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THERAPEUTICS IN PEDIATRIC CARDIOILOGY: MANUAL GUIDE AND ANDROID APPLICATION

THESIS

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بسم الله الرحمن الرحيم
قَالُوا سُبْحَانَكَ لَا
عِلْمَ لَنَا إِلَّا مَا
عَلَّمْتَنَا ط إِنَّكَ
أَنْتَ الْعَلِيمُ
الْحَكِيمُ
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صدق الله العظيم

إهداء

لا تستطيع جميع الحروف أن تجد الكلمات الصحيحة ... كل الكلمات لا يمكنها التعبير عن امتناني وحبي واحترامي لذلك أهدي هذه الأطروحة إلى .....

الى الله العظيم

اللهم ليس بجهدي او اجتهادي , و انما بتوفيقك و رضاك فاالهم لك الحمد حتى ترضى و لك الحمد اذا رضيت و لك الحمد بعد الرضى .

إلى أمي العزيزة فوزية دراغمة

لا يمكنني العثور على الكلمات للتعبير عن مدى شعوري تجاه أمي الاستثنائية أفخر بأن أكون الابن لها. إلى والدتي الحلوة ، الحنونة جدًا لكنها لا تزال قوية جدًا. إلى الشخص الذي أعطاني كل شيء ولم أحسبه أبدًا. لا يوجد تكريم يمكن أن ينقل حقًا الحب والتفاني والاحترام الذي أحمله لك. بدونك ، أنا لا شيء ، لكن بفضلك أصبحت طبيبا . لقد كانت صلواتك دعمًا كبيرًا لي طوال دراستي. أتمنى أن أكون قد حققت الآمال التي وضعتها فيّ وحققت أحد أعز أحلامك اليوم. أسأل الله أن يعطيكي الصحة والعافية ، وأن يجازيكي على كل تضحياتك . أتمنى أن تجدي في هذا العمل المتواضع شهادة على امتناني وحبي غير المشروط واحترامي العميق.

أحبك كثيرا يا أمي.

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أنا ممتن دائمًا لدعمكم المعنوي الذي قدمتموه لي طوال رحلتي. كنتم دائما تبحثون عن سعادتي وابتسامتي في أصعب لحظات حياتي. أهدي لكم هذا العمل كشهادة على مدى شعوري تجاهكم ، والذي لا يمكن لأي كلمات التعبير عنه. أرجو أن نظل متحدين في الحنان ومخلصين للتربية التي تلقيناها.

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أنت أكثر من مجرد صديق لي ، لقد تقاسمنا الكثير من الوقت معًا

و الحزن والإحباط الذي تمكنا من التغلب عليه معًا

.و لحظات الفرح و السعاده و النجاح اللتي عشناها سويا

.أتمنى لك تحقيق ما تريد

إلى أصدقائي الأعزاء ورفقاء الغربة

: حسين ,سعيد ,أسيد ,قصي ,فارس ,صالح ,يحيى ,جلال ,نور الدين ,رئبال ,حسام و جميع أصدقائي وزملائي و رفقاء الغربة

الفلسطينين و الاردنيين :

شكرا لك على حبكم ، صداقتكم. كنتم دائمًا هناك لدعمي ومساعدتي والاستماع إلي. شكرًا لكم على الأوقات الجيدة التي أمضيناها

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الى كوثر ,نهال ,مونيا ,فاطمة الزهراء ، مريم :

قد يكون هذا العمل رمزًا لما أشعر به من امتنان لدعمكم . بارك الله فيكم و منحكم حياة مديدة مليئة بالفرح والنجاح.

ABBREVIATIONS :

ABG : arterial blood gas

ALT : alanine aminotransferase

ARF : Acute Rheumatic Fever

AS : aortic stenosis

ASLO : Anti-StreptoLysines O

AST : Aspartate aminotransferase

AV : Atrioventricular

AVSD : atrioventricular septal defect

AVT : acute vasoreactivity testing

BCPS : bidirectional cavo-pulmonary shunt

BNP : brain natriuretic peptide

BPs : blood pressure

BT : Blalock Taussig

BVH : Biventricular hypertrophy

CAT : Common Arterial Trunk

CCHD : Critical congenital heart disease

CcTGA : Congenitally corrected transposition of the great arteries

CHD : congenital heart disease

CHF : Congestive heart failure

CMR : Cardiovascular magnetic resonance imaging

CNS : Central nervous system

CoA : coarctation of aorta

COPE : Colchicine for Acute Pericarditis

CPET : cardiopulmonary exercise testing

CTA : computed tomography angiogram

EA : Ebstein's anomaly

ECMO : Extracorporeal Membrane Oxygenation

ESR : erythrocyte sedimentation rate

GERD : gastroesophageal reflux disease

GI : Gastrointestinal

HLHS : Hypoplastic left heart syndrome

IAA : interrupted aortic arch

ICD : implantable cardioverter-defibrillator

IE : Infective endocarditis

IVIG : Intravenous immunoglobulin

JET : junctional ectopic tachycardia

LCOS : Low cardiac output syndrome

LVH : Left ventricular hypertrophy

LVH : left ventricular hypertrophy

mPAP : mean pulmonary artery pressure

Mpap : Mean Pulmonary Artery Pressures

MR : mitral regurgitation

PA : pulmonary arteries

PAH : pulmonary arterial hypertension

PAWP : Pulmonary Capillary Wedge Pressure

PBF : pulmonary blood flow

PBF : pulmonary blood flow

PDA : Patent ductus arteriosus

PDA : patent ductus arteriosus

PFO : patent foramen oval

PH : Pulmonary hypertension

PICU : pediatric Intensive Care Unit

PMK : pacemaker

PPHN : Persistent pulmonary hypertension of the newborn

PPHN: Persistent pulmonary hypertension of newborn

PS : pulmonary stenosis

PVR : Pulmonary vascular resistance

PVR : pulmonary vascular resistance

Qp : Pulmonary flow.

Qs : Systemic flow

RA : Rheumatoid Arthritis

RV :right ventricle

RVOT: Right ventricular outflow tract

SBE : Subacute Bacterial Endocarditis

SIDS : Sudden infant death syndrome

SVT : Supraventricular tachycardia

SVT : Supraventricular tachycardia

VADs : Ventricular assist devices

VATS : Video-assisted thoracoscopic surgical

Contents :

LIST OF FIGURES

LIST OF TABLES

Chapter 1 : Cyanotic Neonate

I. Introduction :

- Cyanosis, derived from the Greek word kuaneos meaning dark blue, refers to the bluish discoloration of the skin, nail beds or mucous membranes.
- The clinical detection of cyanosis depends upon many variables and therefore, cannot be relied in isolation to confirm hypoxia .
- The importance of skin color of the neonate and the experience of the clinician cannot be overemphasized .
- The determination of partial pressure of oxygen (PaO2) in arterial blood gas (ABG) remains the gold standard for the diagnosis of hypoxia.
- ABG is not commonly performed in routine as it is invasive and not available widely.
- Also, since majority of the oxygen is carried in the blood bound to Hb, oxygen saturation is more relevant clinically.
- Direct measurement of oxygen saturation by pulse oximetry (SpO2) provides much easier and reliable way to diagnose hypoxia.

II. Classification of Cyanosis :

- Based on the extent of involvement, cyanosis is classified as acrocyanosis, central cyanosis and differential cyanosis :
  1. Acrocyanosis is limited to the extremities and lips with normal SpO2 and arterial PaO2 :
     - This results from local vasoconstriction and sluggish circulation in conditions like hypothermia or cold stress.

- Although a benign condition, it may at times indicate the presence of serious pathologies such as sepsis, hypoglycemia or low cardiac output state.

2. Central cyanosis is present on cutaneous and mucosal surfaces through-out the body and signifies serious pathology :
   - Usually, it is present uniformly in all the four limbs.
3. Differential cyanosis' :
   - Sometimes, cyanosis is not uniform with dissimilar oxygen saturation in upper and lower half of the body.
   - When cyanosis is more pronounced in lower limbs than upper limbs it is labelled as 'differential cyanosis'
   - Causes : patent ductus arteriosus (PDA), persistent pulmonary hypertension of newborn (PPHN) , coarctation of aorta (CoA) or interrupted aortic arch (IAA).
   - In the absence of PPHN, differential cyanosis is virtually diagnostic of cyanotic CHD.
   - In similar instances of PPHN or CoA but with transposition of great arteries (TGA), lower limbs are less cyanosed than the upper limbs. This pattern is due to more oxygenated blood from the left ventricle (LV) reaching lower limbs and is known as 'reverse differential cyanosis.

III. Causes of Cyanosis in Neonates :

- Respiratory and cardiac causes are the most common causes of persistent cyanosis (**Table 1**):

Table 1 : of different causes of cyanosis (2):	
1. Airway :	• Choanal atresia , Micrognathia, • Pierre Robin sequence , Laryngomalacia, • vocal cord palsy, tracheal stenosis, • vascular ring or sling Cystic hygroma or other neck masses Absent pulmonary valve • syndrome with large PA compressing airway.
2. Breathing :	• Parenchymal : Hyaline membrane disease (HMD) . • Aspiration (meconium, blood or milk), pneumonia (congenital or acquired) • Pulmonary hemorrhage , lymphangiectasia • Pulmonary edema Non parenchymal ,Pneumothorax • Congenital diaphragmatic hernia ,Congenital cystic adenomatoid malformation. • Pulmonary sequestration Pleural effusion, • Congenital lobar emphysema , Diaphragmatic palsy.
3. Circulation :	• Persistent pulmonary hypertension of newborn (PPHN) . • Pulmonary arteriovenous fistula , Cyanotic congenital heart diseases. • Reduced PBF Increased PBF , Transposition physiology . • Admixture physiology , No pulmonary stenosis with normal pulmonary blood flow . • Normal PBF with normal PA pressure • Pulmonary venous hypertension Low cardiac output state.
4. Defective Hb :	• Methemoglobinemia, Sulfhemo-globinemia, Hemoglobin M .
5. Miscellaneous	• Sepsis , Hypoglycemia , Polycythemia CNS • Asphyxia/ maternal sedation , Apnea of prematurity.

IV. Approach diagnostic :

1. Clinical Approach to Cyanosis in a Neonate :

- The main goal is identify the most likely cause of cyanosis.
- The distinction between respiratory and cardiac pathologies is an important initial step.

2. Clinical History :

- The evaluation begins with detailed clinical history :
  - Antenatal exposure to teratogens, viral exanthems, radiation or occurrence of gestational hypertension .
  - History mothers with diabetes mellitus during pregnancy , History of polyhydramnios .
  - Prolonged rupture of membranes and maternal fever .
  - History of mother who have received narcotic analgesia .
- It is more likely to have respiratory , if neonates became symptomatic at birth.
- Incoordination sucking and swallowing, vocal cord palsy or laryngeal cleft can cause Cyanosis while feeding.
- If respiratory distress and cyanosis was developed many hours after birth, it is usually related to cyanotic CHD, postnatal aspiration syndrome, or trachea – esophageal fistula.
- Some cases of CDH and congenital lobar emphysema may manifest many hours to days after birth .
- Similarly, some cyanotic CHDs may have clinically apparent cyanosis immediately after birth.
- Late onset cyanosis is typically seen in patients with tetralogy of Fallot (TOF) .

3. Physical Examination :

- Should be performed when the infant is appropriately warm and quiet.
- If absent respiratory distress, generally indicates CHD as the underlying cause.
- Respiratory distress due to lung disease, characterized by:
  - rapid breathing, retractions, use of accessory muscles and crepitations.
- A child with cyanotic CHD and increased pulmonary blood flow (PBF) may also have tachypnea but with fewer retractions and generally no crepitations.
- Neurological pathologies must be suspected if cyanosis is accompanied by hypoventilation, then evaluate :
  - the child's tone and activity.
  - and to assess for periodic breathing and apneic spells.
- The cardiac examination :
  - assessment of the heart rate, peripheral pulses.
  - perfusion and evidence of heart failure .
  - Brachial and femoral pulses should be palpated for their character and volume.
  - Importance of measuring blood pressure in all four limbs.
  - auscultation :
    - on the second heart sound (S2) which is loud and single in patients with pulmonary arterial hypertension (PAH),In contrast, S2 is single with inaudible pulmonic component (P2) in cardiac lesions with reduced PBF.

- Auscultation of cardiac murmurs is often not useful, serious lesions such as TGA and total anomalous pulmonary venous connection (TAPVC) are not associated with murmurs
- loud murmurs are frequently heard in benign lesions : small ventricular septal defect (VSD) and mild pulmonary stenosis (PS).

- Physical examination in neonates with suspected cyanotic CHD :
  - Evaluate Airway, Breathing and Circulation
  - Presence and pattern of respiratory distress
  - Dysmorphism or any other associated anomaly
  - Evidence of heart failure- poor weight gain tachycardia, tachypnea
  - Abdomen for liver sidedness (to assess situs) and hepatomegaly
  - Examine pulse, capillary refill, SpO2 and blood pressure in both pre and post-ductal location
  - Heart rate and rhythm
  - Precordial impulse to assess sidedness of the heart, heart sounds, mainly S2
  - Murmur and thrill—timing, site, intensity and radiation .
- The following physical signs, if present, indicate the presence of specific cardiac lesions :
  - LV type of apex beat : Tricuspid atresia , Single ventricle of LV morphology , DORV with restrictive VSD
  - Pulsation in 2nd left intercostal space due to left and anterior position of aorta : ccTGA
  - Pansystolic murmur of AV valve regurgitation : AV septal defect ccTGA
  - Early diastolic murmur at LUSB Truncus arteriosus with regurgitation

- Sea saw (systolo-diastolic) murmur at LUSB : TOF with absent pulmonary valve
- Complete heart block : ccTGA Heterotaxy syndrome

4. Investigations :

a. Pulse oximeter screen :

- should be done after 24 hours of life or just before early discharge from the hospital.
- The POS done earlier than 24 hours of age increases false-positive results.
- The false-positive test results detect noncardiac conditions that require prompt attention and treatment
- Have good ability to detect CCHD or other life-threatening neonatal conditions before the infant is discharged from the hospital.
- Sensitivity of the POS in detecting CCHD has been demonstrated to be high with a specificity up to 99% with a very low false-positive rate, making it a strong test.
- False-positive cases for heart lesions actually resulted in detection of noncardiac critical conditions that require immediate attention.
- It's Usefulness : it can detect all CCHDs , and also some noncardiac conditions before deterioration occurs
- To detect cyanotic CHDs and ductal-dependent lesions, oxygen saturation should be measured in the right hand (for preductal arterial saturation) and either foot (for post-ductal arterial saturation).
- Test Results :

1- Normal neonates should have oxygen saturation in the right hand and foot higher than 95% and the difference in oxygen saturation between the right hand and the foot should be 3% or less

2- Positive (abnormal) test results include the following three categories.

- Category 1: oxygen saturation 89% or less in either the right hand or a foot .
- Category 2: saturation between 90% and 94% in the right hand and the foot.
- Category 3: difference in the saturation 4% or more between the right hand and the foot

- Interpretation :
  - category 1 positive test results require immediate assessment (Refer for immediate assessment).
  - category 2 or 3 : Repeat screen is recommended for those with positive test results, for up to two times, each separated by 1 hour.
  - Repeat screen may prove negative on some cases.
  - If the positive test results continue to be present on the third screen, action must take as Category 1
- If Pulse oximetry of >95% in both the Right Hand and foot and Difference of < 3% :
  - Do not repeat for screening
  - Provide normal newborn care

b. <u>Hyperoxia Test :</u>

- Usually it is not difficult to differentiate a cardiac and respiratory cause of cyanosis especially when clinical data is combined with electrocardiogram (ECG) and chest X-ray (CXR).

- Some cases nonetheless remain challenging and in them hyperoxia test may be useful .
- It is advisable to use ABG or trans-cutaneous oxygen tension monitor rather than pulse oximeter while performing this test.
- The test consists in measuring an arterial blood gas at room air and 100% inspired oxygen after 10 minutes:
    - Neonates with congenital heart disease are usually not able to increase PaO2 above 100 mm Hg during 100% oxygen administration.
    - In patients with pulmonary disease, PaO2 generally increased greater than or equal to 100 mm Hg with 100% oxygen as ventilation-perfusion discrepancies are overcome.
    - A positive result indicates the cardiac origin and further cardiac workup is indicated to rule out CCHD.

c. <u>Chest X-ray :</u>

- CXR is important while evaluating newborns with cyanosis and respiratory distress .
- The role of CXR in excluding lung parenchymal pathology is well established.
- The locations of stomach, liver, and heart should be determined to rule out dextrocardia and situs inversus.
- A small heart and pulmonary oligemia suggest a malformation with reduced PBF .
- An enlarged heart and increased pulmonary vascular markings points to increased PBF.
- Some typical appearances are specific to some cardiac lesions :
    - Ground glass appearance of obstructed TAPVC ;

- 'Egg on side' appearance, cardiomegaly with narrow pedicle seen in children with TGA .
- 'Snowman or figure of 8' appearance in cases with TAPVC and 'boot-shaped heart' of TOF .
- These radiological appearances may appear late and therefore, may not be apparent in the neonatal period.

d. Electrocardiography :

- Normal neonatal dominance of RV presents as right axis deviation (RAD) and right ventricular hypertrophy (RVH) on ECG.
- Many cyanotic CHDs, including serious malformations like TGA have similar ECG appearance and therefore, even serious CHD may evade detection if ECG alone is relied for the diagnosis.

e. Echocardiography :

- Echocardiography is the gold standard for the diagnosis of CHD.
- In addition to providing anatomic information, echocardiography allows insights into the physiological alterations.
- Combined assessment of anatomic and physiologic aberrations is the basis for ascertaining the definitive management.
- Nevertheless, accurate diagnosis is necessary for immediate stabilization and therefore focus should be on determining the hemodynamic type of underlying CHD.

V. Management of a Neonate with Cyanotic CHD :

A. Immediate Management :

1. Medical Management :

- Medical management is the key to initial stabilization.
- The main goal is avoiding tissue hypoxia and metabolic acidosis.
- Patients who are critically ill must be treated in consultation with a pediatric cardiologist.
- Other patients must receive drug therapy based on the clinical presentation :
  - Heart failure secondary to cyanotic CHD with increased PBF responds well to diuretic therapy .
  - Beta blocker (intravenous metoprolol 0.1 mg/kg/dose 3–4 times/d or oral propranolol 1–4 mg/kg/d in 3–4 divided doses) is prescribed for children with reduced PBF, especially if the saturations are low or spells are present.
- PGE1 Infusion :
  - Neonates with deep cyanosis, especially those with acidosis should be immediately started on PGE1 infusion.
  - Intravenous PGE1 infusion : 0.05–0.4 mcg/kg/min typically improves and maintains oxygen saturation.
  - The infusion dose is guided by the degree of oxygen saturation.
  - The PGE1 infusion is useful in almost all neonates with cyanotic CHD except when associated with severe PVH such as with obstructed TAPVC, HLHS, mitral atresia with restrictive ASD and rarely TGA with intact ventricular septum and restrictive ASD.

- Clinical worsening following PGE1 infusion provides a clue towards the existence of one of these malformations.
- side effects in 10-12 % neonates receiving PGE1 infusion , (apnea which is dose dependent and may need mechanical ventilation is the most serious).

- oxygen :
  - There is only a slight improvement in saturation with the administration of oxygen.
  - However, oxygen supplementation increases dissolved oxygen which is undoubtedly helpful for a child with severe hypoxia.
  - Oxygen supplementation, by causing pulmonary vasodilatation sometimes results in clinical worsening in patient with increased PBF.
  - Oxygen supplementation, therefore, must be restricted to neonates with severe hypoxia and should not be used routinely.
- Iron supplementation : All children with cyanotic CHD should receive it , to aid compensatory erythrocytosis.

2. Percutaneous or Surgical Interventions for Immediate Stabilization :

- Some neonates in whom severe hypoxia or heart failure persists despite medical stabilization, require percutaneous or surgical intervention for stabilization.
- A surgical aorto-pulmonary shunt such as Blalock Taussig shunt or percutaneous PDA stenting improves saturation in patients with TOF physiology.
- Critical PS in neonates necessitate urgent percutaneous pulmonary valve balloon dilation (PVBD).
- Percutaneous balloon atrial septostomy improves saturation in neonates with TGA by enlarging preexisting PFO or ASD.

- Patients with critical lesions such as obstructive TAPVC must be operated upon urgently

B. Definitive Management :

- Surgery remains the destination therapy for almost all children with cyanotic CHD.
- All cyanotic CHDs are not amenable to corrective surgery and only palliative surgery is possible in these circumstances.
- Brief knowledge of surgical management available for various cyanotic CHDs is important as it enables the pediatricians to decide the timing of referral and surgical intervention .
- In addition, it allows preliminary counselling of the parents.
- Indications :
  a) Surgical correction possible :
     1. Neonatal surgery or intervention if :
        - TAPVC , TGA .
        - Critical PS or pulmonary atresia with IVSa
     2. Surgery during infancy if :
        - Truncus arteriosus
     3. Surgery during childhood if :
        - TOF and TOF physiology
        - Single atrium
        - Ebstein's anomaly

  b) Only multistage surgical palliation possible :
        - Single ventricle
        - DORV, Non-routable VSD

- Tricuspid atresia, VSD HLHS and mitral atresia

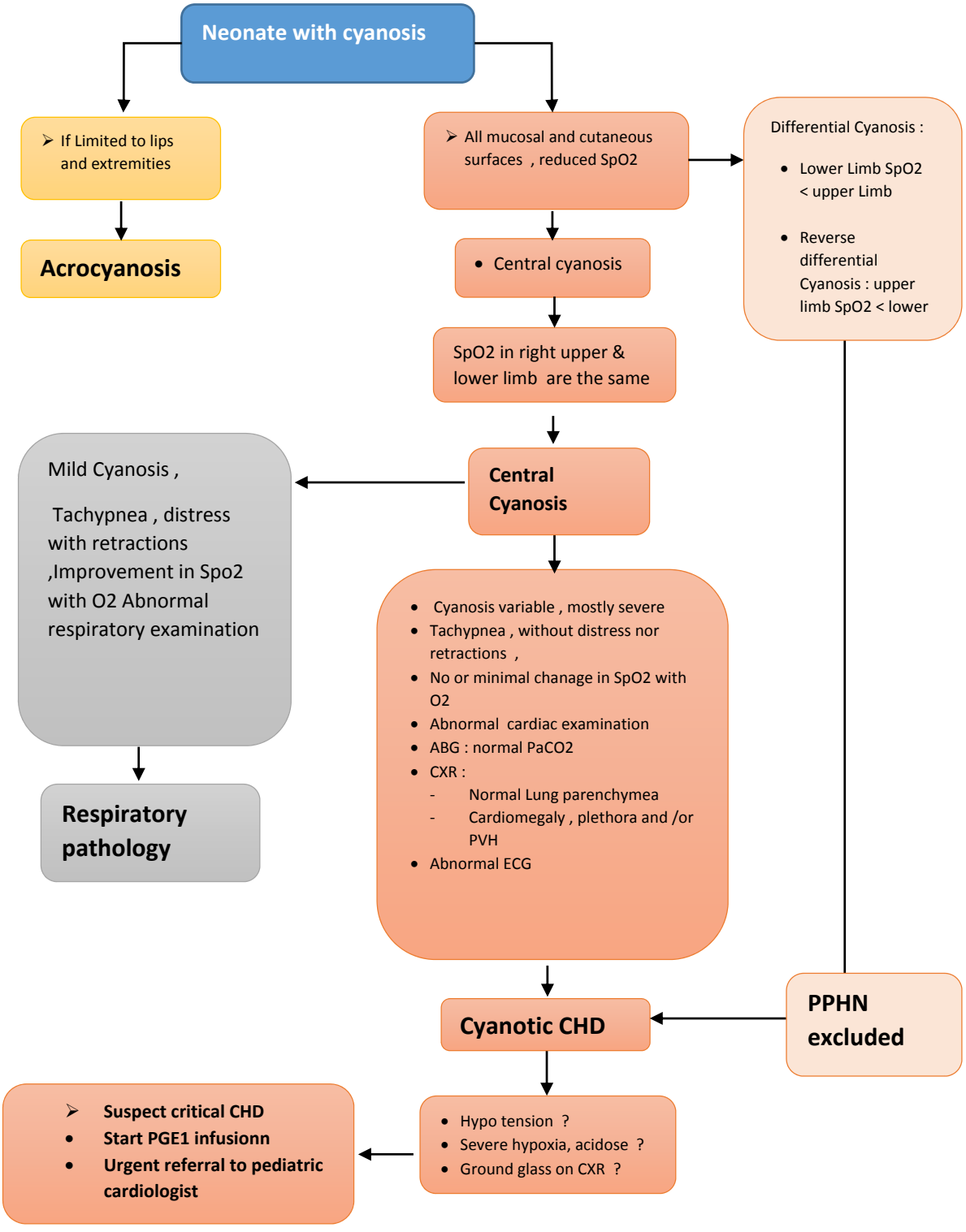

Figure 1 : Algorithmic clinical approach to a neonate with cyanosis (1):

- For more reading :

1. "Gupta, S. K. (2015). *Clinical Approach to a Neonate with Cyanosis. The Indian Journal of Pediatrics, 82(11), 1050–1060."*
2. *"Myung Park, Mehrdad Salamat", "Park's Pediatric Cardiology for Practitioners ","Seventh Edition"," (2020).pages : 107 –118 , 161-223);"*

Chapter 2 : The Child with Chest Pain

I. Introduction :

- After murmurs, chest pain is the second most common reason for referral to a pediatric cardiologist.
- chest pain in children and adolescents frequently involves referral to a pediatric cardiologist.
- The etiology of chest pain in pediatrics is broad, and the vast majority of cases are due to NONCARDIAC CAUSES.
- However, evaluations are often pursued due to fear about missing a potentially serious cardiac diagnosis, which may lead to sudden cardiac death.
- A complaint of chest pain is frequently encountered in children in the office and emergency department .
- Although chest pain does not indicate serious disease of the heart or other systems in most pediatric patients, in a society with a high prevalence of atherosclerotic cardiovascular disease, it can be alarming to the child and parents.
- Physicians should be aware of the differential diagnosis of chest pain in children and should make every effort to find a specific cause before making a referral to a specialist or reassuring the child and the parents of the benign nature of the complaint.
- Making a routine referral to a cardiologist is not always a good idea; it may increase the family's concern and may result in a prolonged and costly cardiac evaluation.

II. CAUSE AND PREVALENCE :

- Chest pain occurs in children of all ages and equally in male and female patients, with an average age of presentation at 13 years.
- By frequency :
  - trauma or muscle strain of the chest wall, costochondritis, and respiratory illness are the three most frequent causes of the pain.
  - Gastrointestinal (GI) and psychogenic causes are identified in fewer than 10% of cases,
  - and a cardiac cause is found infrequently (≤5%).

A. Idiopathic Chest Pain :

- No cause can be found in 12% to 85% of patients, even after a moderately extensive investigation.
- Many cases with chronic chest pain, an organic cause is less likely to be found.

B. Noncardiac Causes of Chest Pain :

- Identifiable noncardiac causes of chest pain include :

1. Musculoskeletal :

- Musculoskeletal chest pain is also common in children.
- The pain is caused by strains of the pectoral, shoulder, or back muscles after exercise, overused chest wall muscle for coughing, or chronic or acute trauma to the chest wall from sports, fights, or accidents as well as continued muscle strain from video gaming.

- A history of vigorous exercise (push-ups, pull-ups), weightlifting, or direct trauma to the chest (boxing) and the presence of tenderness of the chest wall or muscles clearly indicate muscle strain or trauma.
- Abnormalities of the rib cage or thoracic spine can cause mild, chronic chest pain in children.

2. Respiratory :

- Respiratory problems are responsible for about 10% to 20% of cases of pediatric chest pain, which may result from lung pathology, pleural irritation, or pneumothorax.
- A history of severe cough, with tenderness of intercostal or abdominal muscles, is usually present.
- The presence of crackles, wheezing, tachypnea, retraction, or fever on examination suggests a respiratory cause of chest pain.
- Pleural effusion may cause pain that is worsened by deep inspiration.
- Radiographic examination may confirm the diagnosis of pleural effusion, pneumonia, or pneumothorax

3. Exercise-Induced Asthma :

- The prevalence of exercise-induced asthma is probably underestimated.
- The response of the asthmatic patient to exercise is quite characteristic.
- Symptoms range from mild to severe and may include coughing, wheezing, dyspnea, and chest congestion, constriction, or pain.
- They also complain of limited endurance during exercise.

- Environmental factors such as cold temperature, pollens, and air pollution, as well as viral respiratory infection can worsen exercise-induced asthma.
- Exercise-induced bronchospasm provocation test is diagnostic, which is described under Stress Tests in

4. Gastrointestinal :

- Some GI disorders, including gastroesophageal reflux disease (GERD), may present as chest pain in children.
- In addition to chest pain, children with GERD may complain of abdominal pain, frequent sore throat, gagging or choking, extreme pickiness about foods, frequent respiratory problems (such as bronchitis, wheezing, asthma), and poor weight gain.
- The pain is in relation to eating and diet may help clarify the diagnosis.
- The incidence of GERD is higher in patients with Down syndrome, cerebral palsy, and other causes of developmental delay.
- Esophagitis resulting from gastroesophageal reflux should be suspected in a child who complains of burning substernal pain that worsens with a reclining posture or abdominal pressure or that worsens after certain foods are eaten.
- Cholecystitis presents with postprandial pain referred to the right upper quadrant of the abdomen and part of the chest
- Young children sometimes ingest foreign bodies, such as coins, which lodge in the upper esophagus, or they may ingest caustic substances that burn the entire esophagus. In such cases, the history makes the diagnosis obvious.

