during delivery.75–77 In addition, detachable coils are now readily available, which allow the assessment of adequate positioning before release. Figure 4 demonstrates an example of ductus occlusion with a standard Gianturco coil. Figure 4. Example of Gianturco coil occlusion of PDA. A, Views of a Gianturco coil in its stretched out configuration (top) and in its natural coiled configuration (bottom). Note the attached Dacron fibers, which promote thrombosis, along its length. B through D, Lateral angiograms demonstrating closure of a PDA with a single 0.038-in diameter Gianturco coil.In contrast to Gianturco coils, which were designed for occlusion of vascular structures other than the patent ductus, the Nit-Occlud coil occlusion78 system was specifically designed for closure of the PDA. The coil has a biconical shape that is more suitable to the conical shape of most patent ductus than the cylindrical Gianturco coils. Figure 5 demonstrates closure of a PDA with a Nit-Occlud coil. For closure of moderate and large patent ductus, the Amplatzer duct occluder79 is frequently used (Figure 6). This device is made of nitinol wire woven into a mesh in the configuration of a mushroom-shaped plug, and it has a detachable cable, which allows easy repositioning or retrieval if necessary. For some patients with larger type B (short) ductus, the Amplatzer septal occluder device, a Dacron fiber–filled nitinol mesh with 2 disks connected by a short waist, may be effective. Figure 5. Example of PDA closure with a Nit-Occlud PDA occlusion device. A, Image of a Nit-Occlud coil with its biconical configuration. Note the reversed winding on the proximal end. B through D, Lateral angiograms demonstrating closure of a PDA with a single Nit-Occlud coil.Figure 6. Example of PDA occlusion with an Amplatzer duct occluder device. A, Image of an Amplatzer duct occluder device. B through D, Lateral angiograms demonstrating closure of a PDA with an Amplatzer duct occluder device.In addition to the devices described above, newer devices and modifications are in the process of being developed and tested. The Amplatzer duct occluder has been modified such that the retention skirt has an angle and concavity that allows it to fit better at the aortic end, and this device is currently under investigation.80 Other devices that are currently in use and are investigational are the modified folding-plug buttoned device81 and the wireless patch developed by Sideris and associates.82 Given the numerous variations of PDA configuration and size, it is apparent that any individual device will not be optimal for closure of all patent ductus. The availability of a variety of devices and techniques enhances the capability to close the vast majority of patent ductus with catheter-based techniques.Results of transcatheter occlusion of PDA have been excellent. Complete closure rates at follow-up generally exceed 90% to 95% in most studies.82 As a result of device modifications, evolution of new techniques, and increased operator skill, success rates for complete closure have improved significantly over time. Even when a small residual shunt is detected at follow-up, complete occlusion can usually be achieved by delivery of a single small additional coil.Serious complications of transcatheter closure of the patent ductus are rare. The most common complication is device embolization, which was relatively common early in the experience with coils. Embolized coils are usually retrieved, but even in cases in which they cannot be retrieved, adverse consequences are rare. Other potentially important complications are flow disturbance in the proximal left pulmonary artery or descending aorta from a protruding device, hemolysis from high-velocity residual shunting, femoral artery or vein thrombosis related to vascular access, and infection.Surgical TherapyAlthough generally associated with greater pain and morbidity than transcatheter methods, surgical ligation and surgical division are safe and effective procedures that historically have set a high standard by which transcatheter techniques have been judged. Surgical ligation or division of the PDA remains the treatment of choice for the rare very large ductus. Rarely, a large, window-type PDA may have insufficient length to permit ligation, and the appropriate surgical procedure is patch closure on cardiopulmonary bypass.83 Complete closure rates of surgical ligation (often accompanied by division of the ductus) in published reports range from 94% to 100%, with 0% to 2% mortality.84–86 Important complications include bleeding, pneumothorax, infection, and rarely, ligation of the left pulmonary artery or aorta. Surgical morbidity, cost, and hospital length of stay have been decreased with use of transaxillary muscle-sparing thoracotomy87,88 and by the technique of video-assisted thoracoscopic ligation of the PDA.89ConclusionsPDA is a cardiovascular disorder found in patients of all ages and sizes, from tiny premature infants to older adults. The clinical implications vary depending on the anatomy of the ductus arteriosus and the underlying cardiovascular status of the patient. Before the advent of surgical treatment for PDA in 1939, management for this disorder was palliative. Over the past 3 decades, transcatheter techniques have replaced surgical therapy in most patients with PDA. Concurrently, advances in diagnostic echocardiography and the widespread availability of echocardiography have resulted in improved detection and characterization of PDA in patients of all ages. Complications of PDA can be avoided or ameliorated by appropriate diagnosis and management.DisclosuresDr Moore serves as a proctor for AGA Medical Corporation, maker of the Amplatzer PDA occluder device, and as a proctor and consultant for PFM Medical, maker of the Nit-Occlud PDA occlusion device. Dr Schneider reports no conflicts.FootnotesReferences 1 Heymann MA, Creasy RK, Rudolph AM. Quantitation of blood flow patterns in the foetal lamb in utero. In: Proceedings of the Sir Joseph Barcroft Centenary Symposium: Foetal and Neonatal Physiology. 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