5. Psychogenic :

- seen in both boys and girls at equal rates.
- Often a recent major stressful event parallels the onset of the chest pain : a death, divorce or separation in the family, a serious illness, a disability, a recent move, failure in school, or sexual molestation.
- However, a psychological cause of chest pain should not be lightly assigned without a thorough history taking and a follow-up evaluation.
- Psychological or psychiatric consultation may reveal conversion symptoms, a somatization disorder, or even depression.

C. Miscellaneous :

- The precordial catch :
  - a one-sided chest pain, lasts a few seconds or minutes and is associated with bending or slouching.
  - The cause is unclear, but the pain is relieved by straightening and taking a few shallow breaths or one deep breath.
  - The pain may recur frequently or remain absent for months.
- Slipping rib syndrome :
  - results from excess mobility of the 8th to 10th ribs, which do not directly insert into the sternum.
  - In many cases, the ligaments that hold these ribs to the upper ribs are weak, resulting in slippage of the ribs, causing pain.
- Mastalgia :
  - Some adolescents complain of chest pain caused by breast masses .
  - These tender masses may be cysts (in post-pubertal girls)

- or may be part of normal breast development in pubertal boys and girls.

- Pleurodynia (devil's grip) :
  - an unusual cause of chest pain caused by coxsackievirus infection,
  - is characterized by sudden episodes of sharp pain in the chest or abdomen.
- Herpes zoster is another unusual cause of chest pain.
- Spontaneous pneumothorax and pneumomediastinum :
  - are serious but rare respiratory causes of acute chest pain in children;
  - can be seen in children with asthma, cystic fibrosis, or Marfan's syndrome are at risk.
  - inhalation of cocaine can provoke pneumomediastinum and pneumothorax with subcutaneous emphysema.
- Pulmonary embolism:
  - although extremely rare in children, has been reported in female adolescents who use oral contraceptives or have had elective abortions.
  - it has also been reported in male adolescents with recent trauma of the lower extremities and in children with shunted hydrocephalus.
  - It may occur in in children with hypercoagulation syndromes.
  - Affected patients usually have dyspnea, pleuritic pain, fever, cough, and hemoptysis.
- Hyperventilation :
  - can produce chest discomfort
  - it is often associated with paresthesia and lightheadedness

D. Cardiovascular Causes of Chest Pain :

1. Ischemic Myocardial Dysfunction :

- Congenital Heart Defects :
  - Severe obstructive lesions may cause chest pain : such as aortic stenosis (AS), subaortic stenosis, severe pulmonary stenosis (PS), and pulmonary vascular obstructive disease (Eisenmenger's syndrome).
  - Mild stenotic lesions do not cause ischemic chest pain.
  - The pain is usually associated with exercise and may be a typical anginal pain.
  - cardiac examination often reveals a loud heart murmur best audible at the upper right or left sternal border, usually with a thrill, except in patients with Eisenmenger's syndrome.
  - The ECG usually shows ventricular hypertrophy with or without "strain" pattern.
  - Chest radiography films may be abnormal in patients with AS or PS with a prominent ascending aorta or main pulmonary artery trunk, respectively.
  - are definitely abnormal in patients with Eisenmenger's syndrome, with a marked prominence of the main pulmonary artery segment.
  - Echocardiography and Doppler studies permit accurate diagnosis of the type and severity of the obstructive lesion.
- Coronary Artery Disease :
  - Coronary artery anomalies rarely cause chest pain.
  - They include rare cases of proximal intramural course of either coronary arteries, anomalous origin of the left coronary artery from the pulmonary artery (usually symptomatic during early infancy),

single coronary artery, coronary artery fistula, aneurysm or stenosis of the coronary arteries as a result of Kawasaki's disease, or coronary insufficiency secondary to previous cardiac surgery involving the coronary arteries or the vicinity of these arteries.

- Cardiomyopathy :
  - Hypertrophic and dilated cardiomyopathies can cause chest pain from ischemia, with or without exercise, or from rhythm disturbances.
  - Cardiac examination reveals no diagnostic findings, but the ECG or chest radiographic films are abnormal, leading to further studies.
  - Echo studies are diagnostic of the conditions .
- Cocaine Abuse :
  - Even children with normal hearts are at risk of ischemia and myocardial infarction if cocaine is used.
  - The resulting increase in heart rate and blood pressure, increase in myocardial oxygen consumption, possible increase in platelet activation, and myocardial electrical abnormalities may collectively produce anginal pain, infarction, arrhythmias, or sudden death.
  - History and drug screening help physicians in the diagnosis of cocaine-induced chest pain.
- Aortic Dissection or Aortic Aneurysm :
  - Aortic dissection or aortic aneurysm rarely causes chest pain.
  - Children with Turner's, Marfan's, and Noonan's syndromes are at risk

2. Arrhythmias :

- Chest pain may result from a variety of arrhythmias, especially with sustained tachycardia, resulting in myocardial ischemia.

- Even without ischemia, children may consider palpitation or forceful heartbeats as chest pain.
- When chest pain is associated with dizziness and palpitation, a resting ECG and a 24-hour Holter monitor should be obtained.
- Alternatively, an event recorder with telephone transmission device may be used to record the ECG rhythm while the patient experiences symptoms.

3. Mitral Valve Prolapse :

- Chest pain present in about 20% of patients .
- The pain is usually a vague, non- exertional pain of short duration, located at the apex, without a constant relationship to effort or emotion.
- The pain is presumed to result from abnormal tension on papillary muscles, but the causal relationship between chest pain and MVP remains unclear in children.
- Occasionally, supraventricular or ventricular arrhythmias may result in cardiac symptoms, including chest discomfort.
- Thoraco-skeletal deformities commonly occur in these children and may cause chest pain.
- Nearly all patients with Marfan's syndrome have MVP.
- Cardiac examination reveals a mid-systolic click with or without a late systolic murmur, the mid-systolic click becomes more prominent on standing.
- The ECG may show T-wave inversion in the inferior leads (leads II, III, aVF).
- Echo findings of MVP in adults are well established, but diagnostic echo findings of MVP have not been established in children .

- The pain caused by coronary artery abnormalities is expected to be typical of anginal pain.
- Cardiac examination may be normal or may reveal a heart murmur (systolic murmur of mitral regurgitation or continuous murmur of coronary artery fistula).
- The ECG may show myocardial ischemia (ST-segment elevation) or old myocardial infarction.
- Chest radiographs may reveal abnormalities suggestive of these conditions.
- Although echo can be helpful, computed tomography or coronary angiography is usually indicated for the definitive diagnosis.

4. Pericardial or Myocardial Disease :
    - Pericarditis :
    - Myocarditis :

III. DIAGNOSTIC APPROACH :

- The first goal of evaluating children with a complaint of chest pain is to rule out cardiac cause of chest pain, which is usually the main concern to the child and parents, and to look for three common noncardiac causes of chest pain.
- A thorough history taking and careful physical examination will suffice to rule out cardiac causes of chest pain and often to find a specific cause of the pain.
- To rule out cardiac causes of chest pain, it needs :
    - chest radiographic films and an ECG.

- Cardiologists may, in addition, obtain an echocardiogram to accomplish the same.

- Cardiac causes of chest pain can be ruled out by non-exertional nature of pain, negative cardiac examination, and normal results of other investigations, with exception of cardiac arrhythmia as the cause of the pain.
- Even if physicians cannot find a specific cause of chest pain, it is relatively easy to rule out cardiac causes of chest pain by following the steps outlined in this chapter.
- Most patients and parents will be relieved and satisfied to learn that the heart is not the cause of chest pain.

a. History of Present Illness :

- should be directed at determining the nature of the pain :
  - The duration
  - Intensity
  - Frequency,
  - Location,
  - And points of radiation.
- Relation with efforts :
  - during or after heavy physical but dynamic activities
  - or whether it occurred at rest or while sitting in class.
- It is important to remember that ischemic cardiac chest pain is described as a pressure or squeezing sensation, not a sharp pain.
- Associated symptoms, concurrent or precipitating events, and relieving factors may help clarify the origin of the pain.
- The following are some examples of questions to ask.

- When did the pain begin?
- Acute onset of pain (within 48 hours) is more likely to have an organic etiology.
- In young children, a sudden onset of chest pain should raise the possibility of a foreign body (coin or button battery) in the esophagus.
- Those with chronic pain are more likely to be idiopathic or psychogenic, although some children with costochondritis may have chronic pain
- How often have you had similar pain (frequency and chronicity)?
- What is the location (e.g., specific point, localized or diffuse)?
- How severe is the pain?
- What is the pain like (e.g., sharp, pressure sensation, squeezing)?
- The character of the pain is usually nonspecific in children and does not help much in identifying the cause.
- Although classic description of cardiac pain in adults is that of pressure, crushing, or squeezing sensation, it is uncertain whether this classic description is typical in pediatric cases.
- How long does the pain last (seconds, minutes, hours)?
- What triggers the pain (e.g., exercise, eating, trauma, emotional stress)?
- Chest pain precipitated by running or exercise may relate to cardiac disease or more commonly exercise-induced asthma.
- Midsternal or precordial pain that worsens after eating or when lying down may be esophageal.
- History of recent workouts, trauma, or fight may point to the musculoskeletal system.
- A recent stressful event may be important clue to psychogenic etiology of pain (after ruling out organic causes).

- What makes the pain better or worse?
- Pain that worsens with moving, deep breathing, or cough may suggest chest wall pain, pleural pain, or lung pathology.
- Pain that improves by sitting up and leaning forward may be caused by pericarditis.
- Are there associated symptoms, such as cough; fever; syncope; dizziness; tingling in the hands, feet, or around the mouth; or palpitation?
- Pain associated with palpitation or syncope may suggest arrhythmia or other cardiac disease.
- History of fever suggests an infectious process (e.g., pneumonia, myocarditis, pericarditis).
- History of tingling could be suggestive of hyperventilation.

b. Past and Family Histories :

- After gaining some idea about the nature of the pain, the clinician should focus on important past and family histories. Examples of questions are as follows :

1- Have you been hurt while playing, or have you used your arms excessively for any reason?

2- Does the child have any known medical conditions (e.g., congenital or acquired heart disease, cardiac surgery, infection, asthma)?

3- Is there any important past history, such as surgery, Kawasaki's disease, asthma, sickle cell disease, diabetes, or Marfan's syndrome (or other connective tissue disease)?

4- Does any disease run in the family? Is there a family history of heart disease, other conditions, or sudden death?

5- Has there been a recent heart attack or a cardiac death in the family?

6- Is the child taking medicines, such as asthma medicines or birth control pills?

7- Has the child been exposed to drugs (cocaine) or cigarettes?

8- What treatments for the pain have been tried?

9- What is the patient or family member concerned about?

c. Physical Examination :

1- A careful general physical examination should be performed .

2- The clinician should note whether the child is in severe distress from pain, is in emotional stress, or is hyperventilating.

3- The skin and extremities should be examined for trauma or chronic disease. Bruising elsewhere on the body may indicate chest trauma that cannot be seen.

4- The abdomen should be carefully examined because it may be the source of pain referred to the chest.

5- The chest :

- The chest should be carefully inspected for trauma or asymmetry.
- The chest wall should be palpated for signs of tenderness or subcutaneous air.
- Special attention should be paid to the possibility of costochondritis as the cause of chest pain, which is a quite common identifiable cause of the pain.
- Physical examination is all that is needed for the diagnosis of costochondritis.
- Physicians should use the soft part of the terminal phalanx of a middle finger to palpate each costochondral and chondro-sternal junction,

not with the palm of a hand; using the palm may frequently miss the diagnosis.

- Pectoralis muscles and shoulder muscles should be examined for tenderness, which may be caused by excessive weightlifting or other work requiring the use of these muscles.

6- The heart and lungs should be auscultated for arrhythmias, heart murmurs, rubs, muffled heart sounds, gallop rhythm, crackles, wheezes, or decreased breath sounds.

7- Finally, the child's psychological state should be assessed.

d. <u>Other Investigations :</u>

- If the three common causes or other identifiable causes of chest pain are not found by physical examination, the clinician should obtain chest radiographic films and an ECG and direct his or her attention to the cardiac causes of chest pain :

1. Cardiac examination is done to detect a pathological heart murmur. One must be careful not to interpret commonly occurring innocent murmurs as pathologic.
2. Chest radiography should be evaluated for pulmonary pathology, cardiac size and silhouette, and pulmonary vascularity.
3. A resting 12-lead ECG should be evaluated for cardiac arrhythmias, hypertrophy, conduction disturbances (including Wolff-Parkinson-White preexcitation), abnormal T and Q waves, and an abnormal QTc interval.

- If the pain is non exertional, the family history is negative for hereditary heart disease (e.g., long QT syndrome, cardiomyopathies, unexpected sudden death), the past history is negative for heart disease or Kawasaki's disease, the cardiac examination is unremarkable, and the ECG and chest

radiographs are normal, the chest pain is not likely to be of cardiac origin unless palpitation or dizziness is a prominent accompanying symptom.

- At this point, the clinician can reassure the patient and family of the probable benign nature of the chest pain.
- If any of the above aspects is positive, a formal cardiac consultation may be indicated.
- An echocardiographic examination is usually obtained by cardiologists, and it will most likely rule in or out cardiac causes of chest pain.
- If a cardiac cause and the three common noncardiac causes of chest pain are not found, the pain is likely due to a condition in other systems, such as GI or respiratory systems, including psychogenic or idiopathic origin.
- Simple follow-up may clarify the cause. Drug screening for cocaine may be worthwhile in adolescents who have acute, severe chest pain and distress with an unclear cause.

IV. MANAGEMENT

➢ When a specific cause of chest pain is identified, treatment is directed at correcting or improving the cause.

1. Costochondritis :

- Costochondritis can be treated by reassurance and occasionally by nonsteroidal anti-inflammatory drugs (NSAIDs, e.g., ibuprofen) or acetaminophen.
- Ibuprofen is better than acetaminophen because the former is an analgesic and anti-inflammatory agent, and the latter is only analg-esic :
  - ➢ Ibuprofen 10 mg/kg:

- three to four times a day, for 7 days often improves the pain.
- The same course may be repeated two to three times with a 1-week period of no medicine in between the courses.
- Alternatively, for more compliance (because of twice-daily dosing), naproxen could be given for 5 to 7 days.

➢ Weight of backpacks should be reduced to a minimum.

➢ Physical activities requiring the use of shoulder girdle muscles should be avoided, which may include sports using arms, push-ups, pull-ups, certain house chores, and others.

2. Most musculoskeletal and nonorganic causes can be treated

- with rest.
- Acetaminophen.
- or NSAIDs.

3. If respiratory causes are found:

- treatment is directed at those causes.
- Other wise Referral to a pulmonologist should be considered.

4. Exercise-induced asthma:

- is most effectively prevented by inhalation of a β2-agonist 10 to 15 minutes before exercise.
- Inhaled albuterol usually affords protection for 4 hours.
- Other anti asthmatic agents have also been reported to be effective as well.
- Use of a muffler or cold weather mask to warm and humidify air before inhalation also is effective.

5. If gastritis, gastroesophageal reflux, or peptic ulcer disease is suspected:

- Trials of antacids.

- Hydrogen ion blockers.
- Or prokinetic agent (e.g., metoclopramide [Reglan]) are helpful therapeutically .

6. If serious cardiac anomalies, arrhythmias, or exercise-induced asthma is diagnosed, a referral is made to the cardiology or pulmonary service.
7. Cardiac evaluation requires further specialized studies such as echo, an exercise stress test, Holter monitoring, event recorder, or even cardiac catheterization or electrophysiologic study. Depending on the cause, treatment may be surgical or medical.
8. If organic causes of chest pain are not found and a psychogenic etiology is suspected, psychological consultation may be considered.

9. When or if cocaine-associated chest pain is suspected, physicians should arrange a referral to appropriate specialists for confirmation of the diagnosis and management of the problem
    - the following are several points recommended by the American Heart Association's guideline on treatment for cocaine abuse patients.

a. If cocaine intoxication is suspected, benzodiazepines are recommended as the primary treatment for anxiety, tachycardia, and hypertension.
b. Aspirin and nitrates continue to be strongly recommended.
c. However, beta-blockers (including agents with mixed α-adrenergic antagonist effects, such as labetalol) are considered contraindicated because the unopposed α-adrenergic effect leads to worsening coronary vasoconstriction and increasing blood pressure.
d. Calcium channel blockers are not recommended; they might increase mortality rates.

e. Early percutaneous coronary intervention is indicated if myocardial infarction is likely the diagnosis.

V. Referral to Cardiologists

- Referral to Cardiologists The following are some of the indications for referral to a cardiologist for cardiac evaluation:

1. When history reveals that chest pain is triggered or worsened by physical activities, the pain suggests anginal pain .
2. Chest pain is accompanied by other symptoms such as palpitation, dizziness, or syncope .
3. When there are abnormal findings in the cardiac examination or when abnormalities occur in the chest radiographs or ECG, cardiology referral is clearly indicated.
4. The examiner's ability to recognize common innocent heart murmurs minimizes the frequency of such referrals.
5. When there is a positive family history for cardiomyopathy, long QT syndrome, sudden unexpected death, or other hereditary diseases commonly associated with cardiac abnormalities
6. High levels of anxiety in the family and patient and a chronic, recurring nature of the pain are also important reasons for referral to a cardiologist

- For mor reading :

a) Yeh, T. K., & Yeh, J. (2015). *Chest Pain in Pediatrics. Pediatric Annals, 44(12), e274–e278.*

b) "Myung Park, Mehrdad Salamat, "Park's Pediatric Cardiology for Practitioners "," Seventh Edition", (2020).pages : (378- 385)*;"*

Chapter 3 : Common Arterial Trunk

I. Introduction :

- Arterial trunk (CAT), or truncus arteriosus, is a rare cyanotic congenital heart defect, often found in the context of DiGeorge syndrome.
- CAT consists of a single arterial trunk that arises from the ventricles, giving origin to the coronary arteries, aorta, and pulmonary arteries (PA) (**Figure 2**).
- The presentation is highly variable, dependent on the morphological variation, the degree of truncal valve regurgitation, and the relative resistances of the pulmonary and systemic arterial vascular beds, often presenting less with cyanosis, and more with tachypnea from pulmonary over circulation.

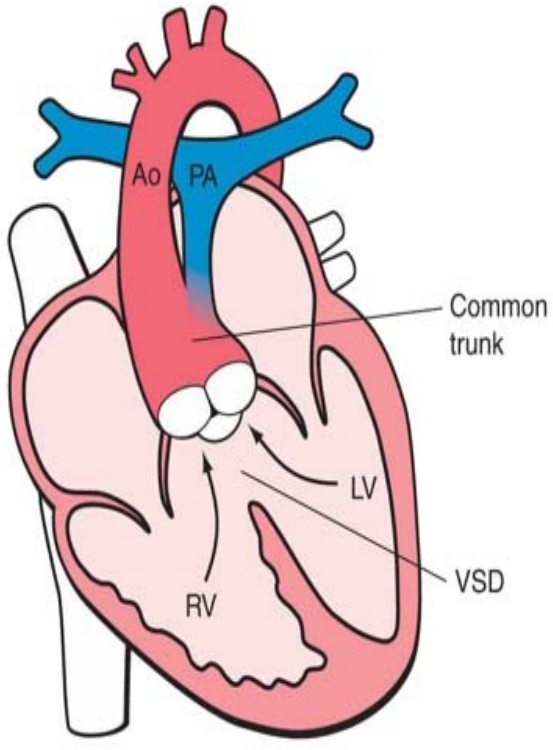

***Figure 2**: Common Arterial Trunk , with VSD(ventricular septal defect)*

source : https://obgynkey.com/common-arterial-trunk/

II. Diagnosis :

- The newly diagnosed patient :
  - Typically during the neonatal period or in early infancy with only mild cyanosis
  - A symptomatology of congestive heart failure(with tachycardia, tachypnea, excessive seating, poor feeding, and poor weight gain) within several days.
- More significant central cyanosis in those with persistently raised pulmonary vascular resistance or branch PA stenosis.
- In those presenting in congestive heart failure, their presentation may be accelerated in the presence of significant truncal regurgitation.
- If left unrepaired into later infancy, with continued pulmonary over-circulation, the child is at high risk for the development of pulmonary arterial hypertension.
- The physical examination findings reflect the infant's state of pulmonary over-circulation with congestive heart failure, and degree of widened pulse pressure.
- the second heart sound is loud and often single, Splitting of the second heart sound may occur.
- There may be an ejection click , a usually a systolic ejection murmur.
- an early diastolic high-pitched murmur can be present present at the left sternal border.
- The peripheral pulses are often bounding secondary to the significant diastolic run off
- Sign of DiGeorge syndrome (22q11 deletion) syndrome .

- Chest Radiography :
  - Usually, demonstrates cardiomegaly and increased pulmonary vascular markings.
  - The aortic arch is right-sided in one-third of patients
  - an absent thymus is seen in those with associated DiGeorge syndrome.
- Fetal Echocardiography
  - In general, prenatal diagnostic accuracy in congenital heart disease, including that of CAT, has improved with the standardization of a more thorough obstetrical screening ultrasound.
- Postnatal Preoperative Imaging :
  - Transthoracic Echocardiogram : Transthoracic echocardiography (TTE) is the initial preoperative imaging modality of choice for all forms of congenital heart disease, and often is the mainstay of diagnosis.
  - Transthoracic echocardiography is the mainstay of diagnosis
  - CT, MRI, and Cardiac Catheterization .
  - Usually 2-dimensional echocardiogram is sufficient to completely delineate the anatomy in CAT. Occasionally, additionally imaging studies are necessary.

III. Management :

a. Preoperative Management :

- In the more common forms of CAT, an arterial duct is absent:
  - prostaglandin E2 is not necessary.
- If pulmonary dominant form(rare) with interruption of the aortic arch or aortic coarctation, a patent arterial duct is often present and necessary to maintain lower extremity perfusion,:
  - prostaglandin E2 should be initiated immediately following birth and continued until surgical repair.
- The newborn often presents with only very mild central cyanosis, often maintaining oxygen saturations >90% in the first days of life, reflecting the large Qp:Qs that is often present.
- If the infant with worsening tachypnea, it may require positive pressure ventilation in an attempt to "stent" open the airways in the presence of interstitial pulmonary edema.
- The fractional percent of inspired oxygen should be kept at room air to avoid further lowering the pulmonary vascular resistance and worsening the congestive heart failure. The target saturation should not exceed 85%
- Diuretic use may be necessary in the preoperative period with worsening pulmonary edema , also anti-congestive measures with and **ACE inhibitors** should be pursued before an operation is undertaken.
- Additional supportive care strategies which may be indicated include :
  - correcting metabolic acidosis, hypoglycemia, and anemia that may contribute to heart failure.

- If lower diastolic pressure , it is prudent to monitor clinically for the occurrence of worsening ventricular systolic function and resulting poor perfusion, with continuous telemetry monitoring and obtaining periodic electrocardiograms to monitor for the development of coronary ischemia.
- Medication that may increase myocardial demands or further compromise diastolic coronary blood flow should be avoided.
- Enteral feeding should be avoided in those with persistently low diastolic pressures as these infants are at increased risk for necr-otizing enterocolitis.
- strategies to improve coronary perfusion in such a patient may include :
  - ventilatory manipulation to increase pulmonary vascular resistance, volume administration to increase cardiac output,
  - and medications to both increase cardiac output and improve ventricular filling pressures.
- Because of the frequent association of DiGeorge (22q11.2 deletion) syndrome:
  - Serum calcium and magnesium levels should be checked (because they may be low from hypo-para-thyroidism); their supplement may be indicated.
  - Only irradiated blood products should be used (to prevent transfusion acquired acute graft-versus-host disease, which destroys lymphocytes) for an urgent surgery (because of an insufficient time for evaluation of immune status accurately).
- Prophylaxis against SBE should be observed when indications arise.

b. Surgical Repair:

- The complete repair in the first few weeks of life has become the standard of care.
- In patients with significant truncal valve regurgitation and/or stenosis, repair of the valve is additionally undertaken.
- Truncal valve manipulation is avoided if possible, as there is an increased mortality and morbidity associated with valve repair in the neonatal period.
- Additional associated anomalies that have been identified as independent risk factors for surgical mortality include interrupted aortic arch and coronary artery anomalies, with poorer outcomes also seen in those with low birth weight and noncardiac abnormalities, including those with DiGeorge syndrome.

- For mor reading :

a) 1= Chikkabyrappa, S., Mahadevaiah, G., Buddhe, S., Alsaied, T., & Tretter, J. (2018). *Common Arterial Trunk: Physiology, Imaging, and Management. Seminars in Cardiothoracic and Vascular Anesthesia, 108925321882138.*

b) 2 . "Myung Park, Mehrdad Salamat. "Park's Pediatric Cardiology for Practitioners"." Seventh Edition". (2020).pages :208-211) "

Chapter 4 : Ebstein's anomaly

I. Introduction

- Ebstein's anomaly (EA) is a malformation of the tricuspid valve (TV) with myopathy of the right ventricle (RV) , characterized by the downward displacement of septal leaflet and atrialized right ventricle (RV) (**Figure 3**).
- Structural abnormalities often seen in Ebstein's anomaly include :
  - atrial septal defect (ASD),
  - patent foramen ovale
  - pulmonary stenosis or atresia,
  - and ventricular septal defect.

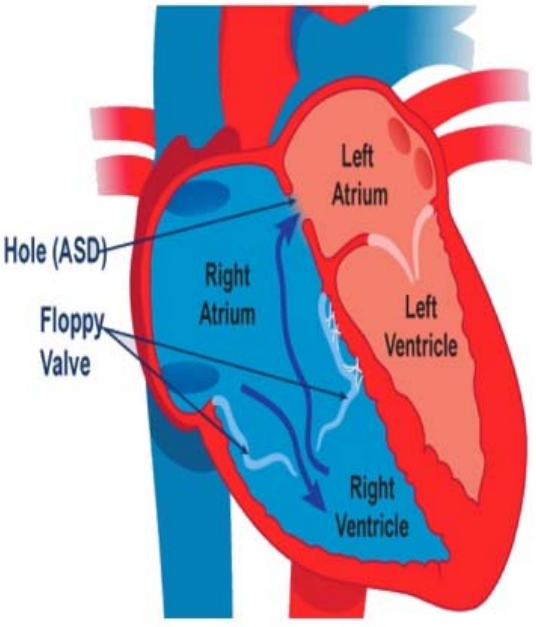

Figure 3: Ebstein's anomaly :

- malformation of the tricuspid valve .
- myopathy of the right ventricle (RV) .
- the downward displacement of septal leaflet .
- and atrialized right ventricle (RV).

(Source :https://kidshealth.org/en/parents/ebstein-anomaly.html)

- The critical distinguishing feature of EA from other congenital regurgitant lesions is the degree of apical displacement of the septal leaflet (≥ 8 mm/m2 body surface area).

II. Diagnosis :

a) Clinical presentation :

- In severe cases, cyanosis and CHF develop during the first few days of life.
- Some subsequent improvement coincides with reduction of the PVR.
- Children with milder cases may complain of dyspnea, fatigue, cyanosis, or palpitation on exertion.
- A history of SVT is occasionally present.

b) Physical Examination :

- Mild to severe cyanosis is present, as well as clubbing of the fingers and toes in older infants and children.
- Characteristic triple or quadruple rhythm is audible. This rhythm consists of a widely split S2, split S1, S3, and S4. A soft holosystolic (or early systolic) murmur of TR is usually audible at the lower left sternal border . A soft, scratchy, mid-diastolic murmur is present at the same location.
- Hepatomegaly is usually present.

c) Paraclinical :

- Baseline testing in patients with EA includes :
  - electrocardiogram,
  - chest radiograph,
  - Echocardiography : is the procedure of choice for the diagnosis and functional assessment of Ebstein's anomal
  - Cardiac catheterization is rarely necessary in patients with Ebstein's anomaly. In the current era, echocardiography and MRI provide superior images.

III. MANAGEMENT :

a. Medical :

- Asymptomatic patients may be managed medically with observation for many years.
- Assessment of arrhythmias, progressive RV enlargement, and/or systolic function deterioration of the RV should be closely followed.
- In severely cyanotic newborns, intensive treatment with :
  - mechanical ventilation .
  - PGE1 infusion.
  - inotropic agents.
  - and correction of metabolic acidosis may be necessary before proceeding with emergency surgery.
- In infants who appear to have a mild form of Ebstein's anomaly and to be improving with the above management, treatment with PGE1 and inotropic support is gradually withdrawn to observe the effect of ductal closure.
- Asymptomatic children with mild Ebstein's anomaly require only regular observation. If CHF develops anti-congestive measures, including :
  - a low sodium diet .
  - oral diuretics .
  - digoxin .
  - and a low dose angiotensin converting enzyme (ACE) inhibitor, for example, enalapril.
- Acute episodes of SVT may be treated most effectively with adenosine.
- Beta-blockers are the most appropriate first-line preventive therapy for SVT.

- For patients with recurrent SVT caused by AV reentrant mechanism, radiofrequency catheter ablation techniques have been successful.
- Varying degrees of activity restriction may be necessary for children with this condition.
- Therapeutic control of acute exacerbation of right heart failure was mainly based on :
  - Diuretics , vasodilators , cardiotonic .
  - Low sodium diet and abdominal paracentesis, which can be effective for relieving the congestive heart failure but is not good for withholding the effusions.
- Patients should be considered for operative intervention :
  - If symptoms and/or worsening exercise capacity, cyanosis, paradoxical embolism, progressive RV dilation or dysfunction, and the onset of arrhythmias
  - If tricuspid repair is feasible and in a setting of low morbidity and mortality.

b. OPERATIVE INTERVENTION :

- Asymptomatic patients with Ebstein's anomaly can be conservatively treated and kept under close follow-up
- Tricuspid valve repair is the goal of operative intervention , typically includes RV plication, right atrial reduction, and atrial septal closure or subtotal closure.
- Surgical operation is indicated for the patients with Ebstein's anomaly:
  - in the presence of right heart dilation and progressive ventricular functional impairment.

- If poor right ventricular function : ventricular repair is indicated .
- If severe left ventricular dysfunction : heart transplantation is indicated .
- In severe form of Ebstein's anomaly in a neonate : tricuspid valve and pulmonary artery closures, residual AV communication that is retained minimal for decompressing the RV when closing the tricuspid valve and construction of atrio-pulmonary artery shunt, followed by late stages of hemi-Fontan and fenestrated Fontan operations were performed.

- BCPS : A bidirectional cavo-pulmonary shunt :
  - If severe RV dysfunction: is applied selectively in adult patients .
  - Pulmonary hypertension is rare in EA, so the BCPS is generally feasible even in the setting of moderate left ventricular (LV) dysfunction.
  - If setting of hypertension or left-sided valve disease, BCPS should be used with caution as it may increase LV end-diastolic pressure.
- Indications for BCPS include both:
  - heart failure indications (RV end-diastolic volume > 250 mL/m2, RV ejection fraction < 25%, D-shaped left ventricle, post-repair right atrial pressure to left atrial pressure ratio > 1.5:1, and post-repair cardiac output depression)
  - and non-heart-failure indications (complex TV repair tension reduction and post-repair TV stenosis with a mean gradient > 8-10 mm Hg).
- BCPS contraindications :
  - related to pulmonary hypertension include a mean pulmonary artery pressure > 20 mm Hg, pulmonary arteriolar resistance > 4 Woods units, and elevated left heart pressures (LV end diastolic pressure or left atrial pressure > 12 mm Hg).

- Another alternative to the BCPS is atrial septal fenestration by either subtotal atrial septal defect closure or by leaving a patent foramen oval open.
- This is applied more to infants and less often in the adult setting due to the risk of left heart dysfunction and risk of paradoxical embolism from right-to-left shunting.
- Intraoperative paroxysmal atrial fibrillation or atrial flutter can be managed with a modified right-sided maze or cavo-tricuspid isthmus ablation using either cryoablation or radiofrequency ablation .

- If atrial fibrillation is best approached with a bi-atrial maze.
- cardiac transplantation may be indicated in patients following single ventricle management strategies in the neonatal period.

For more reading :

1= "Myung Park, Mehrdad Salamat. "Park's Pediatric Cardiology for Practitioners "." Seventh Edition". (2020).pages :204-207 ; "

2= Yuan, S.-M. (2017). Ebstein's Anomaly: Genetics, Clinical Manifestations, and Management. Pediatrics & Neonatology, 58(3), 211–215.

Chapter 5 : Tetralogy of Fallot

I. INTRODUCTION:

- Tetralogy of Fallot (TOF) is the most common form of congenital cyanotic heart disease, occurring in approximately 4 to 5 per 100 000 live births, and represents 7%-10% of all congenital heart defects.
- TOF is often thought of in terms of the tetrad of anomalies (**Figure 4**) :
  - pulmonary stenosis,
  - ventricular septal defect (VSD),
  - aorta overriding the ventricular septum,
  - and right ventricular hypertrophy
- There are several variants of TOF as well, which manifest other abnormal features and are discussed in the following review.
- Left untreated, patients with TOF have a 50%, 5- 10 year survival, with mortality related to hypoxemia, endocarditis, brain abscesses, or cerebral vascular accident. Longevity beyond the fourth decade of life in unrepaired or palliated TOF is rare.
- Forms anatomic :
  a. Tetralogy of Fallot with pulmonary stenosis
  b. Tetralogy of Fallot with pulmonary atresia (PA)
  c. Tetralogy of Fallot with Absent Pulmonary Valve
  d. Tetralogy of Fallot with Complete Atrioventricular (AV) canal

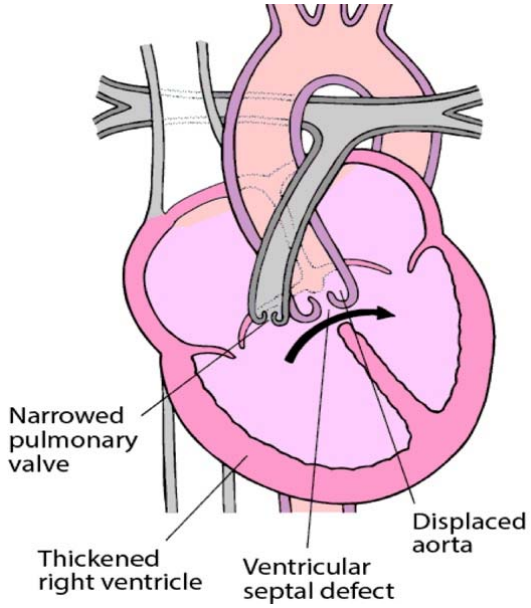

Figure 4 :Tetralogy of Fallot with pulmonary stenosis views :

- pulmonary stenosis,
- ventricular septal defect (VSD),
- aorta overriding the ventricular septum,
- and right ventricular hypertrophy

(source : https://www.msdmanuals.com/home/quick-facts-children-s-health-issues/birth-defects-of-the-heart/tetralogy-of-fallot)

II. Diagnosis :

a. Clinical manifestations and diagnostic :

- varies depending on the severity of the obstruction of blood flow to the lungs :
  - A heart murmur is audible at birth.
  - Most patients are symptomatic with cyanosis at birth or shortly thereafter.
  - Dyspnea on exertion, squatting, or hypoxic spells develop later, even in mildly cyanotic infants
  - Occasional infants with acyanotic TOF may be asymptomatic or may show signs of CHF from a large left-to-right ventricular shunt.
- Physical Examination :
  - Varying degrees of cyanosis, tachypnea, and clubbing (in older infants and children) are present.
  - An RV tap along the left sternal border and a systolic thrill at the upper and mid-left sternal borders are commonly present
  - An ejection click that originates in the aorta may be audible.
  - The S2 is usually single because the pulmonary component is too soft to be heard.
  - A long, loud (grade 3 to 5 of 6) ejection-type systolic murmur is heard at the mid and upper left sternal borders. This murmur originates from the PS but may be easily confused with the holosystolic regurgitant murmur of a VSD.
  - The more severe the obstruction of the RVOT, the shorter and softer the systolic murmur.

- In the acyanotic form, a long systolic murmur, resulting from VSD and infundibular stenosis, is audible along the entire left sternal border, and cyanosis is absent. Thus, auscultatory findings resemble those of a small-shunt VSD (but, unlike VSD, the ECG shows RVH or BVH).

b. Investigations :

- chest x-ray :
  - Cyanotic Tetralogy of Fallot: The heart size is normal or smaller than normal, and pulmonary vascular markings are decreased. “Black” lung fields are seen in TOF with pulmonary atresia.
  - A concave main PA segment with an upturned apex (i.e., “boot-shaped” heart) is characteristic
  - RA enlargement and right aortic arch may be present.
  - If Acyanotic Tetralogy of Fallot: Radiographic findings of acyanotic TOF are indistinguishable from those of a small to moderate VSD (but patients with TOF have RVH rather than LVH on the ECG).
- electrocardiogram :
  - will demonstrate right axis deviation and prominent right ventricular forces,
  - with large R waves in the anterior precordial leads
  - and large S waves in the lateral precordial leads .
  - Although the electrocardiogram is similar to that of a normal newborn, the right ventricular hypertrophy and right axis deviation will not normalize in a patient with tetralogy of Fallot.
- Echocardiography :
  - It is the gold standard for diagnosis of TOF and associated anomalies.

- Doppler :
  - Evaluate severity
  - The size, confluence, and proximal branching of the pulmonary arteries, the presence or absence of a PDA or MAPCAs.
  - Furthermore, determination of an atrial septal defect, anomalous pulmonary venous return, systemic venous anomalies, or other unusual features may be seen.
- Cardiac catheterization is not routinely performed in “classic” cases of TOF :
  - due to the high sensitivity and specificity of echocardiographic images.
- CT angiography or MRI as a diagnostic modality has gained acceptance in many centers.

c. Hyper cyanotic spells The hyperchaotic spell :

- Is characterized by a sudden and striking decrease in the saturation of oxygen due to acute and complete, or near complete, obstruction of the sub-pulmonary outflow tract.
- Not all patients with tetralogy of Fallot will have hyperchaotic spells.
- typically begin to occur at approximately a couple months of age at times of agitation or decreased hydration, both of which exacerbate the dynamic infundibular obstruction.
- The murmur produced by the muscular obstruction is absent during a true spell, due to nearly absent antegrade flow across the right ventricular outflow tract.
- Patients become severely cyanotic, hyperpnea, and lethargic.

- With the development of metabolic acidosis, there is an increase in pulmonary vascular resistance, with a decrease in systemic vascular resistance.
- Cardiac output becomes compromised due to myocardial ischemia. Impending collapse and death can ensue.

III. Management :

- Is determined by the degree and type of sub-pulmonary obstruction, in combination with the preference of the Centre for the timing of surgical intervention.
- on the severity of obstruction within the sub-pulmonary outflow tract, an infusion of prostaglandin may be initiated to preserve ductal patency, and provide a stable source of flow of blood to the lungs.
- Patients who require such an infusion will most likely require surgical intervention prior to discharge from the hospital.
- For those patients who have adequate forward flow through the sub-pulmonary outflow tract after ductal closure, management consists of close follow-up until a complete repair is performed.
- The intervention is routinely done at 3 -6 months
- Some centers will perform complete repairs in all neonates , others will palliate symptomatic neonates, and perform a complete repair in all patients at the age of 4 to 6 months.

A. Medical :

1. Newborns and Infants with Severe Cyanosis

- Infants with severe RVOT , obstruction can become significantly cyanotic when PDA closes , the following should be instituted immediately :
  a. 100% oxygen
  b. Depending on the severity of the clinical condition, the patient likely needs to be intubated and temporarily supported with mechanical ventilation.
  c. Intravascular access (preferably a central venous access).
  d. Appropriate sedation must be carefully planned.
  e. Prostaglandin E1 (alprostadil) infusion :
     - Start at a higher dose of 0.1–0.2 mg/kg/min and once the ductus arteriosus is patent can wean to a lower dose of 0.01–0.05 mg/kg/min.
  f. If there is metabolic acidosis, administer sodium bicarbonate 1–2 meq/kg IV.
  g. If suspected hypovolemia, crystalloid fluid bolus administration 5–15 ml/kg IV.
  h. Optimize electrolytes, including ionized calcium levels.

2. Management of the hyper-cyanotic spell :

- It maneuvers to re-establish adequate balance between the systemic and pulmonary flows.
- Treatment must focus on decreasing pulmonary, and increasing systemic, vascular resistance, hence promoting left to right flow across the ventricular septal defect and into the sub-pulmonary outlet.
- Parents at home with a child suffering such spells are taught to place their child in the knee-to-chest position in an effort to increase systemic vascular resistance and promote systemic venous return to the right heart ,this will

theoretically increase intracardiac shunting from left-to-right across the interventricular communication, as well as increase the preload of the right ventricle , and emergency services should be contacted immediately.

- If the patient remains hyper-cyanotic medical measures:
  - He/she should be paralyzed and intubated, with phenylephrine administered intravenously to increase systemic vascular resistance.
- cyanotic spells "Tet-spells" In the current era, occurrence of "Tet-spells" can be an indication for surgical repair, prior to surgical correction, the following should be considered during an acute episode :
  a. 100% Oxygen.
  b. Positioning- knee-chest position for infants or squatting for toddlers.
  c. Sedation with (decrease the release of catecholamines) :
     - morphine 0.1 mg/kg (IM, IV, SC).
     - midazolam 0.05–0.1 mg/kg (IV, intranasal or intrarectal) .
     - fentanyl 1–2 mg/kg (IV).
     - or dexmedetomidine 0.5 –1 mcg/kg (IV).
  d. Beta-blockers: (used in small doses in the chronic care of patients deemed to be at risk for spells in an effort to minimize the infundibular spasm responsible for the episodes) :
     - Esmolol is a good choice given the possibility of titration between 50 and 200 mg/kg/ min (IV).
     - Intravenous Propranolol is a good alternative .
  e. Phenylephrine (Neo-synephrine®) :
     - 2–5 mg/kg IV every 10–15 min, followed by a continuous infusion 0.1–5 mg/kg/min as needed.

- Alternatively may use vasopressin. Vasoconstrictors are indicated in spells that appear refractory to sedation, volume expansion and beta-blockers.

f. Crystalloid or red blood cell administration 10–15 ml/kg IV.

g. Sodium bicarbonate 1–2 meq/kg IV.

h. Intubation with sedation and muscle relaxation if persistent or refractory spell.

i. If all of the above fail, extracorporeal membrane oxygenation (ECMO) support and emergency Blalock Taussig shunt (BT shunt) should be considered.

- Once a patient requires prophylaxis by betablockade, surgical referral should occur to prevent the potential tragic and unpredictable outcome of a hyper-cyanotic spell

B. Interventional treatment:

1- Balloon dilatation of the RVOT and pulmonary valve, although not widely practiced, has been attempted to delay repair for several months

2- Palliative Shunt Procedures: Shunt procedures are performed to increase PBF , and indicated in :

a. Neonates with TOF and pulmonary atresia .

b. Infants with hypoplastic pulmonary annulus.

c. Children with hypoplastic PAs .

d. Unfavorable coronary artery anatomy .

e. Infants younger than 3 to 4 months old who have medically unmanageable hypoxic spells .

f. Infants weighing less than 2.5 kg.

3- Complete Repair Surgery Indications :

- ✓ asymptomatic patients : undergo an elective one-stage surgical repair during early infancy, usually between 3 and 6 months of age.
- ✓ For symptomatic patients : two approaches are utilized depending on the institutional preference, complete repair vs. a two-stage repair (initial shunt placement followed by complete repair)
- ✓ Situations where surgical intervention needs to be planned urgently include:
  a. Worsening hypoxemia , related to progressive infundibular and valvular obstruction with the saturation less than 80%.
  b. Severe cyanotic spell as discussed above.
  c. Dependence on prostaglandin from early neonatal period (more likely to be observed in TOF with pulmonary atresia).
- ✓ Mildly cyanotic infants who have had previous shunt surgery may have total repair 1 to 2 years after the shunt operation.
- ✓ Neonates born with tetralogy of Fallot with pulmonary atresia who do not have stable flow to the lungs through collateral arteries will require surgical intervention prior to discharge from the hospital.
- ✓ In newborns with tetralogy of Fallot with absent pulmonary valve, surgical repair may be required prior to initial discharge from hospital if obstruction to the airways is a prominent symptom.
- ✓ In cases with tetralogy of Fallot with atrioventricular septal defect, complete repair is usually performed later in life compared to patients with uncomplicated tetralogy of Fallot, typically between the ages of 6 and 12 months.
- ✓ If significantly cyanotic at birth, most centers still opt for initial palliation rather than complete repair in these patients.

- ✓ Patients with coronary artery anomalies may have an early surgery at the same time as those without anomalous coronary arteries.

c. Postoperative Management :

- In some centers, most toddlers and children return to the cardiac ICU already extubated.
- Most patients experience a relatively uneventful postoperative course, some of the most frequent postoperative problems encountered during the first 12–48 h especially in neonates and infants, are the following:

1 Low cardiac output syndrome (LCOS) due to:

a) Right ventricular diastolic and systolic dysfunction.

b) Left ventricular dysfunction (less frequently).

c) Uncontrolled arrhythmias, e.g., junctional ectopic tachycardia (JET), atrial ectopic tachycardia .

d) Residual VSD resulting from either significant VSD patch leak or previously undiagnosed VSD.

2 Arrhythmias:

- Most frequent types of hemodynamically significant arrhythmias encountered after TOF repair include:

a. Junctional Ectopic Tachycardia (5–20%)

b. Atrial Ectopic Tachycardia

c. Re-entry type supraventricular tachycardia (Re-SVT) – Be aware that due to the frequent presence of postoperative right bundle branch block, Re-SVT may resemble ventricular tachycardia.

d. Complete AV Block (<5%) – Mostly transient but occasionally permanent.

IV. Form anatomo-clinical :

A. TETRALOGY OF FALLOT WITH PULMONARY ATRESIA (PULMONARY ATRESIA AND VENTRICULAR SEPTAL DEFECT) :

1. Diagnosis :

- These patients are cyanotic at birth.
- The degree of cyanosis depends on whether the ductus is patent and how extensive the systemic collateral arteries are.
- Usually a heart murmur cannot be heard.
- A faint continuous murmur may be audible from the PDA or collaterals.
- The S2 is loud and single , a systolic click is occasionally present.
- The ECG shows RAD and RVH.
- Chest radiography shows a normal heart size. The heart often appears as a boot-shaped silhouette , and the pulmonary vascularity is usually markedly decreased (i.e., “black” lung field).
- Echo studies is the gold standard for the diagnosis of TOf with pulmonary atresia and associated anomalies .
- Cardiac catheterization and angiograms are sometimes needed for a complete delineation of the collaterals.
- Alternatively, MRI or CT angiography (CTA) is performed for complete anatomic delineation of the aortic collaterals and PA branches.

2. Management :

a. Medical:

- PGE1 infusion :
  - should be started as soon as the diagnosis is made or suspected to keep the ductus open for additional studies and to prepare for surgery.
  - The starting dose of alprostadil solution is 0.05 to 0.1 μg/kg/min.
  - When the desired effect is obtained, the dosage should be gradually reduced to 0.01 μg/kg/min.
- Emergency cardiac catheterization or MRI or CTA is usually needed to delineate the anatomy of the PAs and systemic arterial collaterals.

b. Surgical :

- A connection must be established between the RV and true PA as early in life as possible.
- This may make tiny central PAs to enlarge rapidly during the first year of life with improved arborization (distribution) of the PAs with concurrent development of alveolar units.
- To achieve this goal, a central shunt procedure, or other proceed with an RV-to-PA connection could be used .

B. TETRALOGY OF FALLOT WITH ABSENT PULMONARY VALVE :

1. Clinical Manifestations :

- Mild cyanosis may be present as a result of a bidirectional shunt during the newborn period when the PVR is relatively high.
- Cyanosis disappears, and signs of CHF may develop, after the newborn period.

- Respiratory symptoms vary greatly:
  - Ranging from neonates with severe respiratory compromise, those with wheezing or frequent respiratory infection, and those with no respiratory symptoms at all.
  - At times there may be significant hypoxia secondary to airway compression by the dilated main PA, which would respond to prone positioning of the infant.
- A to-and-fro murmur (with "sawing-wood" sound) at the upper and mid-left sternal borders is a characteristic auscultatory finding of the condition.
- This murmur occurs because of mild PS and free PR.
- The S2 is loud and single. The RV hyperactivity is palpable.

2. Paraclinical :

- The ECG shows RAD and RVH.
- Chest radiography images :
  - Reveal a noticeably dilated main PA and hilar PAs.
  - The heart size is either normal or mildly enlarged, and pulmonary vascular markings may be slightly increased.
  - The lung fields may show hyperinflated areas, representing partial airway obstruction .
- Echo studies is the gold standard for the diagnosis of TOf with pulmonary atresia and associated anomalies .

3. Management :

a) Medical :

- In the past, medical management was preferred because of poor surgical results in newborns; however, the mortality rate of medical management is much higher than for surgical management.
- After the pulmonary symptoms appear, neither surgical nor medical management has good results.

b) Surgical :

- Symptomatic neonates should have corrective surgery on an urgent basis.
- Even asymptomatic child should have elective surgery in the first 3 to 6 months of life.
- Primary Repair: Complete primary repair is the procedure of choice.

➢ For more reading :

1= Wise-Faberowski, L., Asija, R., & McElhinney, D. B. (2018). Tetralogy of Fallot: Everything You Wanted to Know but Were Afraid to Ask. Pediatric Anesthesia. doi:10.1111/pan.13569

2= Bailliard, F., & Anderson, R. H. (2009). Tetralogy of Fallot. Orphanet Journal of Rare Diseases, 4(1), 2. doi:10.1186/1750-1172-4-2

3= Chrysostomou, C., Domnina, Y. A., Kazmerski, T. M., Muñoz, R., & Morell, V. O. (2009). Tetralogy of Fallot. Critical Care of Children with Heart Disease, 199–206. doi:10.1007/978-1-84882-262-7_19

4 = "Myung Park, Mehrdad Salamat. "Park's Pediatric Cardiology for Practitioners "." Seventh Edition". (2020).pages :175-186 ; "

Chapter 6 : COMPLETE TRANSPOSITION OF THE GREAT ARTERIES :

I. Introduction :

- Complete transposition of the great arteries (TGA) is the most common cyanotic CHD presenting in newborn period and comprises approximately 5% of all CHDs.
- In this condition, the aorta arises from the right ventricle (RV), and the pulmonary artery (PA) arises from the left ventricle (LV). As the result, the normal antero-posterior relationship of the great arteries is reversed, so that the aorta is anterior to the PA (transposition), but the aorta usually remains to the right of the PA (**Figure 5**).
- The atria and ventricles are in normal relationship. The coronary arteries arise from the aorta, as in a normal heart.

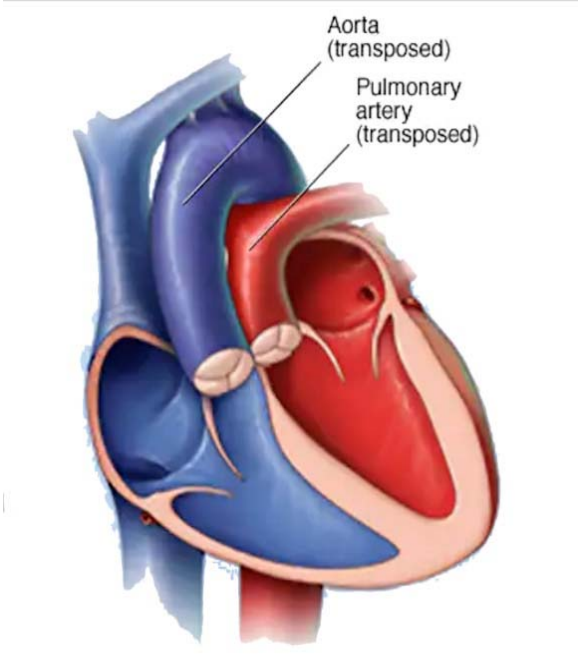

Figure 5 : TRANSPOSITION OF THE GREAT ARTERIES :

- the aorta arises from the right ventricle (RV)
- and the pulmonary artery (PA) arises from the left ventricle (LV).

(source : https://www.mayoclinic.org/diseases-conditions/transposition-of-the-great-arteries/symptoms-causes/syc-2035058)

II. Clinical Manifestations :

a. History

- History of cyanosis from birth is always present. Often the solely sign , should be screened .
- Cyanotic spell .
- Signs of congestive heart failure (CHF) with dyspnea and feeding difficulties can develop during the newborn period .

b. Physical Examination

- Moderate to severe cyanosis is present, especially in large male newborns, such infants are tachypneic but without retraction unless CHF supervenes.
- The S2 is single and loud , no heart murmur is heard in infants with an intact ventricular septum.
- An early or holosystolic murmur of VSD may be audible in less cyanotic infants with associated VSD.
- A soft mid-systolic murmur of PS (LVOT obstruction) may be audible.
- If CHF supervenes, hepatomegaly and dyspnea develop.

III. Paraclinical :

a. Laboratory Studies :

- Hyperoxia Test : severe arterial hypoxemia, usually with acidosis, is present , hypoxemia does not respond to oxygen inhalation.
- Hypoglycemia and hypocalcemia are occasionally present.

b. Electrocardiography :

- Right ventricular hypertrophy (RVH) is usually present after the first few days of life.

- The QRS voltages and the QRS axis may be normal in many newborns with the defect.
- After 3 days of life, an upright T wave in V1 may be the only abnormality suggestive of RVH.
- Biventricular hypertrophy (BVH) may be present in infants with large VSD, PDA, or pulmonary vascular obstructive disease because all of these conditions produce an additional left ventricular hypertrophy (LVH).
- Occasionally, right atrial hypertrophy (RAH) is present.

c. Radiography :

- Cardiomegaly with increased pulmonary vascularity is typically present.
- An egg-shaped cardiac silhouette with a narrow, superior mediastinum is characteristic .

d. Echocardiography Two-dimensional (2D) echo and color-flow Doppler studies usually provide all the anatomic and functional information needed for the management of infants with TGA.

e. Other Studies

- Cardiac catheterization is performed only for the purpose of balloon atrial septostomy to improve mixing at the atrial level. Rarely, it is performed to look for associated anomalies such as abnormal coronary artery, collateral circulation, or a small aortic isthmus.

IV. Evolution :

- Progressive hypoxia, acidosis, and heart failure result in death in the newborn period.

- Without surgical intervention, death occurs in 90% of patients before they reach 6 months of age.
- Infants with an intact ventricular septum are the sickest group but demonstrate the most dramatic improvement after balloon atrial septostomy.
- Infants with large ASD and large VSD are the least cyanotic group but the most likely to develop CHF and pulmonary vascular obstructive disease.
- Many infants with TGA and a large VSD develop moderate pulmonary vascular obstructive disease by 3 to 4 months of age ,where surgical procedures are recommended before this age.
- Infants with a significant PDA are similar to those with a large VSD in terms of their development of CHF and pulmonary vascular obstructive disease.
- The combination of VSD and PS allows considerably longer survival without surgery because the pulmonary vascular bed is protected from developing pulmonary hypertension, but this combination carries a high surgical risk for correction

V. Management :

A.Medical :

1- The following measures should be carried out to stabilize the patient before an emergency cardiac catheterization (if performed) or a surgical procedure is carried out:

- Oxygen should be administered for severe hypoxia:.
- Arterial blood gases and pH : correction of metabolic acidosis if present .
- Hypoglycemia and hypocalcemia it should be treated .
- PGE1 infusion :

- it improves arterial oxygen saturation by reopening the ductus .
- This should be continued throughout the cardiac catheterization or until the time of surgery.

2- CHF may be treated with diuretics (and angiotensin-converting enzyme [ACE] inhibitors).

3- Before surgery:

- A cardiac catheterization and a balloon atrial septostomy are often carried out to have some flexibility in planning surgery.
- If adequate interatrial communication exists and the anatomic diagnosis of TGA is clear by echo examination, the patient may go to surgery without cardiac catheterization or the balloon atrial septostomy.
- The need for the balloon septostomy may be determined :
  - By inadequate atrial mixing through the PFO (evidenced with a high Doppler flow velocity of >1 m/sec, significant hypoxia, or metabolic acidosis)
  - Or lack of readiness for surgical intervention.
  - An increase in the oxygen saturation of 10% or more and a minimal interatrial pressure gradient are considered satisfactory results of the procedure.

4- Cranial magnetic resonance imaging (MRI) is usually performed to rule out associated brain abnormalities preoperatively.

B. Surgical :

- No palliative procedure is performed unless arterial switch operation (ASO) cannot be performed early in life.

- Historically, definitive surgeries performed for TGA were procedures that switched right- and left-sided blood at three levels:
  - The atrial level .
  - The ventricular level .
  - And the great artery level (ASO).
- At this time, ASO is clearly the procedure of choice and intra-atrial repair surgeries are very rarely performed only under unusual situations.

C. Postoperative Follow-up

- A regular follow-up is needed to detect possible complications , such as :
  - stenosis of the PA or aorta in the supravalvular regions,
  - coronary artery obstruction with myocardial ischemia or infarction,
  - ventricular dysfunction, arrhythmias, and semilunar valve regurgitation.
- These complications are, for the most part, hemodynamically insignificant or infrequent.
- A periodic follow-up is recommended with :
  - ECG,
  - echo,
  - exercise stress test (in older children),
  - MRI or computed tomography (CT), or coronary angiography.

➢ For more reading :

1. Warnes, C. A. (2006). *Transposition of the Great Arteries. Circulation, 114(24), 2699–2709.*
2. Martins, P., & Castela, E. (2008). Transposition of the great arteries. Orphanet Journal of Rare Diseases, 3(1), 27.
3. *"Myung Park, Mehrdad Salamat. "Park's Pediatric Cardiology for Practitioners "." Seventh Edition". (2020).pages :* 110 , 164 -171;"

Chapter 7 : Coarctation of the aorta

I. Introduction :

- Coarctation of the aorta is defined as a congenital cardiac anomaly consisting of a constricted aortic segment comprising localized medial thickening with some infoldings of the media and superimposed neointimal tissue (**Figure 6**).
- The localized constriction may form a shelf-like structure with an eccentric opening or it may be a membranous curtain-like structure with a central or eccentric opening.

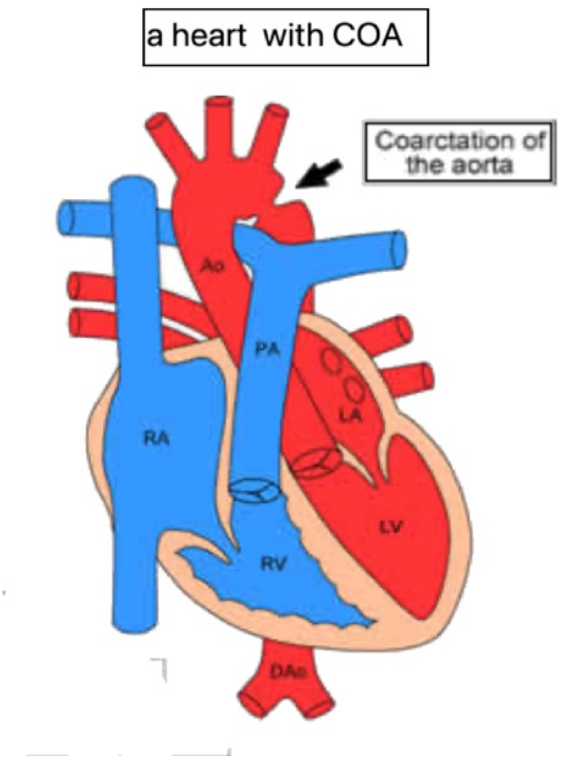

Figure 6 : Coarctation of the aorta :

- Showing a constricted aortic segment

(source : https://www.nationwidechildrens.org/conditions/coarctation-of-the-aorta)

II. Diagnosis :

A. Clinical :

- In clinical practice, it is observed that many patients are undiagnosed due to the lack of a detailed clinical examination, since measuring the pulse of upper and lower limbs is not routine.
- It is estimated that approximately more than 60% of newborns with aortic coarctation are not diagnosed before hospital discharge ,the peripheral pulses may be week as result of congestive heart failure
- Poor feeding, dyspnea and poor weight gain or acute sign of cardiogenic shock may develop in the few first weeks .
- The newborn may be symptomatic as result of incomplete obliteration of the aortic with patent ductus.
- The signs and symptoms in children vary according to the type of clinical manifestation ,The most frequent are :
  - Hypertension , heart murmurs .
  - Headache , Epistaxis .
  - and fatigue in the legs .
- Most often, the coarctation is identified because of a murmur or hypertension detected on routine examination:
  - Palpation of the brachial and femoral artery pulses simultaneously will reveal decreased and delayed or absent femoral pulses .
  - Blood pressure in both arms and one leg must be determined; Arterial hypertension in the upper limbs , and a pressure difference of more than 20 mm Hg in favor of the arms may be considered evidence for AC .
  - A thrill is usually felt in the suprasternal notch.

- The first and second heart sounds are usually normal in isolated aortic coarctation.
- Possible ejection systolic click be heard at the apex and left mid and right upper sternal borders; which is not changed with respiration.
- An ejection systolic murmur may be heard best at the left or right upper sternal borders, but is usually heard best over the back in the left interscapular region.
- Sometimes, a faint continuous murmur may be heard in the left interscapular region, secondary to continuous flow in the coarcted segment or on the back .

B. Investigations :

1- Chest radiograph :

- possible significant cardiomegaly or the heart size may be normal.
- Rib-notching secondary to collateral vessels may also be seen.

2- Electrocardiogram :

- may be normal or it may show LVH.
- Sometimes the LVH may be manifested by increased S waves in leads V5 and V6

3- Echocardiography-Doppler :

- Studies Echocardiographic imaging usually reveals the coarctation in suprasternal notch.
- Two-dimensional echocardiographic views increased Doppler flow velocity in the descending aorta by continuous wave Doppler and a demonstrable jump in velocity at the coarcted segment by pulsed-Doppler technique are usually present.

- Calculate Instantaneous peak pressure gradients across the AC .

4- MRI/MR angiography These studies are useful in demonstrating the anatomy clearly :

- If the intervention is indicates, usually go ahead with catheterization and angiography, and perform interventional procedures.
- If the data are not clear, then MRI or MR angiography are performed to define the problem further

5- Cardiac catheterization and selective cineangiography :

- not required for diagnosis, but helpful in demonstrating the anatomic nature of the aortic obstruction , assessing the extent of collateral circulation, determining the presence and severity of associated lesions, and more recently as a prerequisite to the consideration of transcatheter intervention.

6- Selective aortic root or aortic arch angiography is necessary to clearly demonstrate the aortic narrowing.

7- Aortography is useful in demonstrating the type of AC , extent of collateral circulation, the size of ductus arteriosus, if patent, and presence and degree of hypoplasia of transverse aortic arch and aortic isthmus. If thoracic coarctation is not demonstrated despite clinical features of coarctation or if neurofibromatosis is suspected, abdominal aortography may be needed to demonstrate (or exclude) abdominal coarctation.

III. Treatment :

- Significant hypertension or congestive heart failure are indications of intervention.
- Surgical relief of the aortic obstruction and catheter interventional techniques (balloon angioplasty and stents) are available alternatives.
- Asymptomatic patients should undergo the procedure electively. If neither hypertension nor heart failure are present, elective surgical or balloon therapy between the ages of 2 and 5 years is suggested.
- Waiting beyond 5 years of age is not advisable because of evidence for residual hypertension if the aortic obstruction is relieved after 5 years of age

a. Medical management at initial presentation :

- In symptomatic neonates :
  - PGE1 infusion should be started to promote ductal patency and establish flow to the descending aorta and the kidneys
- In patients with congestive heart failure , initial treatment, consisting of Intensive anti-congestive measures with :
  - short-acting inotropic agents (e.g., dopamine, dobutamine)
  - diuretics, and oxygen should be started.
- If hypertension (rather than heart failure) is the clinical problem:
  - it is better to relieve the aortic obstruction promptly rather than attempting to treat hypertension with antihypertensive medications, although some clinicians use such an approach.
- Metabolic disturbances should be recognized and treated promptly

- When the patient is stabilized, either surgical repair or balloon procedure should be performed because the improvement from anti-congestive measures is usually temporary .

b. Percutaneous intervention

- Balloon angioplasty is done actually for recurrent re-coarctation after surgery or native coarctation with very good outcomes
- It's done as choice rather that alternative option
- The use of stent with balloon angioplasty improve and reduce residual pressure gradient and diminish the incidence of aneurysm formation

c. Surgical :

- Indications and Timing :
  - If CHF or circulatory shock develops early in life, surgical repair should be performed on an urgent basis. a short period of medical treatment, as described earlier, improves the patient's condition before surgery.
  - If there is a large associated VSD, surgery may be performed:

➢ For more reading :

1. Rao, P. S. (2005). *Coarctation of the aorta. Current Cardiology Reports, 7(6), 425–434.*
2. Cangussú, L. R., Lopes, M. R., & Barbosa, R. H. de A. (2019). *The importance of the early diagnosis of aorta coarctation. Revista Da Associação Médica Brasileira, 65(2), 240–245.*
3. "Myung Park, Mehrdad Salamat; "Park's Pediatric Cardiology for Practitioners "; " Seventh Edition"; (2020);pages :152-157 ; "

Chapter 8 : Atrial Septal Defect

I. Introduction :

- Atrial septal defects (ASD) are considered one of the most common congenital heart defects (**Figure 7**) .
- In may occur as isolated anomaly or as associated lesions .
- Atrial septal defects are among the most common types of congenital heart disease that may go undiagnosed in childhood and may initially be found in adulthood , many patients are asymptomatic until the second to fourth decades of life.
- Adults with an atrial septal defect are often asymptomatic, but may present with nonspecific symptoms such as dyspnea on exertion or exercise intolerance.
- Pulmonary arterial hypertension and atrial arrhythmias may develop as a consequence of a longstanding unrepaired atrial septal defect
- Anatomy : There is fours types of ASD , the patent foramen ovale (PFO) do not produce significant shunt :
  - Secudum defect : the most commun type : present at the site of fossa ovalis
  - Primum defect: occur as part of atrioventricular canal
  - Sinus venosus defect : located at the entries of superior vena cava or inferior vena cava
  - Coronary sinus ASD: the defect is in the roof of the coronary sinus

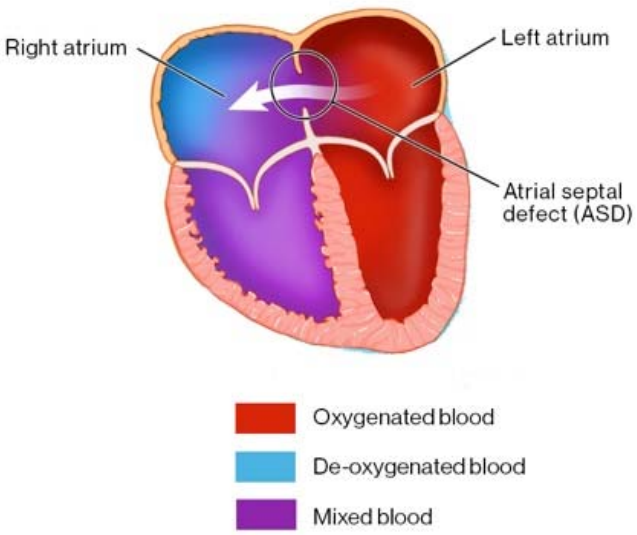

Figure 7 : Atrial Septal Defect :

- Showing left – to – right shunt

(source : https://www.mountsinai.org/locations/childrens-heart/conditions/atrial-septal-defect)

II. CLINICAL PRESENTATION :

- Most patients who present with a newly diagnosed unrepaired ASD are asymptomatic, and the finding is incidental.
- In a minority of patients, the history often reveals a gradual change in exercise capacity, commonly reported as subtle, and occasionally overt, dyspnea on exertion.
- Typically, a patient may describe this change occurring over the preceding months to years; however, if PAH is present, this change can occur more abruptly, on the order of weeks to months.
- Less frequently : palpitations ,with patients developed an occult atrial arrhythmia, which is more common in the patient who presents at an older age.
- On physical examination, may find a soft systolic crescendo–decrescendo outflow tract murmur owing to increased flow across the pulmonary valve, accompanied by a fixed split in the S2 heart sound owing to delayed closure of the pulmonic valve.
- Dysmorphia and others malformation where ASD or other CHD should be searched :
  - Polydactyly , Cleft lip .
  - Tracheoesophageal fistula.
  - Hypertelorism, and hypospadias.
  - Ungual dysplasia , Hypertelorism.
  - webbing of the neck.
  - Kyphoscoliosis.
  - Other somatic anomalies.

- Genetic syndromes where ASD or other CHD should be searched :
  - Down's syndrome (mongolism).
  - Edwards' syndrome.
  - XXX syndrome.
  - Turner's syndrome.
  - Bonnevie-Ulrich syndrome .
  - Noonan's syndrome.
  - Holt-Oram syndrome.
  - Cleido-cranial dysplasia.
  - Deaf mutism.
  - Tracheo-oesophageal-fistula.
  - Cerebral sclerosis plus optic atrophy.
  - BBB syndrome.

III. INVESTIGATION AND ASSESSMENT:

- electrocardiogram :
  - Commonly demonstrate an incomplete right bundle branch block.
  - More specifically, in the presence of a secundum ASD right axis deviation
  - And crochetage (crochet-like hook) of the inferior lead R waves may be seen.
  - In primum ASD, incomplete right bundle branch block is more likely to occur in the presence of left axis deviation.
- Chest radiograph:
  - it is often normal.

- possible cardiomegaly and increased pulmonary vascularity

- Transthoracic echocardiogram
  - The preferred initial imaging test
- In most cases, a transesophageal echocardiogram (TEE) is not required to make the diagnosis of an ASD.
- Additionally, flow quantification on cardiac MRI may be used to evaluate Qp:Qs in the presence of a septal defect in adult patient .

IV. MEDICAL DECISION MAKING AND THERAPEUTIC CONSIDERATIONS

- Indications for Repair :
  - Small ASDs , under 8 mm, may spontaneously close in childhood .
  - larger defects may contribute to hemodynamic abnormalities and clinical symptoms if left unrepaired.
  - The decision to repair an ASD is based on clinical and anatomic information(size and location of the defect), magnitude of hemodynamic impact of the shunt, and the presence and degree of PAH.
  - Patients with decreased functional capacity caused by hemodynamically significant ASD's (moderate or large left-to-right shunts, a Qp:Qs of >1.5:1 and evidence of right heart volume overload in the absence of significant PAH) typically benefit from surgical or transcatheter closure of the ASD.
  - Asymptomatic patients with a significant left-to-right shunt (Qp : Qs of >1.5:1) and evidence of right heart enlargement also benefit from closure.

- If CHF does not respond to medical management, surgery is performed during infancy, again if device closure is considered inappropriate.
- High pulmonary vascular resistance (PVR) (i.e., >10 units/ m2, >7 units/m2 with vasodilators) may be a contraindication for surgery (or device closure).

- Contraindications for Repair :
  - Closure of an ASD is not recommended in patients with a clinically significant right-to-left shunt and those with severe PAH (PVR of >8 Wood units or irreversible pulmonary vascular occlusive disease, desaturated at rest).
  - If pulmonary artery pressure of less than two-thirds of the systemic arterial pressure, a PVR of less than two-thirds of the systemic resistance, or a positive response to pulmonary vasodilator testing may be considered for ASD closure, a fenestrated device is often considered in these cases to ensure that an adequate "popoff" is present so that if RA pressure rises above the LA pressure, cardiac output is conserved.
  - Relative contraindications to closure typically are regarded for percutaneous cases and include:
    - ✓ Defects larger than 36 mm
    - ✓ Inadequate margins and rims to safely anchor the device
    - ✓ And/or interference of the device with the atrioventricular valves or venous drainage.
- Interventional procedure:
  - Catheter delivered closure device has become a preferred method for 5 mm defect and more with significant left to right shunt, applicable only to secundum ASD with an adequate septal rim ,

- Surgery intervention:
  - Usually delayed until 2-5 years of age

➢ For more reading :

1- Bradley, E. A., & Zaidi, A. N. (2020). *Atrial Septal Defect. Cardiology Clinics.*

2- Cascos, A. S. (1972). *Genetics of Atrial Septal Defect. Archives of Disease in Childhood, 47(254), 581–588.*

3- "Myung Park, Mehrdad Salamat ; "Park's Pediatric Cardiology for Practitioners ";" Seventh Edition"; (2020);pages :120-124 ; "

Chapter 9 : Ventricular Septal Defects

I. Definition :

- Ventricular septal defects are the commonest congenital cardiac malformations.
- They can exist in isolation, but are also found as integral components of other cardiac anomalies, such as tetralogy of Fallot, double outlet right ventricle, or common arterial trunk.
- As yet, there is no agreement on how best to classify such defects, nor even on the curved surface that is taken to represent the defect.
- Definition of the defect :
  - the entity is described as an interventricular communication, rather than a ventricular septal defect , in many ways, interventricular communication is a better term (**Figure 8**).
- Despite advances Catheter-based therapy for VSD closure , many patients with small VSDs require only subacute bacterial endocarditis prophylaxis.
- Anatomy and classification , VSD may be classified as :
  - Membranous.
  - Inlet.
  - outlet (or infundibular).
  - muscular : mid-trabecular (or mid-muscular), anterior trabecular (or anterior muscular), posterior trabecular (or posterior muscular), or apical muscular defect

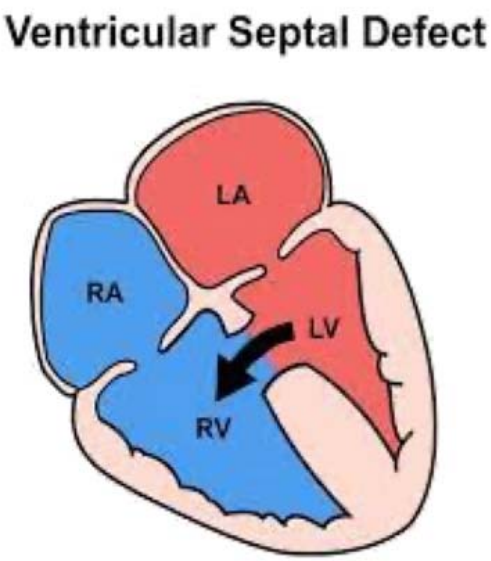

Figure 8 : Ventricular Septal Defects :

- showing Left- to- right shunt

(Source : https://www.drmani.com/ventricular-septal-defect-vsd/)

II. Diagnosis :

a. clinical presentation :

- it is related to its size, and the relationship between systemic and pulmonary vascular resistances .
- It is unusual to find symptoms at birth in infants born with communication between the ventricles.
- The symptoms typically become manifest between the ages of 4 and 8 weeks.
- Symptoms, however, will occur much earlier in infants born prematurely.
- Retardation of growth.
- Decreased exercise tolerance,
- Repeated pulmonary infections,
- And CHF are relatively common during infancy.
- Pulmonary hyperinflation , pulmonary oedema, and combined with compression of the airways, results in lower airway disease, and produces the symptoms :
  - wheezing, tachypnea, and respiratory distress.
  - Some times can be found cyanosis
- Complications :
  - a prolapse of the leaflets of the aortic valve, with ensuing aortic valvar incompetence .
  - muscular obstruction in either the right or left ventricular outflow tracts, or development of a fibrous ridge or shelf in the left ventricular outlet.
  - Eisenmenger reaction, and the development in some patients of bacterial endocarditis.

b. physical examination:

- The murmurs:
  - The murmurs are typically described as holosystolic or pansystolic.
  - The grade depends on the velocity of flow, the location is variable
  - Smaller defects are loudest and may have a thrill.
  - Muscular defects can be heard along the lower left sternal border and may vary in intensity as the defect size changes with muscular contraction throughout systole.
  - A systolic click can be associated.
- In the setting of low pulmonary vascular resistance:
  - larger defects have murmurs of constant quality and less commonly have an associated thrill , and a diastolic rumble at the apex.
  - on palpation of the precordium can find a laterally displaced impulse.
- An increased of the second heart sound is possible .
- Precordial hyperactivity in case of large shunt .
- If Large defects with no shunt and defects with Eisenmenger physiology and right-to-left shunt often do not have a VSD murmur .
- If associated with tricuspid regurgitation have a systolic murmur at the left lower or right lower sternal border.
- Defects with aortic insufficiency have a diastolic decrescendo murmur with the patient sitting and leaning forward.
- A widened pulse pressure may be present.
- Patients with Eisenmenger syndrome often are cyanotic with clubbing. They have a right ventricular heave on palpation of the precordium and a loud pulmonary component of the second heart sound. A VSD murmur may not be present.

- Sign of underlying etiologies: dysmorphia , malformation .

c. Investigations :

- The electrocardiogram :
  - can be normal if small ventricular septal defects.
  - could find to right-ventricular hypertrophy.
- Cross-sectional echocardiography :
  - It is the mainstay of modern diagnosis of ventricular septal defect.
- spectral and color doppler with two dimensional (2D) echocardiography greatly assists with identification and characterization of ventricular septal defects .
- The need for cardiac catheterization to obtain pressure data is indicate in advanced cases.
- Associated extracardiac defects should be explored
- Fetal diagnosis of ventricular septal defect is becoming increasingly frequent as imaging techniques improve.

III. Management :

a. Indications : Depends on symptoms :

- A small defect does not require medical management or likely require any intervention. Ills should be exanimated each year for restrictive VSD complication (aortic insufficiency, sub aortic stenosis and sub pulmonary stenosis)
- The medium and larger defects require various degrees of medical management and eventual surgical closure.
- If Congestive heart failure in the infant is treated with diuretics, and afterload reduction at times.

- If The patient with Eisenmenger syndrome needs very specialized care at centers, with trained personnel capable of managing myriad medical problems : Arrhythmias, endocarditis, gallstones, gouty arthritis, hemoptysis, pulmonary artery thrombosis, and symptomatic hypertrophic osteoarthropathy are frequently seen.
- Echocardiography and magnetic resonance imaging are used to evaluate right ventricular function.
- Cardiac catheterization is reserved for cases in which surgical or device closure is a question.
- Vasodilator therapy is an important adjunct to management and can provide functional improvement.
- Endocarditis is a lifelong risk in unoperated patients and those with residual defects. Proper prophylaxis and periodic follow-up are indicated.

b. Medical Management:

- When interventricular shunting is sufficient to prevent normal growth, producing difficulty in feeding, diaphoresis, or tachypnea,:
  - diuretics are the first line of medical palliation.
  - Attention if high dose's side effects, especially hypokalemia(Addition of spironolactone may be helpful to minimize potassium loss from diuretics)
- Afterload reduction may also be needed :
  - inhibitors of angiotensin converting enzyme.
- In general, if a patient is symptomatic and needs palliation, it is preferable to refer for urgent surgical correction .
- It is only patients with large muscular apical defects that are either difficult to see, or to access, from the right ventricular side, or those with the so-

called swiss-cheese septum presenting as neonates or infants, who require palliation by banding the pulmonary trunk.

- When referring patients for surgical correction, care must be taken to ensure that the shunting across the defect is from left-to-right, rather than right-to-left.
- No exercise restriction is required in the absence of pulmonary hypertension.

c. Surgical Closure :

- Location has been used as an indication for surgical closure
- Chamber enlargement is another measure of the degree of shunting and may indicate the need for closure.
- Catheterization can be used in some individuals to determine Qp:Qs and pulmonary artery pressure and resistance to help guide clinicians.
- Generally, a Qp:Qs of 1.5:1 to 2:1 or evidence of increased pulmonary arteriolar resistance is an indication for closure.
- Multiple “Swiss cheese” defects refractory to medical management may require a palliative pulmonary artery band procedure.
- Advances in surgical and bypass techniques and timing of surgical repair have decreased the morbidity associated with surgical closure.

d. Catheter Closure:

- Advancements in catheter techniques and devices are leading us into the era of percutaneous closure of VSDs.
- The benefits of avoiding bypass are intuitive, and the relative ease of placement makes this procedure ultimately attractive.

- For more reading :

1. Minette, M. S., & Sahn, D. J. (2006). *Ventricular Septal Defects. Circulation, 114(20), 2190–2197.* doi:10.1161/circulationaha.106.618124
2. Penny, D. J., & Vick, G. W. (2011). *Ventricular septal defect. The Lancet, 377(9771), 1103–1112.* doi:10.1016/s0140-6736(10)61339-6
3. Spicer, D. E., Hsu, H. H., Co-Vu, J., Anderson, R. H., & Fricker, F. J. (2014). *Ventricular septal defect. Orphanet Journal of Rare Diseases, 9(1).* doi:10.1186/s13023-014-0144-2
4. "Myung Park, Mehrdad Salamat;"Park's Pediatric Cardiology for Practitioners ";" Seventh Edition";(2020);pages :124-131 ; "

Chapter 10 : Patent ductus arteriosus

I. Introduction :

- Patent ductus arteriosus : is a vascular structure that connects the left pulmonary artery near its origin to the descending aorta just after the left subclavian artery; it is an essential fetal structure that closes spontaneously in about 90% of full-term infants during the first 48 hours of life(**Figure 9**).
- Persistent patency of the PDA beyond a few weeks is considered abnormal and is mainly encountered in neonates with ventilatory or circulatory abnormalities or in premature infants.
- Formally speaking, PDA is considered a form of congenital heart disease, defined as a persistent patency beyond the third month of life in term infants

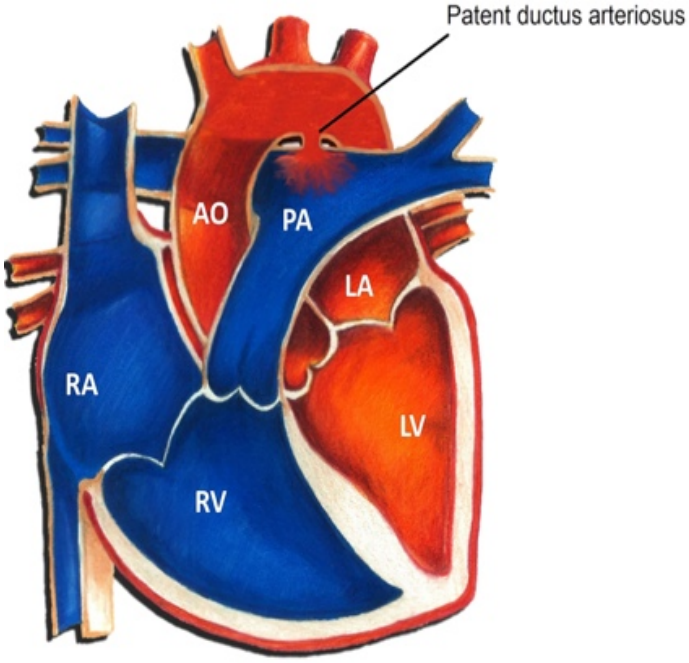

Figure 9: Patent ductus arteriosus showing :

- connection the left pulmonary artery to the descending aorta

(Source : https://www.heart.org/en/health-topics/congenital-heart-defects/about-congenital-heart-defects/patent-ductus-arteriosus-pda)

- it can be associated with various other congenital heart diseases. In the adult PDA is usually an isolated lesion.

II. Diagnosis :

a. Clinical :

- Varies from completely asymptomatic to congestive heart failure in infancy .
- Dictated largely by the size of the left-to-right shunt.
- Patients are usually asymptomatic when the ductus is small.
- Infants with moderate to large ductus arteriosus may present with
  - symptoms of congestive heart failure, including : poor feeding with failure to thrive, tachypnea, and diaphoresis.
  - a lower respiratory tract infection, atelectasis .
- Many PDAs are detected during evaluation of an asymptomatic heart murmur.
- Others are detected incidentally by echocardiograms performed for unrelated reasons in patients without symptoms or clinical manifestations.
- Some children may be healthy but report exercise intolerance or carry the diagnosis of asthma.
- Intolerance to respiratory infections : severe illness when they encounter respiratory infections.
- Although most children with PDAs, even with a moderate shunt and cardiomegaly, compensate well and remain asymptomatic during childhood, many years of chronic shunting may lead to symptoms of congestive heart failure and/or other complications in adulthood.
- Physical Examination :
  - Patients with tiny “silent” PDAs have normal cardiac examinations.
  - Tachycardia and tachypnea may be present in infants with CHF.

- A continuous murmur , often referred to as a “machinery” murmur (in large shunt, the precordium is hyperactive)
- Newborns, a murmur may not be present.
- A thrill may be present, and a diastolic rumble may be audible at the cardiac apex .
- In patients with high pulmonary vascular resistance, there may be no murmur during systole or diastole, as shunting may be minimal.
- A bounding peripheral pulses with wide pulse pressure (with elevated systolic pressure and lower diastolic pressure) are characteristic findings of a large PDA. With a small shunt, these findings do not occur.
- In infants, the pulse may be palpable in the palm.
- The patient with a large shunt and failure to thrive may be poorly nourished and have tachycardia and tachypnea with retractions.
- Except for in premature infants or other patients with underlying lung disease, rales are uncommon in children, even with a large shunt.

b. Investigations : findings are proportionate to the degree of shunting

- **Findings from the chest radiograph** :
  - May be completely normal,
  - or cardiomegaly , signs of left atrial and left ventricular enlargement ,and increased pulmonary vascular markings.
- **The electrocardiogram** :
  - smaller PDA shunts, the electrocardiogram is often completely normal.
  - larger shunts may demonstrate sinus tachycardia, left ventricular hypertrophy, and left atrial enlargement.
  - In the patient with a large ductus arteriosus and elevated pulmonary artery pressure, signs of biventricular hypertrophy may be present.

- **Echocardiography** :
  - Confirms the diagnosis , characterizes the anatomy and physiology of the PDA .
  - Detect the presence of any other associated cardiac defects.
  - In patients with small PDAs, the cardiac chambers are usually normal in size.
  - Mild left atrial and/or left ventricular enlargement may be present.
  - In patients with moderate or large PDAs, the left atrium and left ventricle are enlarged.

    ➔ color Doppler is very sensitive to PDA and employed to qualitatively estimate the degree of shunting.
- **Computed tomography scanning** :
  - can assess the degree of calcification in adults with PDA, which may be important if surgical therapy is considered.
- **Cardiac magnetic resonance imaging** :
  - may be used to noninvasively quantitate the shunt volume
  - but this generally does not add necessary information for clinical decision making.
  - One exception is that computed tomography scanning or cardiac magnetic resonance imaging may be useful to evaluate the anatomy if a ductus arteriosus aneurysm is suspected.
- **Cardiac Catheterization** :
  - Diagnostic cardiac catheterization is no longer necessary in making or confirming the diagnosis of PDA.
  - interventional catheterization for transcatheter PDA closure is currently the treatment of choice for most infants and children with DPA.

III. Treatment :

a. **Medical** : medical management in premature infants consists of pharmacologic closure using :

- Non-selective cyclo-oxygenase inhibitors :
  - Successful PDA closure in 75—93%
  - This efficacy has to be balanced with their significant potential adverse effects on other organ perfusion.
  - Moreover, indications for treatment remain a controversial topic, as 40% of PDAs close spontaneously, even in extremely-low-birthweight neonates.
  - Although efficacious for medical closure of the PDA in the premature infant, a careful assessment of risk/benefit is critical when deciding whether cyclo-oxygenase inhibitors should be used and this decision must be individualized to the particular patient.
- Acute medical treatment before definitive closure is usually not necessary.
- Those with symptoms, however, usually improve with a standard regimen of diuretics ,and after load reduction.
- Medical therapy for congestive heart failure due to PDA should be short term, until definitive surgical or transcatheter closure is performed.
- If patient with PDA and pulmonary vascular disease who are considered unacceptable candidate for definitive closure may be managed with **pulmonary vasodilating agents** :
  - chronic oxygen,
  - prostacyclin,
  - nifedipine,
  - bosentan, or sildenafil.

- The most recent guidelines for endocarditis prophylaxis in patients with isolated PDA no longer recommend pretreatment with antibiotics for dental work or other procedures likely to induce bacteremia.

b. Interventional treatment :

1. Nonsurgical Closure :
   - Currently, transcatheter closure is standard care beyond the neonatal period.
   - Advances in device and delivery system design are extending this option even to very small infants.
   - Indications and contraindications for device closure :
     a. Closure of PDA is definitely indicated in patients with :
        - CHF .
        - Failure to thrive.
        - Pulmonary over-circulation .
        - Enlargement of the LA and LV.
     b. It is reasonable to close a small PDA :
        - If the murmur of PDA is audible by standard auscultation techniques.
     c. There is controversy related to occlusion of so-called “silent ductus.”
     d. In patients with Eisenmenger syndrome or pulmonary vascular obstructive disease, the response of PVR to balloon occlusion or pulmonary vasodilator should be tested in cardiac catheterization laboratory :
        - If a good response is obtained, closure is advised.
        - If the response is poor or equivocal, closure may not be recommended.

e. The presence of severe pulmonary hypertension with irreversible pulmonary vascular obstructive disease is a contraindication to surgery.

2. Surgical Closure :

- Indications and Timing:

a. It is reserved to cases where a nonsurgical closure technique is not applicable.

b. An interventional device rather than surgery is used to close small ductus with no hemodynamic significance.

➢ For more reading :

1. Schneider, D. J. (2012). *The Patent Ductus Arteriosus in Term Infants, Children, and Adults. Seminars in Perinatology, 36(2), 146–153.*

2. Baruteau, A.-E., Hascoët, S., Baruteau, J., Boudjemline, Y., Lambert, V., Angel, C.-Y., … Pass, R. (2014). *Transcatheter closure of patent ductus arteriosus: Past, present and future. Archives of Cardiovascular Diseases, 107(2), 122–132.*

3 . "Myung Park, Mehrdad Salamat; "Park's Pediatric Cardiology for Practitioners ";" Seventh Edition"; (2020).pages :131-133 ; "

Chapter 11 : Patent Ductus Arteriosus in Preterm Neonates

I. Diagnosis :

1. The history :

- Is important in suspecting a significant PDA in a premature neonate.
- Typically, a premature infant with hyaline membrane disease shows some improvement during the first few days after birth.
- This is followed by an inability to wean the infant from the ventilator or a need to increase ventilator settings or oxygen requirements in 4- to 7-day-old premature infants.
- Episodes of apnea or bradycardia may be the initial sign of PDA in infants who are not on ventilators.

2. The physical examination :

- commonly reveals bounding peripheral pulses, a hyperactive precordium, and tachycardia with or without gallop rhythm.
- The classic continuous murmur at the left infraclavicular area or upper left sternal border is diagnostic, but the murmur may be only systolic and is difficult to hear in infants who are on ventilators.
- Premature infants who are fluid overloaded or retaining fluid may also present with findings of PDA as described earlier (hyperdynamic precordium, systolic ejection murmur, bounding pulses, and wide pulse pressures), requiring differentiation from PDA.

3. The ECG: It usually is normal but occasionally shows LVH.

4. Chest radiographs :

- show cardiomegaly in larger premature infants who are not intubated.
- The infant may have evidence of pulmonary edema or increased pulmonary vascular markings, but these may be difficult to assess in the presence of hyaline membrane disease.
- In infants who are intubated and on high ventilator settings, chest x-ray films may show the heart to be either of normal size or only mildly enlarged.

5. Echocardiographic and Doppler :

- Provide accurate anatomic and functional information.
- Show the following findings :
  - Ductal shunt pattern .
  - Estimation of PA pressures.
  - Perfusion status .
  - Hemodynamic significance of PDA : volume overload , Cavities sizes and function with left atrium-diameter/aortic route diameter ratio greater than 1,4 .

II. Management

- If symptomatic neonate , either pharmacologic or surgical closure is indicated.
- If a small PDA that have no symptoms , it should be followed medically for 6 months without surgical ligation because of the possibility of spontaneous closure.

1)Medical :

a. Fluid restriction to 120 mL/kg per day and a diuretic (e.g., chlorothiazide) :

- may be tried for 24 to 48 hours, but these regimens have a low success rate.
- Use of furosemide is not recommended because it is known to stimulate prostaglandin E2 synthesis and thus dilate the PDA.
- Digoxin is not used because it has little hemodynamic benefit and a high incidence of digitalis toxicity.

b. Pharmacologic closure of the PDA :

i. Indomethacin :

- It is prostaglandin synthetase inhibitor .
- Prostaglandins play a major role in maintaining ductal patency during fetal life.
- Many dosage regimens exist, and dose is dependent on postnatal age of the infant at time of first dose; one example is as follows.
  - The dose is given intravenously every 12 hours a total of 3 doses.
  - For infants less than 48 hours old, 0.2 mg/ kg is followed by 0.1 mg/kg times 2 is given .
  - For those who are 2 to 7 days old, 0.2 mg/kg times 3 is given .
  - for those who are more than 7 days old, 0.2 mg/kg followed by 0.25 mg/kg times 2 is given.
- Contraindications to the use of indomethacin include high blood urea nitrogen (>25 mg/dL) or creatinine (>1.8 mg/dL) levels, low platelet count (<80,000/mm3), bleeding tendency (including intracranial hemorrhage), necrotizing enterocolitis, and hyperbilirubinemia

ii. Ibuprofen,:

- another inhibitor of prostaglandin synthesis, has also been used in ductal closure in premature infants.
- A multicenter prospective study from Europe showed that intravenous ibuprofen (10 mg/kg, followed at 24-hour intervals by two doses of 5 mg/kg) starting on the third day of life was equally effective in closing the ductus in preterm newborns as indomethacin. Ibuprofen had a significantly lower incidence of oliguria, and it does not appear to have a deleterious effect on cerebral blood flow.
- Ibuprofen significantly reduces plasma concentrations of prostaglandin.

iii. Acetaminophen :

- recently was being used for PDA closure in preterm infants.
- oral or intravenous, has become another alternative pharmaceutical method for PDA closure with success rates comparable to indomethacin or ibuprofen.
- Acetaminophen is believed to block the peroxidase segment of prostaglandin synthetase, thus inhibiting prostaglandin production.
- Because of its different site of action, this drug may not generate vasoconstriction; thus, a non-surgical option for preterm infants with gastrointestinal perforations or reduced renal blood flow.
- However, its use has been reported to cause elevation of transaminase, so caution is warranted is patient with hepatic injury.
- A current recommended dosing is 15 mg/kg given every 6 hours.

2)Interventional closure: can safely performed in infant as small as 700 g

3)Surgical closure :

- If medical treatment is unsuccessful or if the use of indomethacin is contraindicated, surgical ligation of the ductus may be indicated.
- The standard operative approach to PDA is through a posterolateral thoracotomy.
- The PDA is simply ligated or hemoclipped (without division).
- PDA ligation in the neonatal intensive care unit at the bedside.
- The operative mortality rate is 0% to 3%.
- Recently, the use of minimally invasive VATS (Video-assisted thoracoscopic surgical) has been reported for the management of PDA in low-birth-weight infants.
- This technique allows PDA interruption without the muscle cutting or rib spreading of a standard thoracotomy. Reduced compromise of respiratory mechanics and less chest wall deformity associated with a large thoracotomy incision may also be advantages.

➢ For more reading :

1. Jain, A., & Shah, P. S. (2015). *Diagnosis, Evaluation, and Management of Patent Ductus Arteriosus in Preterm Neonates. JAMA Pediatrics, 169(9), 863.*
2. *"Myung Park, Mehrdad Salamat; "Park's Pediatric Cardiology for Practitioners ";" Seventh Edition"; (2020).pages :* 133 -135*; "*

Chapter 12 : Atrioventricular canal

I. Definition:

- There are two general types of AVSD that can occur, depending on which structures are not formed correctly :
- **Complete AVSD (Figure 10) :**
  - A complete AVSD occurs when there is a large hole in the center of the heart which allows blood to flow between all four chambers of the heart.
  - This hole occurs where the septa (walls) separating the two top chambers (*atria)* and two bottom chambers (*ventricles*) normally meet. There is also one common atrioventricular valve in the center of the heart instead of two separate valves – the *tricuspid valve* and the *mitral valve* on.

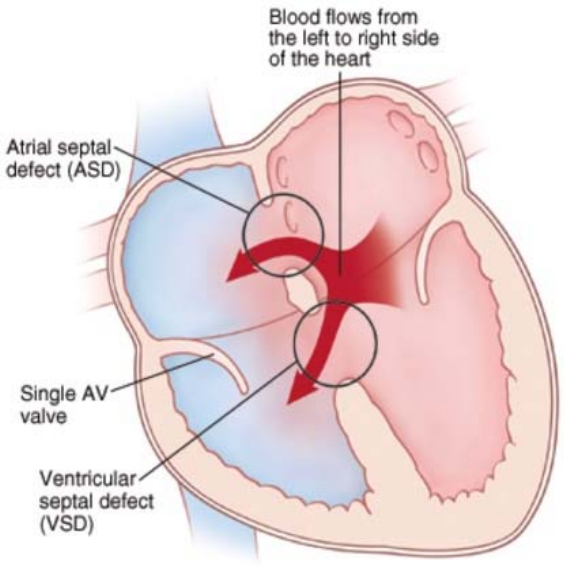

Figure 10: AVSD complete :

- showing the communication between all cardiac compartments

(Source : https://www.fairview.org/patient-education/89102)

- This common valve often has leaflets (flaps) that may not be formed correctly or do not close tightly. A complete AVSD arises during pregnancy when the common valve fails to separate into the two distinct valves (tricuspid and mitral valves) and when the septa (walls) that split the upper and lower chambers of the heart do not grow all the way to meet in the center of the heart.

- **Partial or Incomplete AVSD (Figure 11):**
  - A partial or incomplete AVSD occurs when the heart has some, but not all of the defects of a complete AVSD.
  - There is usually a hole in the atrial wall or in the ventricular wall near the center of the heart .
  - A partial AVSD usually has both mitral and tricuspid valves, but one of the valves (usually mitral) may not close completely, allowing blood to leak backward from the left ventricle into the left atrium.

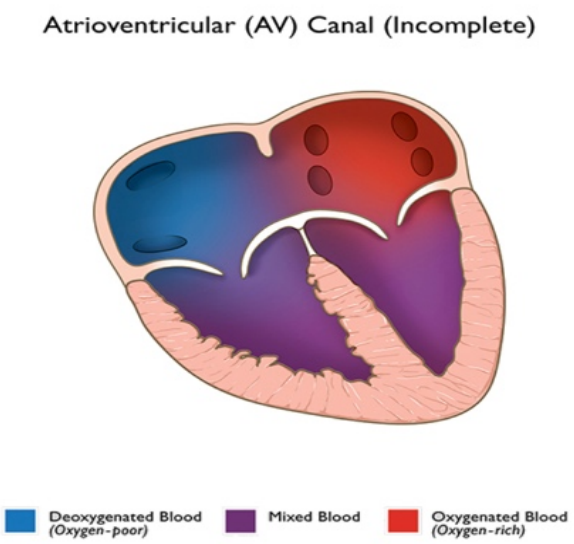

Figure 11: AVSD incomplete :

(source : https://pedecho.org/library/chd/partial-av-canal)

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II. Clinical description :

a. Complete atrioventricular canal :

- Symptoms occur in infancy : Failure to thrive, as well as congestive heart failure and frequent repeated pulmonary infections, are invariably seen.
- feeding problems and are virtually symptomatic in the first few months of life.
- Signs of congestive heart failure consist in
  - feeding difficulties,
  - excessive sweating,
  - tachycardia, tachypnea,
  - subcostal and intercostal retractions,
  - mild wheezing, hepatic enlargement and poor peripheral blood perfusion.
- systolic cardiac murmur and gallop rhythm are frequent.
- Sign of underlying cause : genetics , dysmorphia , malformation
- Over time, irreversible pulmonary hypertension develops, improving the signs of congestive heart failure but worsening tolerance to effort.
- Lately cyanosis develops, further decreasing the exercise capacity.

b. Partial atrioventricular canal defect :

- Signs and symptoms might not appear until early adulthood and might be related to complications that develop as a result of the defect.
- These signs and symptoms can include:
  - usually free from symptoms in infancy
  - some may have recurrent chest infection
  - wide splitting of the second heart sound with ejection systolic murmur

- the infant may be symptomatic early in life if the defect is associated with major valvar regurgitation or common atrium

- Symptoms which might indicate that a child's complete AVSD or partial AVSD is getting worse include:
  - Arrhythmia,
  - Congestive heart failure
  - Pulmonary hypertension
  - Associated Dysmorphia and malformation (trisomy, Noonan syndrome….)

III. Diagnosis criteria :

a. Complete atrioventricular canal :

- Diagnosis of CAVC might be clinically suspected in patients presenting in the first few months of life with:
  - congestive heart failure, especially I Down's case syndrome, in this case the cardiac abnormalities should be screened
  - Cardiomegaly on chest X-ray : Cardiomegaly is always present and involves all four cardiac chambers. Pulmonary vascular markings are increased, and the main PA segment is prominent.
  - left axis deviation, bi-atrial enlargement and bi-ventricular pressure and volume overload on electrocardiogram (ECG).
- Echocardiography is the key tool for the diagnosis and anatomic classification of this malformation. It shows the ostium primum atrial septal defect, with the underlying common atrioventricular valve, and the defect of the ventricular septal inflow .

b. During Pregnancy:

- prenatal tests to check for birth defects and other conditions. AVSD may be diagnosed during pregnancy with an ultrasound test .

c. **An echocardiogram** to confirm the diagnosis if AVSD is suspect-ed .

IV. Treatment :

➔ All AVSDs, both partial and complete types, usually require surgery

a. Medical treatment:

- Medical therapy aims to improve the signs and symptoms of congestive heart failure.
- Thus, it should be just considered as a bridge toward surgery.
- Pharmacological therapy is based on digitalis, diuretics and vasodilators:
  - Diuretic therapy is mainly based on furosemide, at the dose of 1–3 mg/kg/ day, and spironolactone, at the dose of 2–3.5 mg/kg/day.
  - Vasodilator therapy consists chiefly in the angiotensin converting enzyme inhibitors, captopril (0.5–3 mg/kg/ day, tid) or enalapril (0.1–0.4 mg/kg/day, bid).
- Nutrition should be optimized.

b. Surgical treatment :

- Surgical treatment is preferably scheduled before 6–12 months of life , except in case of Down's syndrome , before 6 months maximum. generally the great majority of surgeons perform the repair between the 3rd and the 6th month of life.

- Surgical palliation with pulmonary artery banding is now seldom indicated in high-risk infants (very low weight and/or in critical conditions). It reduces the pulmonary artery flow and pressure, so controlling the congestive heart failure, promoting the patient's growth and preventing the development of pulmonary vascular disease, but is contra-indicated in patients with severe atrioventricular valve regurgitation.
- However, more frequently complete intracardiac repair is indicated .
- Patients with an unbalanced AV canal (with hypoplasia of the right or left ventricle) may be treated by an earlier PA banding and later by a modified Fontan operation.
- Risk factors for surgical repair include :
  - the patient's age,
  - the severity of pre-operative common valve incompetence,
  - the presence of associated cardiac malformations
  - and the degree of the functional class .
- The prognosis is directly related to the repair of the left AV valve .
- The overall mortality for primary repair of CAVC is below 5-10%. Long-term survival is good and in 80%-95% of cases there is no need for reoperation.
- Of note, the closure of the cleft results in longer times before a reoperation is necessary .

➢ For more reading :

1: Calabrò, R., & Limongelli, G. (2006). *Orphanet Journal of Rare Diseases*

2: https://www.cdc.gov/ncbddd/heartdefects/avsd.html

3 . “Myung Park, Mehrdad Salamat”; ”Park's Pediatric Cardiology for Practitioners ”;” Seventh Edition”;(2020);pages :135-140 ; "

Chapter 13 : Pulmonary stenosis :

I. INTRODUCTION :

- Pulmonic stenosis is a defect of the pulmonic valve in which the valve is stiffened, causing an obstruction to flow,(**Figure 12**) .
- It typically congenital, benign, and diagnosed in pediatric patients with potentially curative treatments.
- Neonates usually present with severe cyanosis and right heart dysfunction right after birth .
- Many fetuses presenting with pulmonary valve stenosis (PS) and right ventricle dysplasia who are diagnosed as fetal CPS/IVS or PA/IVS are always turned out to be isolated mild-moderate pulmonary valve stenosis.

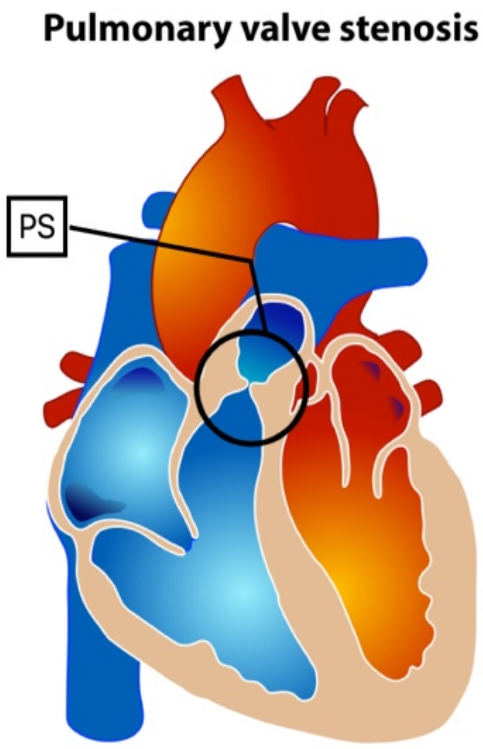

Figure 12 : Pulmonary valve stenosis

(Source : https://en.wikipedia.org/wiki/Pulmonary_valve_stenosis)

II. Diagnosis :

a) CLINICAL PRESENTATION :

- Most patients with mild to moderate PS are asymptomatic and will be discovered by a murmur during routine physical examination in infancy or childhood. There can be mild exertional dyspnea and fatigue.
- In patients with moderate stenosis, exertional dyspnea and easy fatigability may be present.
- In untreated severe PS, the inability to increase pulmonary blood flow during exercise can lead to chest pain or syncope (and even sudden death may occur with strenuous exercise).
- In the newborn with a critical PS, the supra-systemic RV pressure may result in RV dilatation and failure with severe tricuspid regurgitation (TR) and cyanosis due to right-to-left shunting over the foramen ovale or an ASD. These infants may present in heart failure and will often be duct dependent.
- Newborns with critical PS may present with poor feeding, tachypnea, and cyanosis.

b) Physical Examination :

- Most patients are acyanotic and well developed.
- Newborns with critical PS (who have hypoplastic RV and a right-to left atrial shunt) are cyanotic and tachypneic.
- A right ventricular tap and a systolic thrill may be present at the upper left sternal border (and occasionally in the suprasternal notch).
- A systolic ejection click is present at the upper left sternal border only with valvular stenosis.

- The S2 may split widely, and the P2 may be diminished in intensity.
- An ejection-type systolic murmur (grade 2–5 of 6) is best audible at the upper left sternal border, and it transmits well to the back, too.
- The louder and longer the murmur, the more severe the stenosis is.
- Hepatomegaly may be present if congestive heart failure (CHF) develops.
- In newborns with critical PS, cyanosis may be present (caused by a right-to-left atrial shunt), and signs of CHF with hepatomegaly and peripheral vasoconstriction may be found.
- In patients with peripheral PA stenosis, a mid-systolic murmur in the pulmonary valve area is well transmitted to the axillae and back. Occasionally, a continuous murmur is audible over the involved lung field

c) paraclinical diagnosis :

- ECG :
  - The electrocardiogram (ECG) findings are normal in mild cases.
  - Right-axis deviation (RAD) and right ventricular hypertrophy (RVH) are present in moderate PS.
  - Right atrial hypertrophy (RAH) and RVH with “strain” may be seen in severe PS.
  - Neonates with critical PS may show left ventricular hypertrophy (LVH) because of a hypoplastic RV and relatively large left ventricle (LV)
- Radiography :
  - Heart size is usually normal, but the main PA segment may be prominent with valvular stenosis
  - Cardiomegaly is present only if CHF develops

- Pulmonary vascular markings are usually normal but may decrease with severe PS.
- In neonates with critical PS, lung fields are oligemic with a varying degree of cardiomegaly.

- Echocardiography:

- Transthoracic two dimensional (2D) echocardiography and Doppler imaging is the clinical standard to detect PS and quantify its severity.
- Pulsed wave Doppler is useful to discriminate between sub-valvular, valvular and supravalvular stenosis.

III. TREATMENT :

A.Medical management and Balloon Valvuloplasty :

1- Newborns with critical PS :

- These cyanotic neonates require emergency treatment to reduce mortality.

a. temporarily improvement with prostaglandin E1 (PGE1) infusion, which reopens the ductus arteriosus, and other supportive measures.
b. Balloon valvuloplasty is the procedure of choice in critically ill neonates.
c. Some of Patients are not able to maintain effective forward flow through the pulmonary valve because of noncompliant or hypoplastic RV. Some of them may need one of the following:
   (1) A prolonged PG infusion .
   (2) Ductal stenting .
   (3) systemic-to-pulmonary shunt surgery.

2- Balloon valvuloplasty : it is the procedure of choice for the valvular stenosis at all ages.

a. Indications: Indications for the procedure may include the following.
   - A resting pressure gradient of greater than 40 mm Hg with the patient sedated in the catheterization laboratory .
   - If the catheterization gradient is 50 mmHg, the balloon procedure may be reasonable.
   - Symptoms attributable to PS with a catheterization gradient greater than 50 mm Hg : and may include angina, syncope or presyncope, and exertional dyspnea.
   - The procedure is useful and reasonable in patients with dysplastic pulmonary valve, as commonly seen in Noonan's syndrome.
   - It has a lower success rate with the valvuloplasty (65%). If balloon valvuloplasty is unsuccessful, surgery is indicated.

b. Results: The balloon procedure carries an extremely low risk, is painless, is less costly than surgery, and shortens hospital stay.

3- Restriction of activity is not necessary in children with this condition, except in cases of severe PS (Doppler gradient >70 mm Hg).

B. Surgical : Indications and Timing :

- Surgical valvotomy should be limited to patients with more complex lesions or those in whom balloon procedure is contraindicated or failed.
- Other types of obstructions (e.g., infundibular stenosis, anomalous RV muscle bundle) with significant pressure gradients require surgery on an elective basis.
- If balloon valvuloplasty is unsuccessful or unavailable, infants with critical PS and CHF require surgery on an urgent basis.

- For more reading :

1. Cuypers, J. A. A. E., Witsenburg, M., van der Linde, D., & Roos-Hesselink, J. W. (2013). Pulmonary stenosis: update on diagnosis and therapeutic options. Heart, 99(5), 339–347.
2. Wang, Q., Wu, Y. R., Jiao, X. T., Wu, P. F., Zhao, L. Q., Chen, S., & Sun, K. (2018). Fetal pulmonary valve stenosis or atresia with intact ventricular septum: Predictors of need for neonatal intervention. Prenatal Diagnosis, 38(4), 273–279.
3. "Myung Park, Mehrdad Salamat"; "Park's Pediatric Cardiology for Practitioners ";" Seventh Edition";' (2020);pages :143-146 ; "

Chapter 14 : Infective Endocarditis:

I. Definition :

- It is an infection of the endocardium of the heart and vascular endothelium.
- This process can include the native endocardium of the heart chambers or the endothelium associated with the cardiac valves or prosthetic hardware or material (prosthetic valves, conduits, grafts, patches, or pacemaker generator or leads).
- IE development is a complex process that involves the susceptibility of a valve or tissue to bacterial adherence, survival of the bacteria on the tissue or associated structure, and propagation of the infected vegetation.
- Endocarditis is rare in infancy; at this age, it usually follows open-heart surgery

II. Diagnosis :

A. Clinical :

- Most patients have a history of an underlying heart defect.
- A history of a recent dental procedure or tonsillectomy is occasionally present, but a history of toothache (from dental or gingival disease) is more frequent than a history of a procedure.
- A history of recent cardiovascular procedures or surgeries or hospital care may be present.
- Unexplained and persistent fevers without a potential source in a patient who carries a high risk for IE should be evaluated thoroughly.
- Nonspecific : fatigue , night sweats or chills, generalized malaise, and weight loss.
- With IE associated with a cardiac valve, a murmur will likely become evident.

- A new diastolic murmur or an abnormal systolic murmur (often regurgitant or holosystolic) should raise suspicion in a patient without a history of structural heart disease.
- In patients with bioprosthetic valves, a new diastolic murmur or a rapidly changing or progressive systolic ejection murmur should also raise high suspicion.
- myalgias, neurologic changes, dermatologic findings such as splinter hemorrhages, Roth spots (retinal hemorrhagic lesions), Janeway lesions (painless hemorrhagic lesions of the distal extremities), or Osler nodes (painful nodules of the distal extremities). The skin manifestations, if present, are associated with an increased risk of complications. skin manifestations consisting of purpura , Osler nodes , and Janeway , lesions in Visual changes such as a sudden or complete loss of vision in 1 eye or eye pain should prompt an ophthalmologic evaluation to look for retinal or ophthalmic artery occlusion or associated endophthalmitis.
- Systemic manifestations: sepsis, shock, respiratory sign , Embolic or immunologic phenomena ,
- Complication : neurologic, respiratory, renal , vascular .
- The modified Duke criteria for diagnosis of IE incorporate pathologic and clinical criteria to assist in the diagnosis of IE

B. <u>Paraclinical:</u>

- blood count , platelet count.
- erythrocyte sedimentation rate,
- reactive protein,
- blood cultures : Blood cultures are the mainstay of diagnosis.

- Echocardiogram :
  - echocardiographic imaging , transesophageal echocardiographic ,
  - a negative echocardiogram does not mean that the patient does not have endocarditis.
  - In some cases, repeat imaging may be indicated.
  - Serial imaging studies can also provide valuable information in regard to therapy success or progressive disease.
- Other imaging modalities such as computed tomography scans, MRI, and cardiac PET may be used in select situations.
- electrocardiogram, in general, is not helpful in the diagnosis , but a new conduction abnormality or bundle branch block should raise
- concern for abscess formation affecting the conduction system.

C. <u>The modified Duke criteria for the diagnosis of IE :</u>

- See （**Box 1**）

Table 1 : : The modified Duke criteria for the diagnosis of IE

1- <u>Definitive IE : if one of the following 2</u>

a. Pathologic criteria :

- Micro-organisms demonstrated by culture or histologic examination of vegetation, vegetation that has embolized, or an intracardiac abscess specimen; or
- Pathologic lesions; vegetation or intro cardiac abscess confirmed by histologic examination showing active endocarditis.

b. Clinical criteria :

- Two major and 0 minor criteria; or
- One major and 3 minor criteria; or
- No major and 5 minor criteria.

➔ Major criteria :

- Positive blood culture positive for IE :
  - Typical endocarditis organism from 2 separate blood cultures :
    - Viridans streptococci or Streptococcus bovis
    - HACEK organisms
    - Staphylococcus aureus
    - Community-acquired enterococcus in absence of primary focus
  - Micro-organisms consistent with IE from persistently positive blood cultures:
    - Two separate blood cultures from samples drawn greater than 12 hours apart
    - Three, or a majority of 4 or more, separate blood cultures (first and last sample drawn 1 hour apart)
    - Single positive blood culture for Coxiella burnetii or an antiphase I IgG antibody titer of greater than 1:800
- Evidence of endocardial involvement
- Echocardiogram positive for IE Oscillating intracardiac mass on valve or supporting structures, in the path of regurgitant jets, or on implanted material in the absence of an alternative anatomic explanation; or Abscess; or New partial dehiscence of prosthetic valve or new valvular regurgitation.
- New valvular regurgitation (worsening or changing of preexisting murmur not sufficient)

➔ Minor criteria

- Predisposing heart condition or intravenous drug use
- Fever, temperature greater than 38 C (100.4 F)
- Vascular phenomena: major arterial emboli, septic pulmonary infarcts, mycotic aneurysm, intracranial bleed, conjunctival hemorrhages, Janeway lesions
- Immunologic phenomena: glomerulonephritis, Osler nodes, Roth spots, rheumatoid factor
- Microbiological evidence: positive blood culture, but does not meet a major criterion as noted or serologic evidence of an active infection with organism consistent with IE (excluding single positive culture for coagulase-negative staphylococci and other common contaminants)

2- <u>Possible IE :</u>

If clinical criteria:

- One major criterion and one minor criterion; or
- Three minor criteria

3- <u>Rejected diagnosis : if</u>

- Firm alternative diagnosis explaining evidence of IE; or
- Resolution of IE syndrome with antibiotic therapy for less than or equal to 4 days; or
- No pathologic evidence of IE at surgery or autopsy, with antibiotic therapy for less than or equal to 4 days; or
- Does not meet criteria for possible IE, as described

III. Treatment :

- The management of patients with infective endocarditis necessitates a multidisciplinary approach with input from pediatrics , cardiologists, cardiothoracic surgeons, and infectious disease specialists.
- Blood cultures are indicated for all patients with fever of unexplained origin and a pathologic heart murmur, a history of heart disease, or previous endocarditis.
  - Usually three blood cultures are drawn by separate venipunctures over 24 hours unless the patient is very ill.
  - In 90% of cases, the causative agent is recovered from the first two cultures.
  - If there is no growth by the second day of incubation, two more may be obtained. There is no value in obtaining more than five blood cultures over 2 days unless the patients received prior antibiotic therapy.
  - It is not necessary to obtain the cultures at any particular phase of the fever cycle.
  - Aerobic incubation alone suffices because it is rare for IE to be caused by anaerobic bacteria.
- It is highly recommended that consultation from an infectious disease specialist be obtained when IE is suspected or confirmed because antibiotics of choice are continually changing and there may be special situation pertaining to the local area.

a. medical:

- Antibiotics should be started as soon as blood cultures have been acquired, but clinicians can also await culture results if the patient is clinically stable.
- In general, combination intravenous therapy is preferred over monotherapy, to reduce emergence of resistance and provide synergistic antimicrobial activity.
- The exception is methicillin sensitive S aureus, for which flucloxacillin monotherapy is sufficient and addition of gentamicin increases nephrotoxicity.
- Empirical antibiotic regimens for native valve endocarditis and prosthetic valve endocarditis are based on definitive guidelines produced by the British Society for Antimicrobial Chemotherapy (**Table1**).
- The usual initial regimen is an anti-staphylococcal semisynthetic penicillin (nafcillin, oxacillin, or methicillin) and an aminoglycoside (gentamicin). This combination covers against S. viridans, S. aureus, and gram-negative organisms.
- Some experts add penicillin to the initial regimen to cover against S. viridans, although a semisynthetic penicillin is usually adequate for initial therapy.
- If a methicillin-resistant S. aureus is suspected, vancomycin should be substituted for the semisynthetic penicillin.
- Vancomycin can be used in place of penicillin or a semisynthetic penicillin in penicillin-allergic patients.
- The final selection of antibiotics depends on the organism isolated and the results of an antibiotic sensitivity test .
- The antimicrobial regimen can be modified according to :

- culture results,
- resistance patterns,
- severity of infection,
- and the presence or absence of prosthetic material.

- Treatment for at least 4–6 weeks is usually necessary, and for substantially longer in some cases (eg, Q fever infective endocarditis).
- Patients with uncomplicated native valve endocarditis due to highly sensitive streptococci might be suitable for a short 2-week course of intravenous benzylpenicillin or ceftriaxone in combination with gentamicin.
- Other selected patients who are responsive to treatment and have suitable domestic living circumstances could be eligible for home or outpatient antibiotic care after the first 2-week period in which the frequency of complications is highest.

Table 2: Empirical treatment for different clinical scenarios in patients with suspected infective endocarditis (7)

Native valve endocarditis—indolent presentation	**Amoxicillin :**	**(2 g, every 4 h, intravenously)**
	+ gentamicin:	(optional; 1 mg/kg of actual bodyweight)
Native valve endocarditis—severe sepsis (without risk factors for multi-resistant enteric Gram-negative bacilli, pseudomonas)	Vancomycin :	(dose as per local guidelines)
	+gentamicin:	(1 mg/kg of ideal bodyweight, every 12 h, intravenously)
Native valve endocarditis—severe sepsis (with risk factors for multi-resistant enteric Gram-negative bacilli, pseudomonas)	Vancomycin:	(dose as per local guidelines) +
	+meropenem :	(2 g, every 8 h, intravenously)
Prosthetic valve endocarditis—pending blood cultures or with negative blood cultures	Vancomycin:	(1 g, every 12 h, intravenously)
	+gentamicin:	(1 mg/kg, every 12 h, intravenously)
	+ rifampicin :	(300–600 mg, every 12 h, orally or intravenously)

b. Surgery :

- There are three principal indications :
  - valve dysfunction leading to heart failure,
  - uncontrolled or complex infection,
  - and for prevention of embolism.
- The aims of surgery are to eradicate infection and reconstruct cardiac anatomy.
- Both valve repair and replacement are options for reconstruction, and no definitive evidence favors a bioprosthetic valve more than a mechanical replacement.

➢ For more reading :

1- Cox, D. A., & Tani, L. Y. (2020). Pediatric Infective Endocarditis. Pediatric Clinics of North America, 67(5), 875–888.
2- (n.d.). 2.. Sullam PM, Drake TA, Sande MA. Pathogenesis of endocarditis. Am J Med 1985;.
3- Li, J. S., Sexton, D. J., Mick, N., Nettles, R., Fowler, V. G., Ryan, T., … Corey, G. R. (2000). Proposed Modifications to the Duke Criteria for the Diagnosis of Infective Endocarditis. Clinical Infectious Diseases, 30(4), 633–638.
4- Cahill, T. J., & Prendergast, B. D. (2016). Infective endocarditis. The Lancet, 387(10021), 882–893.
5- Gould FK, Denning DW, Elliott TSJ, et al. Guidelaines for the diagnosis and antibiotic treatment of endocarditis in adults: a report of the Working Party of the British Society for Antimicrobial Chemotherapy. J Antimicrob Chemother 2012; 67: 269–89.
6- Prophylaxie : Wilson, W., Taubert, K. A., Gewitz, M., Lockhart, P. B., Baddour, L. M., … Levison, M. (2007). Prevention of Infective Endocarditis: Guidelines From the American Heart Association: A Guideline From the American Heart Association Rheumatic Fever, Endocarditis, and Kawasaki Disease Committee, Council on Cardiovascular Disease in the Young, and the Council on Clinical Cardiology, Council on Cardiovascular Surgery and Anesthesia, and the Quality of Care and Outcomes Research Interdisciplinary Working Group. Circulation, 116(15), 1736–1754.
7- “Myung Park, Mehrdad Salamat;”Park's Pediatric Cardiology for Practitioners ”;” Seventh Edition”;”(2020)”;”pages :264-271” ;

Chapter 15 : MYOCARDITIS

I. Definition :

- Myocarditis is an inflammatory disease of the myocardium with numerous different etiologies, the vast majority of which are infectious in origin.
- Patients affected with myocarditis can have variable presentations from flu-like symptoms to cardiogenic shock and sudden death, thus making the diagnosis difficult.
- The presentation is variable, degeneration into florid right heart failure or life threating arrhythmia .
- Acute myocarditis is a serious pediatric problem, with high mortality rates, debilitating sequelae such as chronic dilated cardiomyopathy, no globally accepted treatment or protocol, and under recognition.

II. Diagnosis :

a. Clinical Manifestations :

- May start with a sudden onset in newborns and vomiting, lethargy, and occasionally circulatory shock.
- Older children may have a history of an upper respiratory infection.
- Sudden infant death syndrome (SIDS) autopsies and a cause of sudden cardiac death .
- The presentation of myocarditis may often mimic the presentation and findings of acute coronary syndrome.
- The most commonly presenting symptoms by order of frequency : respiratory , cardiac , hypoperfusion , and gastrointestinal.

- Chest pain , tachypnea, hepatomegaly, respiratory distress, fever, and abnormal lung exam .
- Viral symptoms, and shortness of breath is possible .
- Specific symptoms: arthritis, cutaneous eruption , septic pyohemia , neuralgic injuries,
- In fulminant myocarditis, cardiogenic shock could be the result
- On examination : respiratory distress, poor perfusion ,hypotension
- A soft, systolic heart murmur and irregular rhythm caused by supraventricular or ventricular ectopic beats may be audible.
- Hepatomegaly (evidence of viral hepatitis) may be present

b. Investigations :

1. Electrocardiography:
   - Should eliminate rhythmic myocardiopathy
   - The most common findings on ECG were ST or T wave abnormalities and axis deviations.
   - T-wave inversion as the most common finding, followed by ST segment elevation, prolonged PR interval, ST segment depression, Q waves, and low-voltage QRS complexes
   - ST segment elevation signifies bad prognosis.
2. Radiography :
   - CXR alone was an insufficient screening test.
   - Cardiomegaly.
3. Echocardiography
   - Echocardiogram is the initial imaging technique .

- Should eliminate others etiologies: aortic stenosis, coarctation , origin coronary anomalous, metabolic etiology .
- Demonstrate ventricular dilatation with hypokinemia
- Should be done in whenever suspicion of myocarditis.
- Search atrial thrombus
- The diagnostic value of echocardiography is limited by the fact that many patients with less severe myocarditis have a normal echocardiogram and the highly variable echocardiographic findings lack specificity .
- Fulminant myocarditis : severe hemodynamic compromise compared to acute myocarditis as well as a greater chance of progressing towards dilated cardiomyopathy
- Echocardiography as a means of differentiating acute and fulminant myocarditis

4. Cardiac magnetic resonance imaging :
   - Cardiac magnetic resonance imaging (cMRI) is currently considered to be the noninvasive gold standard for diagnosing myocarditis and is only secondary to an EMB.
   - cMRI can detect tissue injury, including edema, hyperemia, and fibrosis
5. Laboratory Studies :
   a. elevated cardiac enzymes :

➔ Troponin I Versus Troponin T :

- The diagnostic workup in any patient with a suspected diagnosis of myocarditis involves obtaining serum cardiac biomarkers including troponin testing.
- Superior sensitivity of troponin I over troponin T or vice versa with regards to sensitivity or specificity for the diagnosis of myocarditis.

b. Additional Labs :

- Aspartate aminotransferase (AST) .
- No associated increase in alanine aminotransferase (ALT) level.
- Complete blood count, erythrocyte sedimentation rate (ESR).
- C-reactive protein (CRP), and brain natriuretic peptide .
- Antibodies anti corps .
- Metabolic parameters .
- ASLO .

6. Endomyocardial biopsy :

- The first pathological definition of myocarditis was the Dallas criteria
- Inflammation in an EMB specimen is defined by the detection of mononuclear infiltrates with >14 cells/mm2 , with enhanced expression of HLA class II molecules.
- Not done in routine practice ,The current recommendations state that an EMB should only be performed in patients with new-onset heart failure < 2 weeks.
- Dallas Criteria :
  - The gold standard histological criteria, the Dallas Criteria, defining myocarditis as a process characterized by an inflammatory infiltrate of the myocardium with necrosis and/or degeneration of adjacent myocytes not typical of the ischemic damage associated with coronary artery disease

III. Treatment :

1- Initial measures of myocarditis treatment include :

- Oxygen .
- Bed rest and , limitation in activities are recommended.
- Salt and fluid restriction, supplemental oxygen..
- And correction of any identified anemia.

2-Symptomatic management : Supportive therapy is the mainstay of therapy in myocarditis :

a. treatment of heart failure :

- for preload reduction : the use of diuretics, :
  - Rapid-acting diuretics (furosemide or ethacrynic acid, 1 mg/kg, each one to three times a day)
- for afterload reduction :
  - angiotensin-converting enzyme (ACE) inhibitors (captopril)
  - or angiotensin receptor blockers (ARB)
- Beta-blockers :
  - are not recommended in the acute phase but may be required as long-term maintenance drug.
  - Carvedilol was shown to protect against acute autoimmune myocarditis .
- Aldactone is an aldosterone antagonist : beneficial in the long-term treatment of patients with heart failure:
  - eplerenone (an aldosterone antagonist) : have anti-inflammatory .
- Some patients may require positive pressure ventilation to reduce cardiac demand and left ventricular afterload .

b. Therapy for advanced heart failure (more severe cases of myocarditis) :

- Myocarditis may progress to severe heart failure unresponsive to conventional medical therapy.
- The initial therapy in these cases is the initiation of inotropic support.
- even intense medical therapy may also fail and these patients often require mechanical circulatory support, the most common of which is ECMO.
- Though ECMO can provide effective short-term (<2 weeks) survival is poor in patients requiring >2 weeks of support in the ELSO registry..
- Ventricular assist devices (VADs) are being increasingly used in pediatric myocarditis with a favorable initial experience.
- Currently, the pulsatile Berlin Heart EXCOR is the most commonly used VAD in the pediatric population, and it allows support for infants as small as 3.5 kg.
- The primary use of pediatric VADs is as a bridge to heart transplantation

c. In patients with chronic myocarditis:

- therapy is usually limited to the treatment of arrhythmias and implantable cardioverter-defibrillator (ICD) for higher risk cases.

d. Conduction problems :

- If complete or high-grade atrioventricular block which does not recover, a pacemaker implantation decisions should be taken in consideration
- if the complete heart block does not resolve within 1 week : A permanent pacemaker is indicated.

e. Ventricular arrhythmias :

- Arrhythmias are a common sequela and/or manifestation of myocarditis.
- They may sometimes be the only manifestation of myocarditis

- It is treated based on current guidelines, with β-blockers being the most common therapy.
- Digoxin is not recommended for the treatment of acute myocarditis , may increase myocardial injury may worsen the inflammation associated with viral myocarditis.
- arrhythmias is a significant cause of sudden cardiac death in these patients.
- ECG changes may be used in identification of the onset of subacute arrhythmia as well as follow-up post-discharge to monitor for the recurrence
- the recommendations emphasized that athletes with "probable or definite evidence of myocarditis should be withdrawn from all competitive sports and undergo a prudent convalescent period of about 6 months following the onset of clinical manifestations."

f. Athletes were able to return to training after this time period had elapsed provided that there was echocardiograph and/ or radionuclide studies proven return of cardiac dimensions, LV function and wall motion to baseline, Holter, and exercise testing proven absence of clinically relevant arrhythmias as well as normalization of serum inflammatory/heart failure markers and 12 lead EKG

3- Etiological treatment :

a. Anti-Viral Treatments :

- drug that prevents Enterovirus, such as Coxsackie virus, from infecting target cells .
- HIV, CMV, and HSV should be treated with already established antiviral therapies.

b. Immunosuppressant therapy and immune modulation :

- Could be useful if autoimmune and idiopathic myocarditis
- Immune therapy remains as an area of great controversy in the treatment of pediatric myocarditis.
- Intravenous immunoglobulin (IVIG) has antiviral, anti-inflammatory, and immunomodulatory effects.
- The immunosuppressive agents: Prednisone, IVIG, cyclosporine, azathioprine, interferon-alpha, and Orthoclone OKT®
- The use of high-dose IVIG 2 g/kg over 24 hours is associated with improved recovery of left ventricular function and enhanced survival for the first year post presentation.
- However, this treatment(IVIG) had a high risk of bias .
- recent interest in interferon-α and interferon- β as possible therapeutic options for myocarditis.

c. The nonsteroidal anti-inflammatory drugs :

- is also controversial in this patient population, indomethacin can decrease interferon production, increased - coxsackievirus four titers, and enhance the virulence of coxsackievirus B4.
- However, nonsteroidal anti-inflammatory drugs may be used discriminately in patients with coexisting signs of pericarditis and/or pericardial effusion.
- The clear benefit of nonsteroidal anti-inflammatory drugs in the treatment of pericarditis is difficult to extrapolate to acute myocarditis

4- ICU Admission :

- Parvovirus B19 positive myocarditis cases, that children presenting in fulminant myocarditis .
- EKG with ST segment changes (especially ST elevation) .
- History of a short prodromal illness (< 48 h).
- Those in severe heart failure have worse outcomes .
- However, not all myocarditis patients require PICU admission.
- Stratified patients based on a severity score as minor, moderate, major, and extreme .

Table 3: Medical therapeutic used in myocarditis (2) :

Medication	Indication
Diuretics	Anti-congestive therapy for relief of symptoms
Angiotensin-converting enzyme inhibitors	Asymptomatic left ventricular dysfunction
B-blockers	Added when there is symptomatic heart failure May be considered for ventricular ectopy
Aldosterone antagonists	Added when there is symptomatic heart failure, beneficial in the long term May be considered for asymptomatic left ventricular dysfunction
IVIG	No recommendation for the routine use in myocarditis
Immunosuppressive therapy	No recommendation for the routine use in myocarditis, useful for the management of giant cell myocarditis

Myocarditis symptoms identified in clinic or the Emergency Department

Fever/prodromal illness with:
- **Cardiovascular Symptoms:** Poor perfusion and hypotension, chest pain, shortness of breath or tachypnea, shock
- **Gastrointestinal Symptoms:** nausea, vomiting, diarrhea or abdominal pain
- **Neurological symptoms:** lethargy, weakness, altered mental status, syncope
- Neonates may present with nonspecific signs such as fever, irritability, poor intake, color change, apnea. *Presenting symptoms may have significant overlap with symptoms of sepsis. Myo-pericardial disease should be included within the differential diagnosis.*

↓

Suspicion for myocarditis and initial diagnostic evaluation

- **12 lead EKG:** findings may include T wave inversion, ST segment elevation or depression, prolonged PR interval, Q waves, low voltage QRS complexes, non specific T wave and ST segment changes
- **Chest X-ray:** Cardiomegaly is commonly associated with myocarditis, pleural effusions, peri-hilar congestion may be present or it may be normal
- **Echocardiogram:** global left ventricular or bi-ventricular dysfunction, dilated cardiomyopathy, reduced LVEF, significant regurgitation of the mitral and tricuspid valves or atrial enlargement may be observed. May be normal
- **Troponin testing:** elevated levels support diagnosis of myocarditis, use a cut off value of 0.01ng/mL
- **Lab work:** CBC, CMP: elevated AST with normal ALT correlates with myocarditis), ESR, CRP, BNP, Respiratory Viral Panel
- *Recommend early cardiology consultation and placing on cardiac monitoring*

↓

Patient placement after initial workup

- Patients who display any signs of fulminant myocarditis such as ***short < 48 hours prodrome illness or echocardiographic findings suggestive of fulminant myocarditis***, Reduced LVEF, ST elevation, Arrhythmias on cardiac monitoring, signs of hemodynamic instability or tested positive for Parvovirus on RVPCR should be immediately transferred to the intensive care unit.
- For patients who do not meet the above criteria, and are deemed otherwise stable in conjunction with a cardiac consultation may be monitored closely on the floor with full cardiac monitoring for observation and or further management.

↓

Management in the PICU

Cardiac monitors with ECG monitoring, Cardiology consultation , Continue echocardiographic monitoring
Diagnosis:
Consider Cardiac MRI
Consider EBM testing with viral PCR if patient is not improving.
Infectious Work-up:
Consider RVPCR
Consider Rickettsia Panel when history of fever, headache, and rash
Consider Parvovirus B19, Enterovirus, Adenovirus, EBV, & CMV PCR
Consider HIV/Lyme disease testing
Review immunization status, *especially MMRV*
Review TB exposure risk and consider placing PPD and drawing IGRA

Treatment:
No IVIG
Consider steroids usage for severe impairment of LVEF
Cardiac medications and Ionotropic support per the ICU team
Arrhythmia Monitoring
Mechanical Ventilation
Cardiac Transplant Criteria to be followed if deemed necessary based on heart failure

Figure 13 : Algorithm general of myocarditis (1)

- For more reading :

1 . Howard, A., Hasan, A., Brownlee, J., Mehmood, N., Ali, M., Mehta, S., & Fergie, J. (2019). Pediatric Myocarditis Protocol: An Algorithm for Early Identification and Management with Retrospective Analysis for Validation. Pediatric Cardiology.
2. Soham Dasgupta, Glen Iannucci, Chad Mao, Martha Clabby, and Matthew Oster contributed equally to the genesis of the research design, analysis and interpretation of data, initial drafting of the manuscript and review, and approval of the submitted and final version.
3. “Myung Park, Mehrdad Salamat; Park's Pediatric Cardiology for Practitioners; Seventh Edition;(2020); pages :269-271 "

Chapter 16 : ACUTE PERICARDITIS

I. Definition :

- ACUTE PERICARDITIS :is a common disorder caused by inflammation of the pericardium and can occur as an isolated entity or as a manifestation of an underlying systemic disease .
- In most patients, the cause of acute pericarditis is thought to be idiopathic because the yield of diagnostic tests to confirm etiology has been relatively low .
- An acute inflammatory disease of the pericardium, which may occur in many different disease states (both infectious and non-infectious).
- Cause :

- Viral infection is probably the most common cause of pericarditis in the developed world.
- Bacterial infection (purulent pericarditis) is a rare , but serious form of pericarditis.
- Tuberculosis is a common cause in developing countries ,and it is an occasional cause of constrictive pericarditis, with an insidious onset.
- Acute rheumatic fever is a common cause of pericarditis.
- Heart surgery is a possible cause (see Post pericardiotomy Syndrome).
- Collagen disease such as rheumatoid arthritis can cause pericarditis.
- Pericarditis can be a complication of oncologic disease or its therapy, including radiation.
- Uremia (uremic pericarditis) is a rare cause.

II. Diagnosis :

a. clinical :

- Non specific symptoms: frequent in child and infant: fever, respiratory symptoms , anorexia, and dyspnea …
- In purulent pericarditis, septic fever [38.3°–40.5°C]), tachycardia, chest pain, and dyspnea are almost always present
- Although no criteria for the diagnosis of acute pericarditis have been established, studies have suggested that at least 2 of the followings criteria's should be present :

1. characteristic chest pain :
   - sudden in onset, retrosternal, and pleuritic exacerbated by inspiration, can be affected by position, lessening of the pain when they lean forward or are in the upright position, chest pain can radiate to the neck, arms, or left shoulder, radiation of the pain to 1 or both trapezius muscle ridges , pain can also occur in pericarditis, making it difficult to distinguish from myocardial ischemia.
2. pericardial friction rub :
   - The classic friction rub consists of 3 phases during 3 phases of the cardiac cycle, some rubs are present in only 1 (monophasic) or 2 (biphasic) , and it is difficult to know whether these rubs are truly due to pericardial disease.
3. Systemic manifestation: as part of etiologies; sepsis, arthralgia, myalgia, eruption, arthritis …
4. Typical suggestive electrocardiographic (ECG) changes:
   - wide spread upward concave ST-segment elevation and PR-segment depression .

- Four stages of ECG abnormalities have been described previously.
  - In stage 1, diffuse ST-segment elevation and PR-segment depression can be seen within the first hours to days with reciprocal ST-segment depression in the aVR and V1 leads. There can also be PR-segment elevation in the aVR lead.
  - stage 2 : the ST and PR segments normalize
  - stage 3 : followed by the development of widespread T-wave inversions .
  - stage 4 : findings on ECG may become normal or the T-wave inversions may persist indefinitely.

5. New or worsening pericardial effusion :
   - Cardiomegaly with clear lung fields suggests a significant pericardial effusion and indicates at least 200 mL of pericardial fluid.
   - Cardiomegaly is an uncommon finding, and most findings on chest radiography are normal in patients with acute pericarditis.
6. Signe of cardiac tamponade (see sub : CARDIAC TAMPONADE)

b. Investigations :

1. Lab tests :
   - Serologic testing : viral , streptococcal , antibodies .
   - Hemocultures .
   - Markers of inflammation: white blood cell count, erythrocyte sedimentation rate, and serum C-reactive protein concentration, are usually elevated .

- Serum cardiac troponin I levels have been shown to be minimally elevated ,most patients with an elevated troponin level and acute pericarditis have normal findings on coronary angiography

2. CHEST RADIOGRAPHY :
   - most findings on chest radiography are normal in patients with acute pericarditis
   - Cardiomegaly with clear lung fields suggests a significant pericardial effusion
   -
3. ECHOCARDIOGRAPHY :
   - Transthoracic echocardiography is recommended if acute pericarditis is suspected with evidence of hemodynamic compromise
   - The finding of a significant pericardial effusion supports the diagnosis and guides further management, especially if there is evidence of cardiac tamponade and a need for emergent pericardiocentesis.
4. CARDIAC COMPUTED TOMOGRAPHY AND CARDIAC MAGNETIC RESONANCE IMAGING :
   - very sensitive in the detection of generalized or loculated effusions and can also be used to measure pericardial thickness.
   - Normal pericardial thickness is less than 4 mm and is usually 1 to 2 mm.
5. Etiological Diagnose :
   - Other tests are demanded based on the context :
     - Infection
     - Inflammation ; Vasculitis
     - Neoplasia
     - Traumatic

- Iatrogenic
- post operatory

c. High-risk features :

- If the following is present :
  - Fever
  - Leukocytosis
  - large pericardial effusion
  - cardiac tamponade
  - acute trauma
  - oral anticoagulation
  - NSAID therapy failure
  - elevated troponin level
  - relapsing pericarditis

III. Treatment :

1. Physical activity and restriction:

- patients with acute pericarditis should be advised to restrict physical activity (other than ordinary sedentary life) until resolution of symptoms and normalization of CRP .
- For athletes, it is recommended to return to competitive sports only after symptoms and diagnostic tests are normalized (including CRP, EKG, echocardiogram), but at least 3 months of exercise restriction should be considered.

2. Medical :

- If etiology is identified (not viral or idiopathic), management should be directed toward treating the underlying cause.
- Patients with no high-risk features can be managed as outpatients.
- Medical management for viral or idiopathic acute pericarditis has been centered on 3 major agents—NSAIDs, colchicine, and corticosteroids :

a. Nonsteroidal Anti-inflammatory Drugs :

- recommended for the treatment of idiopathic or viral acute pericarditis
- the goal of therapy being the relief of pain and the resolution of inflammation :
  - Ibuprofen or aspirin has been most commonly used , does not alter the natural history of the disease.
  - High-dose aspirin (every 6 to 8 hours for 7 to 10 days followed by gradual tapering of the dose by 800 mg per week for 3 additional weeks)
  - excellent efficacy in patients with mainly idiopathic or presumed viral pericarditis.
  - Indomethacin 25 and ketorolac have also shown efficacy in treating acute pericarditis.
- In patients who do not respond to NSAID therapy in 1 week, an etiology other than idiopathic or viral pericarditis is likely.
- Aspirin is preferentially used in patients with acute pericarditis in the setting of myocardial infarction (the requirement for antiplatelet therapy; the anti-inflammatory actions of an NSAID other than aspirin may interfere with myocardial healing and scar formation) .

- Indomethacin should be avoided in patients with coronary artery disease because it decreases coronary blood flow.
- A proton pump inhibitor or another form of gastric protection should be provided in all patients treated with an NSAID.

b. Colchicine :

- Colchicine has been shown in observational studies to be effective in relieving pain in patients with acute pericarditis and in preventing recurrences.
- Routine use of colchicine in the treatment of acute pericarditis has been supported by the COPE (Colchicine for Acute Pericarditis)
- reduced symptoms at 72 hours and recurrence at 18 months, and prevent cardiac tamponade or pericardial constriction.
- The major adverse effect prompting discontinuation is diarrhea, less common adverse effects include bone marrow suppression, hepatotoxicity, and myotoxicity, Chronic renal insufficiency can lead to increased colchicine levels and appears to be the major risk factor for adverse effects.
- recommend for 4 to 6 weeks of colchicine therapy be considered in all patients with acute pericarditis, especially in patients who have not benefitted from NSAID therapy after 1 week.
- Colchicine should be avoided or used with caution in patients with severe renal insufficiency, hepatobiliary dysfunction, blood dyscrasias, and gastrointestinal motility disorders.

c. Corticosteroids :

- Although acute pericarditis appears to respond dramatically to corticosteroids, early use of corticosteroids has been associated with an increased risk of relapsing pericarditis in multiple studies.
- corticosteroid use was an independent risk factor for recurrence .
- corticosteroids should only be considered if the patient has clearly received no benefit from NSAID and colchicine therapy and a specific cause for pericarditis has been excluded.
- It is recommend the use of systemic corticosteroids as an initial treatment of acute pericarditis when the underlying cause is an immune-mediated disease , or with severe rheumatic carditis or post-pericardiotomy syndrome
- It is recommend slow tapering of high-dose prednisone (1 mg/kg per day) when corticosteroid treatment is indicated in acute pericarditis.
- Tapering should begin after approximately 2 to 4 weeks and only when the patient is asymptomatic and the serum C-reactive protein concentration has normalized.
- Slow tapering is often the key in preventing recurrence.
- Intrapericardial administration of corticosteroids has been effective in acute pericarditis, but its invasive nature limits its clinical utility.

d. Anti biotherapy : for bacterial etiology based on Lab results results , and tuberculosis .

e. PERICARDIOCENTESIS

- use of pericardiocentesis if purulent, tuberculous, or neoplastic pericarditis is suspected.
- With Pericardial fluid studies .
- Pericardiocentesis can also be performed for patients with persistent symptomatic pericardial effusions.

IV. RELAPSING PERICARDITIS :

A.Diagnosis :

- requires a documented first episode of acute pericarditis and evidence of recurrent pericardial chest pain plus one of the following :
  - Fever, pericardial friction rub, ECG changes typical of acute pericarditis , pericardial effusion on echocardiography, or an elevation in white blood cell count, erythrocyte sedimentation rate, or C-reactive protein concentration .
  - Cardiac CT can be used to evaluate pericardial thickness and pericardial effusions, which can be helpful in the diagnosis of recurrent pericarditis
  - Delayed gadolinium enhancement of the pericardium by CMR is a reliable and objective method to detect inflammation of the pericardium.
- The first symptoms of recurrent pericarditis usually occur within 18 to 20 months after the initial attack.
- The initial episode of acute pericarditis is usually more severe than subsequent episodes.
- Chest pain is usually sharp and progressive, worsens with recumbency, and is relieved by leaning forward.

- Most patients are well between attacks , however some patients have a more persistent or chronic course.

B. TREATMENT:

- Although constrictive pericarditis, myocardial disease, and tamponade are rare in patients with relapsing pericarditis.
- Incessant recurrences can severely impair quality of life in some patients.
- The goals of management should be symptomatic relief, prevention of recurrences, and restriction of physical activity.
- The underlying disease should be treated in recurrent pericarditis :
  - Idiopathic and viral relapsing pericarditis can be treated with aspirin , other NSAIDs (eg, ibuprofen, , and indomethacin,), or acetaminophen, alone or in combination.
  - Colchicine is effective in preventing relapses when given after the first episode of recurrent pericarditis.
  - colchicine can be administered to patients after the first episode of acute pericarditis but should be avoided or used with caution in patients with severe renal insufficiency, hepatobiliary dysfunction, blood dyscrasias, and gastrointestinal motility disorders. Starting dosages of 2 to 3 mg/d can be followed by maintenance dosages of 0.5 to 1 mg/d, which should be given for at least 1 year after the last episode of pericarditis.
  - It is recommend limiting the use of corticosteroids in the treatment of relapsing pericarditis .
  - Corticosteroids should be avoided when possible (may favor relapses), it is recommend limiting corticosteroid treatment to patients in whom

NSAIDs and colchicine are contraindicated or in whom recurrent pericarditis has an autoimmune or rheumatologic etiology.

- Although pericardiectomy could proposed for the relief of refractory relapsing pericarditis, though it does not always result in cessation of recurrences.
- However, pericardiectomy should be considered in patients with severe relapsing pericarditis that has not responded to adequate treatment.

V. CARDIAC TAMPONADE

a. Definition :

- Cardiac tamponade is characterized by the accumulation of pericardial fluid under pressure, as the pericardial effusion increases, the movement of the parietal pericardium decreases.
- Tamponade occurs when all cardiac chambers are compressed as a result of increased intrapericardial pressure to the point of compromising systemic venous return to the right atrium (RA).
- can be acute, subacute, regional, or characterized by low pressure.
- Acute tamponade is sudden, life-threatening if not treated promptly, and often associated with hypotension as well as chest pain and dyspnea.
- Cardiac tamponade should be considered in patients in cardiogenic shock, especially if they have increased jugular venous pressure or pulseless electrical activity.

b. Diagnosis :

- Physical Examination "Depending on the type and severity of tamponade, a variety of physical findings may be present:
  - Chest pain ,typically, substernal chest discomfort radiates up to the neck and jaw.
  - Atypical symptoms include shoulder discomfort, abdominal discomfort, or even nausea.
  - In patients with subacute tamponade, a prominent presenting symptom can be right upper quadrant pain due to hepatic venous congestion and peripheral edema.
  - Sinus tachycardia occurs in most patients as response to maintain cardiac output.
  - Pulsus paradoxus, is commonly found in tamponade and can be quantified by an inspiratory reduction in systolic blood pressure of greater than 10 mm Hg Pulsus paradoxus (predictive of the severity of cardiac tamponade).
  - A pericardial friction rub is not common.
  - Kussmaul sign is an elevation in the jugular venous pressure during inspiration and can be seen in tamponade, but not usually in the absence of pericardial constriction.
- Electrocardiography :
  - Sinus tachycardia,
  - low-voltage QRS complex,
  - and typical ECG findings in acute pericarditis
  - Electrical alternans is specific , but not very sensitive for cardiac tamponade.

- Electrical alternans reflects the swinging motion of the heart in pericardial fluid.

- Chest Radiography :
  - In acute tamponade, findings on chest radiography are usually normal
  - and the cardiac silhouette does not enlarge until at least 200 mL of pericardial fluid has accumulated.
  - as the pericardial effusion becomes larger, the cardiac shadow becomes globular on chest radiography
- Echocardiography :
  - The use of echocardiography in cardiac tamponade is a class I indication.
  - It is the mainstay of diagnostic .
- Cardiac CT and CMR are not usually needed if 2-dimensional and Doppler echocardiography are available.

c. TREATMENT :

- Acute cardiac tamponade with hemodynamic compromise requires urgent pericardiocentesis or surgical removal of pericardial fluid. Pericardiocentesis , is the most direct means to relieve cardiac tamponade: .
- If hemodynamically stable: careful hemodynamic monitoring with serial echocardiography and treatment of the cause of tamponade may be sufficient.
- In hypotensive patients :
  - volume expansion with saline, blood, plasma, and dextran can be used as a temporary measure.
  - Inotropic therapy is controversial in cardiac tamponade (endogenous inotropic stimulation is usually maximal in tamponade).

- Positive-pressure mechanical ventilation should be avoided (it further reduces cardiac filling).
- Evacuation of pericardial fluid in cardiac tamponade : by percutaneous catheter pericardiocentesis or surgical pericardiectomy.
- In patients with malignant effusions, percutaneous balloon pericardiotomy is an alternative approach .
- Percutaneous catheter pericardiocentesis is the treatment of choice in most patients and is less expensive and less invasive than surgery, while allowing for accurate hemodynamic measurement.
- pericardiocentesis is almost always performed under echocardiographic guidance.
  - The para-apical site was the most common entry site for pericardiocentesis and, in 89% of procedures, only 1 attempt at needle passage was necessary to gain access to the pericardial space.
  - The following tests should be performed on the pericardial fluid, as clinically indicated: Gram stain, bacterial cultures, acid-fast bacilli and culture, polymerase chain reaction, and cytology.
  - In the setting of aortic dissection, pericardiocentesis is relatively contraindicated, and an urgent surgical evaluation should be obtained.

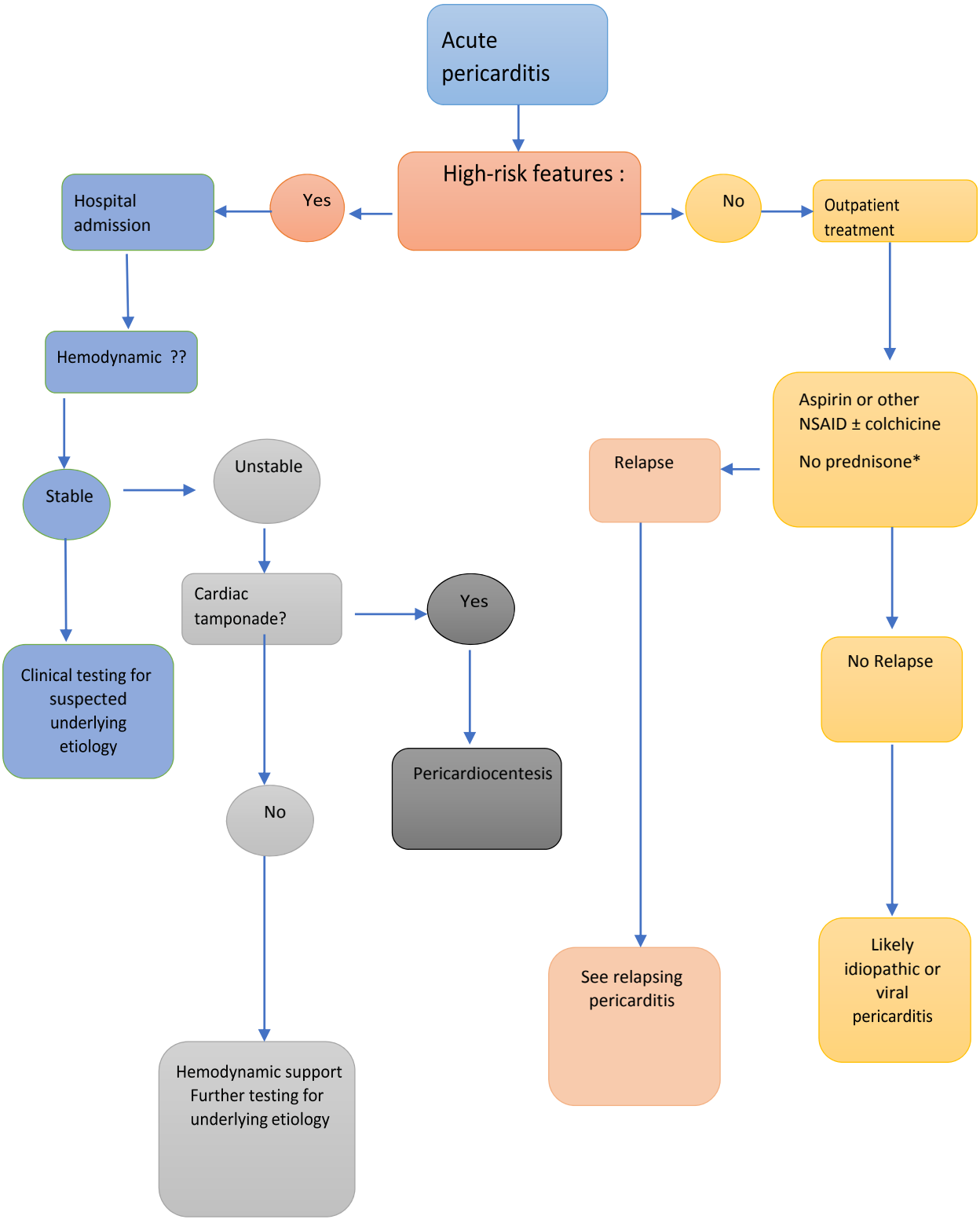

Figure 14 : Algorithm for decision in case of acute pericarditis (1)

- **For more reading :**

1- **Khandaker, M. H., Espinosa, R. E., Nishimura, R. A., Sinak, L. J., Hayes, S. N., Melduni, R. M., & Oh, J. K. (2010).** ***Pericardial Disease: Diagnosis and Management. Mayo Clinic Proceedings, 85(6), 572–593.***

2- **Doctor, N. S., Shah, A. B., Coplan, N., & Kronzon, I. (2017). Acute Pericarditis. Progress in Cardiovascular Diseases, 59(4), 349–359.**

3- **Tombetti, E., Giani, T., Brucato, A., & Cimaz, R. (2019).** ***Recurrent Pericarditis in Children and Adolescents. Frontiers in Pediatrics, 7.***

4- **"Myung Park, Mehrdad Salamat; "Park's Pediatric Cardiology for Practitioners ";" Seventh Edition";(2020).pages :271-273 ; "**

Chapter 17 : Acute Rheumatic Fever :

I. Introduction :

- Rheumatoid Arthritis (RA) is a systemic inflammatory autoimmune disease with a prevalence of 1% and with a female predominance .
- CAUSE :

1- ARF is believed to be an immunologic response that occurs as a delayed sequela of group A streptococcal (GAS) infection of the pharynx but not of the skin . The attack rate ARF after streptococcal infection varies with the severity of the infection, ranging from 0.3% to 3%.

2- Important predisposing factors include family history of rheumatic fever indicative of genetic disposition as well as low socioeconomic status (poverty, poor hygiene, medical deprivation) and age between 6 and 15 years (with a peak incidence at 8 years of age).

II. CLINICAL MANIFESTATIONS :

1. History :

- History of streptococcal pharyngitis, 1 to 5 weeks before the onset of symptoms, is common.
- The latent period may be as long as 2 to 6 months in cases of isolated chorea.
- Pallor, malaise, easy fatigability, and other history, such as epistaxis (5%–10%) and abdominal pain, may be present .

2. Major Manifestations :

a) Carditis (50%- 79%) :

1. Clinical presentation may be quite variable from the asymptomatic patients with characteristic heart murmur to the critically ill patients presenting in heart failure .
2. Tachycardia (out of proportion to the degree of fever) is common; its absence makes the diagnosis of myocarditis unlikely.
3. A heart murmur of MR or AR is almost always present.
4. Echocardiography :
   - Echocardiography and Doppler studies should be performed in all cases of confirmed and suspected cases of ARF.
   - it can determine the presence and severity of MR and AR more objectively than auscultation can.
   - Inclusion of echocardiography and Doppler findings can enhance correct diagnosis of acute rheumatic carditis, including those with subclinical carditis (The prevalence of subclinical carditis may reach as high as 50%.)

b) Arthritis (35%-66%) :

- Arthritis is the second most common manifestation of ARF (occurring in 35%-66%).
- Arthritis of ARF is typically a migratory polyarthritis, and the joints most frequently involved are large ones, including :
  - knees, ankles, elbows, and wrists.
- Swelling, heat, redness, severe pain, tenderness, and limitation of motion are common.
- If the patient was given salicylate-containing analgesics, these signs of inflammation may be mild or resolved.

- The arthritis responds dramatically to salicylate therapy; if patients treated with salicylates (with documented therapeutic levels) do not improve in 48 hours, the diagnosis of ARF probably is incorrect
- Generally, the arthritis in ARF runs a self-limited course, even without therapy, lasting about 4 weeks.

c) Sydenham's Chorea (10%–30%), :

- Sydenham's chorea or St. Vitus' dance , it occurs more often in prepubertal girls (8–12 years) than in boys.
- Sydenham's chorea is a neuropsychiatric disorder consisting of both neurologic (choreic movement and hypotonia) and psychiatric signs (e.g., emotional lability, hyperactivity, separation anxiety, obsessions and compulsions).
- It begins with emotional lability and personality changes. These are soon replaced (in 1–4 weeks) by the characteristic spontaneous, purposeless movement of chorea (which lasts 4–18 months) followed by motor weakness.
- The distractibility and inattentiveness outlast the choreic movements.
- The adventitious movements, weakness, and hypotonia continue for an average of 7 months (≤17 months) before slowly waning in severity.

d) Subcutaneous Nodules (0%–10%) :

- Subcutaneous nodules are found in 2% to 10% of patients, particularly in cases with recurrences;
- It is almost never present as a sole manifestation of rheumatic fever.
- They are firm, painless, nonpruritic, freely movable, swelling, and 0.2 to 2 cm in diameter.

- They usually are found symmetrically, singly or in clusters, on the extensor surfaces of both large and small joints, over the scalp, or along the spine.
- They are not transient, lasting for weeks, and have a significant association with carditis. Subcutaneous nodules are not exclusive to rheumatic fever.
- They occur in 10% of children with rheumatoid arthritis, and benign subcutaneous nodules have been described in children and adults. In adults, they occur with rheumatoid arthritis, systemic lupus erythematosus, and other diseases.

e) Erythema Marginatum (< 6%) :

- Erythema marginatum occurs in fewer than 10% of patients with ARF
- It is the unique, evanescent, pink rash seen with pale centers and rounded or serpiginous margin.
- They are most prominent on the trunk and the inner proximal portions of the extremities; they are never seen on the face. The rashes are evanescent, disappearing on exposure to cold and reappearing after a hot shower or when the patient is covered with a warm blanket.
- They seldom are detected in air-conditioned rooms.

3. Minor Manifestations :

a. **Polyarthralgia** refers to multiple joint pain without the objective changes of arthritis.
b. **Fever** (usually with a temperature of ≥[38.5°C is present early in the course of untreated rheumatic fever.
c. In laboratory findings, elevated acute-phase reactants : **elevated C-reactive protein [CRP] levels and elevated erythrocyte sedimentation rate [ESR]) are objective evidence of an inflammatory process.**

d. A prolonged PR interval on the **electrocardiogram (ECG) is** neither specific for ARF nor an indication of active carditis.

4. Other Clinical Features

a. Abdominal pain, rapid sleeping heart rate, tachycardia out of proportion to fever, malaise, anemia, epistaxis, and precordial pain are relatively common but not specific.
b. A positive family history of rheumatic fever also may heighten the suspicion

5. Evidence of Antecedent Group A Streptococcal Infection :

- Because other illness may closely resemble ARF, laboratory evidence of antecedent GAS infection is needed whenever possible, and the diagnosis is in doubt when such evidence is not available.
- The exception to this includes chorea, which usually has a long latent period and insidious onset of the illness. Any one of the following can serve as evidence of preceding infection according to a recent AHA statement:

a. Increased or rising anti-streptolysin O (ASO) titer or other streptococcal antibodies (anti-DNASE B) .
b. Positive throat culture for group A beta-hemolytic streptococcus .
c. A positive rapid group A streptococcus carbohydrate antigen test result in a child whose clinical presentation suggests a high pretest probability of streptococcal .

III. DIAGNOSIS :

- Acute rheumatic fever is diagnosed by the use of revised Jones criteria (see box 1). The criteria are three groups of important clinical and laboratory findings:
  1) five major criteria,
  2) four minor criteria, and supporting evidence of preceding GAS infection.
  3) three minor criteria in the presence of evidence of preceding GAS infection suffice.
- A diagnosis of ARF is highly probable :
  - If two major criteria or one major and two minor criteria
  - plus evidence of antecedent streptococcal infection are present
- The following tips help in applying the Jones criteria:
  a. The absence of supporting evidence of a previous GAS infection makes the diagnosis doubtful (except when chorea is present).
  b. Two major criteria are always stronger than one major plus two minor criteria.
  c. Polyarthralgia or a prolonged PR interval cannot be used as a minor criterion when using arthritis and carditis, respectively, as major criterion.
  d. The vibratory innocent (Still's) murmur is often misinterpreted as a murmur of MR and thereby is a frequent cause of misdiagnosis (or overdiagnosis) of ARF.
  e. The murmur of MR is a regurgitant-type systolic murmur (starting with the S1) caused by MR, but the innocent murmur is low pitched and an ejection type. A cardiology consultation and echocardiography and Doppler study during the acute phase will minimize the frequency of misdiagnosis.

f. The possibility of the early suppression of full clinical manifestations should be sought during the history taking. Subtherapeutic doses of aspirin or salicylate-containing analgesics (e.g., Bufferin, Anacin) may suppress full manifestations.

- Exceptions to the Jones criteria include the following two specific situations:

a) Chorea may occur as the only manifestation of ARF.

b) Indolent carditis may be the only manifestation in patients who come to medical attention months after the onset of rheumatic fever.

Table 4 : Revised Jones Criteria (3)

Major Criteria • **Carditis (clinical or subclinical)** • **Arthritis (polyarthritis only)** • **Chorea** • **Erythema marginatum** • **Subcutaneous nodules**	**Minor Criteria** • Polyarthralgia • Fever ≥38.5°C • ESR ≥60 mm/hr and/or CRP ≥3.0 mg/dL • Prolonged PR interval for age
Evidence of Preceding Group A Streptococcal Infection (Any One of the Following) • **Increased or rising ASO titer (or anti-DNASE B)** • **Positive throat culture for group A beta-hemolytic streptococci** • **Positive rapid group A streptococcal carbohydrate antigen**	
Diagnosis - **Initial ARF: Two major or one major + two minor** - **Recurrent ARF: Two major, 1 major + two minor, or three minor** - **Evidence of preceding GAS infection**	

IV. MANAGEMENT :

1. When ARF is suggested by history and physical examination, one should obtain the following laboratory studies:

- complete blood count,
- acute-phase reactants (ESR and CRP),
- throat culture,
- ASO titer (and a second antibody titer, particularly with chorea),
- chest x-ray films,
- and ECG.
- Cardiology consultation is indicated to clarify whether there is cardiac involvement; two-dimensional echo and Doppler studies are usually performed at that time.

2. Anti-biotherapy :

- Benzathine penicillin :
  - G, 0.6 to 1.2 million units intramuscularly, is given to eradicate streptococci.
  - This serves as the first dose of penicillin prophylaxis as well (see later discussion).
- In patients allergic to penicillin, erythromycin :
  - 40 mg/kg/day in two to four doses for 10 days, may be substituted for penicillin.

3. ARF is confirmed : one must educate the patient and parents about the need to prevent subsequent streptococcal infection through continuous antibiotic prophylaxis.

4. Bed rest :

- Bed rest of varying duration is recommended.
- The duration depends on the type and severity of the manifestations and may range from a week (for isolated arthritis) to several weeks for severe carditis.
- Bed rest is followed by a period of indoor ambulation of varying duration before the child is allowed to return to school.
- The ESR is a helpful guide to the rheumatic activity and therefore to the duration of restriction of activities.
- Full activity is allowed when the ESR has returned to normal, except in children with significant cardiac involvement.

Table 5 : General Guidelines for Bed Rest and Indoor Ambulation (3)

	Arthritis Alone	Mild Carditis	Mild Carditis	Severe Carditis
Bed rest	1–2 wk	3–4 wk	4–6 wk	As long as CHF is present
Indoor ambulation	1–2 wk	3–4 wk	4–6 wk	As long as CHF is present

5. Anti-inflammatory or suppressive therapy :

- Early suppressive therapy may interfere with a definite diagnosis of ARF by suppressing full development of joint manifestations and suppressing acute-phase reactants
- With salicylates or steroids should be started once the diagnosis is confirmed , but must not be started until a definite diagnosis is made :

a. For mild to moderate carditis :

- aspirin alone is recommended : 90 to 100 mg/kg/day in four to six divided doses.
- An adequate blood level of salicylates is 20 to 25 mg/100 mL.
- This dose is continued for 4 to 8 weeks, depending on the clinical response.
- After improvement, the therapy is withdrawn gradually over 4 to 6 weeks while monitoring acute-phase reactants.

b. For severe carditis:

- prednisone (2 mg/kg/day in four divided doses) for 2 to 6 weeks is indicated.
- The dose of prednisone should be tapered and aspirin started during the final week of prednisone to prevent rebound.

c. For arthritis :

- aspirin therapy is continued for 2 weeks and gradually withdrawn over the following 2 to 3 weeks.
- Rapid resolution of joint symptoms with aspirin within 24 to 36 hours is supportive evidence of the arthritis of ARF

6. Treatment of CHF includes the following :

a. Complete bed rest with orthopneic position and moist, cool oxygen

b. Prednisone for severe carditis of recent onset

c. Furosemide: 1 mg/kg every 6 to 12 hours, if indicated

d. Afterload reduction may be beneficial

7. Management of Sydenham's chorea:

a) Reduce physical and emotional stress and use protective measures as indicated to prevent physical injuries.

b) Give benzathine penicillin G:

- 1.2 million units, initially for eradication of streptococcus
- and also every 28 days for prevention of recurrence, just as in patients with other rheumatic manifestations.
- Without the prophylaxis, about 25% of patients with isolated chorea (without carditis) develop rheumatic valvular heart disease in 20-year follow-up.

c) Anti-inflammatory agents are not needed in patients with isolated chorea.

d) For severe cases, any of the following drugs may be used: phenobarbital (15–30 mg every 6–8 hours), haloperidol (starting at 0.5 mg and increasing every 8 hours to 2 g), valproic acid, chlorpromazine (Thorazine), diazepam (Valium), or steroids.

e) Results of plasma exchange (to remove antineuronal antibodies) and intravenous immune globulin therapy (to inactivate the effects of the antineuronal antibodies) are promising in decreasing the severity of chorea and they were better than prednisone .

f)

V. PROGNOSIS

- The presence or absence of permanent cardiac damage determines the prognosis. The development of residual heart disease is influenced by the following three factors.

1. Cardiac status at the start of treatment:
   - The more severe the cardiac involvement at the time the patient is first seen, the greater the incidence of residual heart disease.
2. Recurrence of rheumatic fever:

- The severity of valvular involvement increases with each recurrence.

3. Regression of heart disease:
   - Evidence of cardiac involvement at the first attack may disappear in 10% to 25% of patients 10 years after the initial attack. Valvular disease resolves more frequently when prophylaxis is followed.

VI. PREVENTION :

A. Primary Prevention :

- Group A streptococcal infection of the pharynx is the precipitating cause of rheumatic fever. Primary prevention of rheumatic fever is possible by appropriate antibiotic treatment of streptococcal pharyngitis in most cases. However, primary prevention is not possible in all patients because about 30% of the patients develop subclinical pharyngitis and therefore do not seek medical treatment. In addition, some symptomatic patients do not seek medical care. In these instances, rheumatic fever is not preventable.
- Throat culture or a rapid antigen detection test is required for the diagnosis of GAS pharyngitis. Streptococcal skin infection (impetigo or pyoderma) have not been proven to lead to ARF. After positive throat culture result for GAS, either oral penicillin V or intramuscular benzathine penicillin G is the treatment of choice, because it is cost effective, has a narrow spectrum of activity, and has long-standing proven efficacy, and GAS resistant to penicillin have not been documented. For individuals allergic to penicillin, cephalosporin, clindamycin, azithromycin, or clarithromycin may be given.

B. Secondary Prevention :

- An individual with a previous attack of rheumatic fever in whom GAS pharyngitis develops is at high risk of a recurrent attack of rheumatic fever
- . Prevention of recurrent rheumatic fever requires continuous antimicrobial prophylaxis rather than recognition and treatment of acute episode of streptococcal pharyngitis.

1- Who should receive prophylaxis? Patients with documented histories of rheumatic fever, including those with isolated chorea and those without evidence of rheumatic heart disease, must receive prophylaxis.

2- For how long? Ideally, patients should receive prophylaxis indefinitely. For patients who had ARF without carditis, the prophylaxis should continue for at least 5 years or until the person is 21 years of age, whichever is longer. Patients who have history of carditis or persistent valvular disease (clinical or echocardiographic evidence) should receive secondary prophylaxis for a longer period of time (Table 20.2)

3- Choice of antibiotics :

a. Benzathine penicillin G, 600,000 U units given intramuscularly every 28 days (not once a month) for children weighing less than 27 kg (60 lb) and 1.2 million units for children weighing more than 60 lb is the drug of choice.

b. Alternatively, penicillin V (250 mg twice a day, oral) or sulfadiazine (oral), 0.5 g once daily for children weighing less than 27 kg (60 lb) or 1.0 g once a day for children weighing more than 60 lb, is given.

c. For individuals allergic to penicillin and sulfadiazine, a macrolide or azalide may be given.

Table 6 : Recommended Duration of Secondary Rheumatic Fever Prophylaxis(3)

Category	Duration After Last Attack
Rheumatic fever with carditis and residual heart disease (persistent valvular disease)	10 yr or until 40 yr of age (whichever is longer)
Rheumatic fever with carditis but no residual heart disease (no valvular diseasea)	10 yr or until 21 yr of age (whichever is longer)
Rheumatic fever without carditis disease)	5 yr or until 21 yr of age (whichever is longer)

- **For mor reading :**

1. ***Carapetis, J. R., McDonald, M., & Wilson, N. J. (2005). Acute rheumatic fever. The Lancet, 366(9480), 155–168.***
2. **Webb, R. H., Grant, C., & Harnden, A. (2015).** ***Acute rheumatic fever. BMJ, h3443.*** **doi:10.1136/bmj.h3443**
3. ***"Myung Park, Mehrdad Salamat. "Park's Pediatric Cardiology for Practitioners "." Seventh Edition". (2020).pages :*** **282-287;"**

Chapter 18 : Pediatrics hypertension

I. Definition :

- The definition of hypertension in younger children is statistical, in which the patient's BP is compared with a compilation of approximately 50,000 BPs of normal weight children from ages 1 through 17 years , categorized by age, sex and height .
- For children under the age of 13 years , a normal BP is defined as a measurement that falls below the 90th percentile (matched for age, sex and height ;
  - elevated BP is defined as 90th or greater percentile but less than the 95th percentile;
  - stage I hypertension is defined as s BP that is greater than or equal to the 95th percentile;
  - stage II hypertension is defined as BP that is greater than or equal to the 95th percentile plus 12 mm Hg.
  - Reference tables for BP are used to find the 50th, 90th, 95th, and 95^{th} + 12 cut offs specific to the sex, age and height of the child. Additional normative tables with the 95th and 99th percentiles are available for patients 26 to 44 weeks postmenstrual age and for infants up to 1 year of age.
- In teens the newer thresholds used to define hypertension are static :
  - a normal BP defined as less than 120/80 mm Hg,
  - an elevated BP as greater than or equal to 120/less than 80 mm Hg ,
  - a stage 1 hypertension as greater than or equal to 130/ greater than 80 mm Hg.

- Stage 2 hypertension is defined as a BP of greater than or equal to 140/greater than or equal to 90 .

II. *Diagnosis* :

a- Clinical Presentation and Diagnosis Hypertension :

- can present with non specific symptoms (e.g., headache, fatigue); polyuria, polydipsia, enuresis, dehydration …) .
- commonly remains asymptomatic until the blood pressure reaches very high levels, at which point severe headache, blurry vision, fatigue, or confusion may develop
- It is therefore recommended that blood pressure be checked routinely at each well-child visit for patients >= 3 years of age, with screening for patients <3 years of age only if they have specific risk factors for hypertension.
- Blood pressure should be compared with age , sex , and height specific norms so that elevated blood pressure is not overlooked .
- The diagnosis of prehypertension can be made on the basis of the average of blood pressure measurements on a single occasion, while diagnosis of hypertension requires measurements on three separate occasions .
- Repeat blood pressure measurements increase precision and reproducibility of results, and taking at least three measurements per clinic visit is recommended .

b- Ambulatory Blood Pressure :

- Analysis of ABPM data in children should be done according to the American Heart Association guidelines as published in the 2014 update on ABPM in children and adolescents

Table 7 : New blood pressure classifications 2017 (1)

BP Classification	Children Aged 1–12 y (Percentile)	Everyone≥ 13 y Old (mm Hg)
Normotensive	<90th and <120/80	<120/<80
Elevated blood pressure	≥90th and <95th Or ≥120/80 mmHg , < 130/80	120–129/<80
Stage 1 hypertension	≥95th to < 95th +12 mmHg Or ≥ 130–139/80 –89 mmHg	130–139/80–89
Stage 2 hypertension	≥95th +12 mmHg Or ≥ 140/90	≥ 140/90

III. Treatment :

- The goals of treatment include achieving a systolic and diastolic BP of less than the 90th percentile in younger children and less than 130/80 mm Hg for children greater than 13 years old :

1 The first-line treatment for primary hypertension consists of non-pharmacologic therapy :

- Such as nutritional intervention and exercise , moderate decreases in sodium intake and a high potassium diet have been associated with improved BPs.

- The DASH diet, which is a diet high in fruits and vegetables and low in fat and sodium, has been found to be associated with significantly lower BPs compared with the BP in those receiving usual care.
- Additionally, at least 60 minutes of physical activity 3 times per week can confer modest reductions in BP.

2 The second -line treatment pharmacologic therapy :

- Indication:
  - For patients who are still hypertensive despite a 6-month trial of lifestyle modification,
  - who have symptomatic hypertension,
  - who have stage II hypertension,
  - or who have evidence end-organ disease.
- The initiation of antihypertensive medication should begin with lowest dose as monotherapy and titrated upward or with a second agent added every 2 to 4 until the goal BP is achieved (BP $<90^{th}$ percentile or $<50^{th}$ percentile if chronic kidney disease) :

  - Preferred agents include ACE inhibitors, angiotensin receptor blockers, calcium channel blockers, and diuretics, although no specific class has been shown superior as a first-line agent

  - Other classes of antihypertensives should be reserved for patients who remain hypertensive despite treatment with 2 or more of the preferred drugs.

  - Unless contraindicated, ACE inhibitors or ARBs should be first line in patients with diabetes or proteinuria chronic kidney disease .

  - African American children may require higher doses of ACE inhibitors owing to racial differences in response to ACE inhibitor

- Last, ACE inhibitors and ARBs are teratogenic; if used in adolescent females, these classes of medications require counseling over the teratogenic effects and may require prescription of oral contraceptive medication as appropriate.

Table 8 : Oral Antihypertensive Drugs (3)

Class	Drug	Dose	Dosing interval
Calcium-channel blocker	Amlodipine	Initial: 0.05–0.1 mg/kg/day, up to 5 mg/day Maximum: 0.6 mg/kg/day, up to 10 mg/day	Daily
	Extended-release nifedipine	Initial: 0.25–0.5 mg/kg/day, up to 60 mg/day Maximum: 3 mg/kg/day up to 120 mg/day	Daily–BID
	Other available drugs in this class include isradipine, felodipine, verapamil, and diltiazem		
ACE inhibitor	Captopril	Initial: 0.9–1.5 mg/kg/day up to 40 mg/day Maximum: 6 mg/kg/day	TID
	Enalapril	Initial: 0.08 mg/kg/day, up to 5 mg/day Maximum: 0.6 mg/kg/day, up to 40 mg/day	Daily–BID
	Lisinopril	Initial: 0.07 mg/kg/day, up to 5 mg/day Maximum: 0.6 mg/kg/day, up to 40 mg/day	Daily
	Other available drugs in this class include benazepril, fosinopril, and quinapril		
Angiotensin-receptor blocker (ARB)	Losartan	(Children > 6 years of age): Initial: 0.7 mg/kg/day, up to 50 mg/day Maximum: 1.4 mg/kg/day, up to 100 mg/day	

	Valsartan	Children 1–5 years of age, weighing C8 kg: Initial: 0.4 mg/kg/day Maximum: 3.4 mg/kg/day up to 40 mg/dose if < 18 kg, up to 80 mg/dose if >18 kg Children 6–16 years of age: Initial: 1.3 mg/kg/day up to 40 mg/day Maximum: 2.7 mg/kg/day up to 160 mg/day	Daily
	Other available drugs in this class include candesartan, irbesartan, and telmisartan		
Thiazide diuretics	Chlorthalidone	Initial: 0.3 mg/kg/day up to 12.5 mg/day Maximum: 2 mg/kg/day up to 50 mg/day	Daily
	Chlorothiazide	Initial: 10–20 mg/kg/day Maximum: Age < 2 years—375 mg/day Age 2–12 years—1000 mg/day Age>12 years—2000 mg/day	BID
	Hydrochlorothiazide	Initial: 1 mg/kg/day up to 25 mg/day Maximum: 3 mg/kg/day up to 50 mg/day	Daily–BID
Potassium-sparing diuretic	Spironolactone	Initial: 1 mg/kg/day up to 50 mg/day Maximum: 3.3 mg/kg/day up to 100 mg/day	Daily–BID
	Other available drugs in this class include triamterene and amiloride		

b-Blocker	Atenolol	Initial: 0.5-1 mg/kg/day up to 50 mg/day Maximum: 2 mg/kg/day up to 100 mg/day	Daily-BID
	Metoprolol tartrate	Initial: 1-2 mg/kg/day up to 100 mg/day Maximum: 6 mg/kg/day up to 200 mg/day	BID
	Metoprolol succinate (extended release)	Age > or = 6 years— Initial: 1 mg/kg/day up to 50 mg/day Maximum: 2 mg/kg/day up to 200 mg/day	Daily
	Propranolol	Initial: 1-2 mg/kg/day up to 80 mg/day Maximum: 4 mg/kg/day up to 640 mg/day	BID-TID
	Other available drugs in this class include bisoprolol/HCTZ		
a- and b-blocker	Labetalol	Initial: 1-3 mg/kg/day up to 200 mg/day Maximum: 10-12 mg/kg/day up to 1200 mg/day	BID
Direct vasodilator	Hydralazine	Initial: 0.75-1 mg/kg/day up to 25 mg/day Maximum: 7.5 mg/kg/day up to 200 mg/day	QID
	Minoxidil	Age < 12 year s: Initial: 0.1-0.2 mg/kg/day up to 5 mg/day Maximum: 50 mg/day Age > or =12 years : Initial: 5 mg/day Maximum: 100 mg/day	Daily
Peripheral a-blocker	Prazosin	Initial: 0.05-0.1 mg/kg/day up to 2 mg/day	TID

		Maximum: 0.5 mg/kg/day up to 20 mg/day	
	Other available drugs in this class include doxazosin and terazosin		
Central a-agonist	Clonidine	Initial: 5-10 Ig/kg/day up to 0.2 mg/day Maximum: 0.9 mg/day	q8 h-q12 h Patch: weekly
BID twice daily **HCTZ hydrochlorothiazide,** **TID three times daily,** **QID four times daily,** **q8 h every 8 h,** **q12 h every 12 h**			

- For mor reading :

1- **Guzman-Limon, M., & Samuels, J. (2019). Pediatric Hypertension. Pediatric Clinics of North America, 66(1), 45–57.**
2- **Flynn JT, Kaelber DC, Baker-Smith CM, et al. Clinical practice guideline for screening and management of high blood pressure in children and adolescents. Pediatrics 2017;140(3) [pii:e20171904].**
3- **Whelton, P. K., Carey, R. M., Aronow, W. S., Casey, D. E., Collins, K. J., Dennison Himmelfarb, C., Wright, J. T. (2017). 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: Executive Summary: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Hypertension, 71(6), 1269–1324.**
4- **Chobanian AV, Bakris GL, Black HR, et al. the National High Blood Pressure Education Program Coordinating Committee. Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. Hypertension**

Chapter 19 : Pulmonary Hypertension

I. Definitions and classification

- PH is defined as a mean pulmonary artery pressure (mPAP) ≥25 mmHg in individuals >3 months of age at sea level, diagnosed by cardiac catheterization. The mPAP in healthy people is 14 ± 3 mmHg, rarely exceeds 20 mmHg, and is relatively unchanged regardless of gender, age, or ethnicity.
- Note that the definition of PH does not include PVR(pulmonary veinous resistance); rather, it simply denotes an elevated PAP from any cause.

II. Diagnosis :

1. CLINICAL PRESENTATION :
   - Common symptoms of PH :
     - exertional dyspnea,
     - fatigue, weakness,
     - angina, presyncope, and syncope
     - Fluid retention leading to abdominal distention and ankle edema can develop with progressive RVF.
   - Physical findings may include :
     - left parasternal lift or retraction,
     - augmented second heart sound,
     - an RV third heart sound,
     - elevated jugular venous pressure with abnormal waveform,
     - low volume arterial pulses,

- hepatomegaly, ascites, peripheral edema, and a tricuspid regurgitant murmur.

2. Paraclinical :

a. Echocardiography :

- is the primary diagnostic tool to screen for the presence of PH and associated cardiac malformations
- and it is usually the only test for diagnosis in neonates with transient forms of PH.

b. Cardiac catheterization (gold standard).

- confirm the diagnosis, evaluate PH severity, and perform acute vasoreactivity testing (AVT).
- **A diagnosis of PH** is confirmed with mPAP $\geq$25 mmHg, and PAH is diagnosed with mPAP $\geq$25 mmHg, PAWP $\leq$15 mmHg, and PVRi $>$ 3 WU$\cdot$m^2. If PAWP is $>$15 mmHg, which signifies PH due to left heart disease, then a left heart catheterization is required to investigate the underlying etiology.

c. Other tests are indicated during the diagnostic workup and possibly routinely thereafter to supplement clinical decisions, including brain natriuretic peptide (BNP) or N -terminal (NT) proBNP as an indication of ventricular function, 6 -minute walk test to follow changes in exercise tolerance, imaging to assess underlying pulmonary pathology, cardiopulmonary exercise testing (CPET), polysomnography in those at risk for sleep disordered breathing, and cardiac magnetic resonance.

d- Cardiac magnetic resonance imaging (CMR) :

- It is recommend the use of CMR during diagnostic evaluation and routine follow up in those who do not require anesthesia.

Treatment :

- The approach to treatment is not the same across the various subsets of pediatric PH;
- We will focus on treatment of PAH, understanding that PAH-CHD has additional considerations that influence treatment.

1- The treatment strategy for pediatric PAH :
   - entails pulmonary arterial vasodilation,
   - treatment of RV failure,
   - avoidance of coronary ischemia and biventricular failure
   - and optimizing functional capacity and survival.
   - Underlying disease states that may exacerbate PH, such as obstructive sleep apnea, must be aggressively treated .

2- Many PAH-targeted pharmaceuticals are used as mono- or combination therapy in children, which underscores the importance of treatment in centers with specialized pediatric pulmonary hypertension programs.

3- Initiation of PAH pharmacotherapy depends on the diagnostic cardiac catheterization results and the child's risk stratification:

- Acute responders to AVT who are over 1 year of age :
   - oral calcium channel blocker therapy and observed closely for potential clinical deterioration as a result of the negative inotropic effects of calcium channel blockade.
- AVT non-responders or those who fail calcium channel blocker therapy are then risk stratified:

- Lower risk children may be initiated on oral therapy with endothelin receptor antagonists (ERA) or phosphodiesterase (PDE5) inhibitors. Addition of inhaled prostacyclin (iloprost, treprostinil) may be considered.
- Children who are high risk or experiencing acute deterioration on oral therapy are initiated on aggressive combination therapy, often including an intravenous or subcutaneous prostanoid (epoprostenol, treprostinil, iloprost, beraprost).

- Children with drug-refractory PAH and deteriorating functional status
  - should be assessed for definitive treatment with lung transplantation, which itself carries a high rate of morbidity and mortality
  - An atrial septostomy may be considered prior to lung transplant in children without current shunt; an ASD will augment LV preload in the setting of acute and chronic RV failure.

Figure 15: Algorithm for pediatric PAH. This algorithm applies to IPAH and HPAH (1)

Table 9: Commonly used pediatric pulmonary arterial hypertension-targeted therapies (1)

Medication Class	Medications	POSOLOGY
Calcium channel blockers	Diltiazem	Initial dose: 1.5–2 mg/kg/day in 3 divided doses Maintenance dose: 3–5 mg/kg/day in 3 divided doses Maximum adult dose: 240–720 mg/day
	Nifedipine	Initial dose: 0.6–0.9 mg/kg/day in 3 divided doses Maintenance dose: 2–5 mg/kg/day Maximum adult dose: 120–240 mg/day
	Amlodipine	Initial dose: 2.5–5 mg/day Maintenance dose: 2.5–5 mg/kg/day twice daily Maximum adult dose: 20 mg/day
Endothelin receptor antagonists (ERAs)	Bosentan	2 mg/kg bid 10–20 kg: 31.25 mg bid 20–40 kg: 62.5 mg bid > 40 kg: 125 mg bid After uptitration
	Ambrisentan	2.5/5/10 mg daily
Phosphodiesterase type 5 (PDE5) inhibitors	Sildenafil	*Oral* Initial dose: 0.5 mg/kg/dose Maintenance dose: 1 mg/kg/dose tid : < 20 kg 10 mg tid > 20 kg 20 mg tid *Intravenous* 0.4 mg/kg bolus over 3 h 1.6 mg/kg/day: continuous infusion
	Tadalafil	Preliminary studies suggest 1 mg/kg/day
Prostacyclin analogs (prostanoids)	Epoprostenol	Initial dose: 1–3 ng/kg/min Maintenance dose: 50–80 ng/kg/min
	Treprostinil	*Intravenous/subcutaneous:* Initial dose: 1.25–2 ng/kg/min Maintenance dose: 50–80 ng/kg/min *Inhaled:* Initial dose: 3 breaths (18 µg) 4 times per day Maintenance dose: 9 breaths (54 µg) 4 times per day
	Iloprost	Initial dose: 2.5 µg per inhalation 6–9 times per day Maintenance dose: 5 µg per inhalation Maximum 9 times per day

- For mor reading :

1- Hansmann, G. (2017). *Pulmonary Hypertension in Infants, Children, and Young Adults. Journal of the American College of Cardiology, 69(20), 2551–2569.*
2- Kovacs G, Berghold A, Scheidl S, et al. Pulmonary arterial pressure during rest and exercise in healthy subjects: a systematic review. Eur Respir J 2009; 34: 888 -894.
3- Latham, G. J., & Yung, D. (2018). Current understanding and perioperative management of pediatric pulmonary hypertension. Pediatric Anesthesia
4- Simonneau, G., Gatzoulis, M. A., Adatia, I., Celermajer, D., Denton, C., Ghofrani, A., … Souza, R. (2013). Updated Clinical Classification of Pulmonary Hypertension. Journal of the American College of Cardiology, 62(25), D34–D41.
5- Mandras, S. A., Mehta, H. S., & Vaidya, A. (2020). Pulmonary Hypertension: A Brief Guide for Clinicians. Mayo Clinic Proceedings, 95(9), 1978–1988.
6- Davidson LM, Berkelhamer SK. Bronchopulmonary Dysplasia: Chronic Lung Disease of Infancy and Long -Term Pulmonary Outcomes. Journal of clinical medicine 2017; 6.
7- Hansmann G, Apitz C, Abdul -Khaliq H, et al. Executive summary. Expert consensus statement on the diagnosis and treatment of paediatric pulmonary hypertension. The European Paediatric Pulmonary Vascular Disease Network, endorsed by ISHLT and DGPK.
8- Abman SH, Hansmann G, Archer SL, et al. Pediatric Pulmonary Hypertension: Guidelines From the American Heart Association and American Thoracic Society. Circulation 2015; 132: 2037 - 2099
9- McLaughlin VV, Archer SL, Badesch DB, et al. ACCF/AHA 2009
10- Hansmann G, Apitz C, Abdul -Khaliq H, et al. Executive summary. Expert consensus statement on the diagnosis and treatment of paediatric pulmonary hypertension. The European Paediatric Pulmonary Vascular Disease Network, endorsed by ISHLT and DGPK.
11- Moledina S, Pandya B, Bartsota M, et al. Prognostic significance of cardiac magnetic resonance imaging in children with pulmonary hypertension. Circ Cardiovasc Imaging 2013; 6: 407 - 414.
12- Ivy DD, Abman SH, Barst RJ, et al. Pediatric pulmonary hypertension. J Am Coll Cardiol 2013; 62: D117 -126.
13- Avitabile, C. M., Vorhies, E. E., & Ivy, D. D. (2020). Drug Treatment of Pulmonary Hypertension in Children. Pediatric Drugs. doi:10.1007/s40272-019-00374-2.

Chapter 20 : Neonatal and Pediatric Arrhythmias :

I. Introduction :

- Junctional Rhythm (normal) :
  - Junctional beats or rhythm can be found during phases of sinus arrhythmia and, for this reason, they are common in the pediatric population. On the ECG, we can observe
    1) a regular rhythm with narrow QRS (or QRS resembling the patient's normal QRS),
    2) heart rates between 40 and 100 bpm (according to the age), and
    3) P waves dissociated from or after each QRS (retrograde conduction).
- Sinus Arrhythmia :
  - On the ECG, an irregular rhythm can be observed, with gradual variations in PP intervals, a sinus P wave that precedes each QRS, and rates varying with phase of breathing (increase with inspiration and decrease with expiration).
  - During increased vagal tone, sinus pauses of various degree interrupted by escape beats and/or rhythms may be detected (escape beats may be of atrial, junctional, or ventricular origin).
- Wandering Pacemaker :
  - This terminology is used when the ECG shows an irregular rhythm with ongoing changes in P wave morphology, with associated changes in PP interval during more than 2 beats, often appearing during period of low heart rates.
  - Atrial ectopic rhythm is distinguished from wandering atrial pacemaker rhythm by its unchanging P wave axis/morphology.

II. PEDIATRIC ARRHYTHMIAS and Classification treatment :

A. TACHYARRHYTHMIAS :

1. Premature Supraventricular Beats :

- Generally, premature supraventricular beats are an idiopathic and clinically silent cardiac arrhythmia.
- it is origin from the atria or the AV junction and are diagnosed occasionally (sometimes during fetal life).
- Supraventricular extra beats, in neonates, can determine the so-called pseudo-bradycardia, when conduction to the ventricles is blocked, and usually disappears during the first year of life. This arrhythmia does not need to be treated.

2. Premature Ventricular Beats :

- Premature ventricular beats are usually idiopathic and not associated with symptoms.
- However, when they are documented, a cardiac disease or arrhythmias that are more complex must be excluded.
- Premature ventricular beats can be considered benign when they occur in normal heart as isolated beats, with 1 morphology, and are suppressed by exercise.
- In this case, they do not need any treatment and disappear spontaneously as the patients grows .

3. Paroxysmal Supraventricular Reentry Tachycardia :

- It is the most common arrhythmia in pediatric patients .
- 2 peaks of incidence: the first year of life and ages 8 to 12
- Often, preschool children can describe palpitations as “precordial pain”
- it can manifest with : weakness, dizziness, and syncope .
- Reentry tachyarrhythmias can have a heart rate from 180 to 340 bpm.
- In neonates, SVT can be frequent because it is initiated by atrial extra beats, or only by the rapid acceleration of sinus rhythm during feeding or crying.
- Usually , it is occurs in children with a structurally normal heart but, sometimes, it can be associated with an:

- Ebstein anomaly,
- mitral valve prolapse,
- ventricular septal defect,
- and congenitally corrected transposition of the great arteries.

- Clinical manifestations of this tachycardia are variable and usually females are more symptomatic than male.
- About its prognosis, AV nodal reentry tachycardia is a benign tachyarrhythmia and, nowadays, very safe. Effective ablation techniques exist for its treatment (such as cryoablation with 3-dimensional mapping system guide).
- Among the pediatric SVTs, there is a particular type of AV reentry tachycardia called permanent junctional reentry tachycardia,It represents 4% of all pediatric SVTs and it is due to the presence of an accessory pathway (usually on the right side of the heart, around the tricuspid annulus) capable of decremental retrograde conduction, In general, this is an incessant form of tachycardia very often responsible for left ventricular dysfunction.

- ECG :

- tracings of this SVT are characterized by negative P wave in inferior leads
- and an RP interval that is longer than the PR interval.

- Usually, permanent junctional reentry tachycardia onset is caused by an increase in sinus rate. Permanent junctional reentry tachycardia is often resistant to drug therapy and, for this reason, the only treatment may be transcatheter ablation (recurrence rate of 20%). Nevertheless, spontaneous resolution has been described as well.

➔ Therapy :

- Vagal maneuvers are effective in 70% of cases (diving reflex, Valsalva maneuver, carotid sinus massage, squatting position).
- When the SVT does not stop, antiarrhythmic drugs can be administered.
- When the hemodynamic condition is stable :
  - the first choice drug is adenosine fast bolus intravenously (IV) ; It can be repeated 3 times (100 mg/kg the first 2 times and then a double dose as a last attempt).
  - If adenosine is unsuccessful, 1C class drugs are recommended (flecainide 1.5–2 mg/kg in 3–5 minutes, propafenone 1.5 mg/kg in 3–5 minutes).
  - Amiodarone is used only in refractory cases or in patients with a reduced ejection fraction (5 mg/kg in 20 minutes followed by infusion of 10 mg/kg in 24 hours).
- In cases of severe heart failure or cardiogenic shock, synchronized external electric cardioversion (0.5–1.5 J/kg) or transesophageal atrial pacing should be used.
- In all forms of paroxysmal SVTs, antiarrhythmic prophylaxis should be started to avoid recurrences, using :

- flecainide (2–7 mg/kg/d in 3 doses),
- propafenone (10–15 mg/kg/d in 3 doses),
- amiodarone (loading dose of 10–20 mg/kg/d in 1–2
- administrations for 7–10 days; maintenance

4. Atrial Flutter :

- Atrial flutter is an intra-atrial macro-reentry tachycardia that can involve the whole atrium or just a part of it.
- The ECG is quite typical,:
  - with characteristic saw-tooth P waves.
  - in pediatric patients, it has very fast atrial rate (275–580 bpm) but functional block in the AV junction (more often 2:1) slows down the ventricular rate.
- Less than1/3 of cases, it is associated with the presence of accessory pathways.
- In contrast, atrial flutter is common in patients with congenital heart disease, in particular when right atrial hypertrophy or dilation is present.
- Therapy :
  - In neonates, if well-tolerated, cardioversion can be delayed because sometimes the arrhythmia terminates spontaneously after 24 to 48 hours (26% of cases).
  - For a persistent atrial flutter, electric or pharmacologic cardioversion using :
    a. amiodarone (5 mg/kg in 20 minutes) can be practiced.
    b. In cases of hemodynamic intolerance : the electric cardioversion is the first-line therapy.

- In general, in neonates with no other arrhythmic substrate (eg, accessory pathways) there are no recurrences.
- Instead, in older patients a prophylactic therapy is needed: 1C antiarrhythmic drugs associated with beta-blockers or, as an alternative, amiodarone.
- In patients weighing more than 30 kg, transcatheter ablation can be considered.

5. Automatic Supraventricular Tachycardias :

- These tachyarrhythmias are generally owing to enhanced phase 4 automaticity, with "warm up/ cool down" behavior, often with wide fluctuations in the atrial rate secondary to the autonomic tone.
- Can be paroxysmal or permanent, and isolated or associated with structural heart disease, also AV conduction can be variable.
- Automatic tachycardias are often associated with a heart rate only slightly higher than normal sinus rhythm, causing persistent weakness and reduced exercise tolerance , However, after a while, it can provoke heart failure.
- A characteristic clinical scenario can be "tachy-cardiomyopathy," which can regress through an effective rate control.
- An IV bolus of adenosine can cause persistence of atrial tachycardia with complete or incomplete AV block, this tool can be useful in making the differential diagnosis and to evaluate the morphology and axis of ectopic P waves.

a. Ectopic atrial tachycardia

- Ectopic atrial tachycardia is a rare tachycardia in pediatric patients .
- On the ECG :

- the P wave can be visible and different from the sinus rhythm
- Atrial rate during tachycardia ranges from 130 to 300 bpm, and it is influenced by autonomic tone variations.
- First- and second-degree AV blocks can be present .

b. Multifocal atrial tachycardia :

- Is more common in neonates and in males.
- It is usually idiopathic, although it can be associated with syncytial respiratory virus infection.
- Multifocal atrial tachycardia is characterized by 3 or more different P wave morphologies and it is often incessant.
- First and second-degree AV blocks cause variable PR and RR interval, and a relatively slow heart rate rarely driving to heart failure .

c. Junctional ectopic tachycardia :

- Junctional ectopic tachycardia is distinguished in 2 forms:
  - congenital junctional ectopic tachycardia, which is quite rare,
  - and postoperative junctional ectopic tachycardia, which occurs after surgery for a congenital heart defect involving the AV junction (tetralogy of Fallot, ventricular septal defect, AV canal, truncus arteriosus, etc).
- Both forms are associated with high mortality and morbidity.
- On the ECG :
  - AV dissociation is generally present, as with ventricular tachycardia, but with a narrow QRS.
  - However, in neonates and infants, a 1:1 ventriculo-atrial retro-1conduction with negative P waves in inferior leads can be possible owing to a lower effective refractory period of AV node in this particular patients.

- The heart rate is between 140 and 370 bpm, and it can change with autonomic changes and body temperature .

d. Therapy

- Automatic tachycardias owing to an enhanced automatic activity cannot be terminate by pacing maneuvers.
- Pharmacologic therapy is usually effective, with the exception of idiopathic junctional ectopic tachycardia, which can be resistant to many drugs, and sometimes rate control is the only possible target to reach.
- In case of a stable hemodynamic state:
- first choice drug are beta-blockers (propranolol, nadolol, metoprolol);
- as an alternative class 1C antiarrhythmic drugs can be used (flecainide, propafenone).
- In cases of reduced ejection fraction or resistance to other antiarrhythmic drugs:
- the use of amiodarone is suggested.
- Transcatheter ablation can be effective in 80% to 85% of the cases and can be performed at any age when necessary or, electively, when the patient weights more than 20 kg.
- Cryoablation is suggested as a first-line strategy for junctional ectopic tachycardia, because radiofrequency transcatheter ablation can determine more easily damage to the His bundle with consequent need of PMK implant.

6. Ventricular Tachycardia :

- VT is rare in pediatric patients .
- It can be idiopathic or an expression of a structural heart disease .

- Secondary forms are more frequent than idiopathic ones.
- Idiopathic VTs are generally associated with a benign prognosis.
- In contrast, for VTs that are an expression of a structural disease, the prognosis depends on the primary disease.
- The ECG shows typical signs of ventricular tachycardias:
  - a large QRS, QRS axis different from the sinus rhythm,
  - AV dissociation, fusion, and capture beats.
- An echocardiogram, Holter monitoring, exercise stress testing, and serum electrolytes check are indicated for all patients. In some cases, electrophysiologic study and more advanced imaging techniques are needed.
- Therapy :
  - If symptoms are severe or in cases of heart failure, synchronized electric cardioversion (or a DC shock for ventricular fibrillation) must be delivered (3–7 J/kg).
  - Then, pharmacologic therapy to prevent recurrences can be started:

→ lidocaine (1 mg/kg in bolus to repeat if necessary every 5 minutes, followed by infusion of 20–50 mg/kg/min),

→ magnesium sulfate (30–50 mg/kg in bolus),

→ and/or amiodarone.

  - When the tachycardia is hemodynamically well-tolerated, amiodarone is the drug of choice in case of a reduction in ejection fraction.
  - If the ejection fraction is preserved : propafenone, flecainide, sotalol, propranolol, nadolol, and metoprolol can be used alone or concomitantly.
  - VTs can be treated by transcatheter ablation in case of refractoriness to drug therapy or in older patients (weight >30 kg or in patients after puberty .

a. Neonatal ventricular tachycardia

- Usually, it does not require any treatment and it tends to disappear spontaneously after the first year of life.
- However, when VT is secondary to cardiac disease, it can be malignant, with a high and variable heart rate, and it can cause heart failure. Thus, it requires drug therapy, often combining different drugs, or surgical or transcatheter treatment.

b. Ventricular tachycardia

- originating from the right ventricle VT originating from the right ventricle is the most frequent type of VT.
- From a clinical point of view, these tachycardias can be or not be associated with symptoms (from palpitations to syncope).
- They are usually due to a triggered activity, but sometimes increased automaticity or reentry can be responsible for the cardiac arrhythmia.
- The ECG shows a left bundle branch block and inferior axis.
- This VT can be paroxysmal (in this case, it is usually triggered by a physical activity), incessant, or iterative.
- The paroxysmal form is usually present in short runs of VT at 130 to 150 bpm, suppressed by an increase in sinus rhythm, not associated with symptoms, and carries a good prognosis.
- The incessant form causes longer runs of VT at heart rate greater than 150 bpm, which can cause heart failure.
- This form is treated by drugs (beta-blockers, class 1C, class III antiarrhythmic drugs) or by transcatheter ablation.

c. Fascicular ventricular tachycardia :

- a Fascicular VT originates from the inferior/septal wall of the left ventricle, sometimes from the inferior-posterior portion of the left bundle branch.
- It shows right bundle branch block QRS complexes with superior axis (more rarely inferior axis) and a heart rate of 120 to 250 bpm.
- It usually occurs as a paroxysmal arrhythmia, during the second to fourth decades of life, and more frequently in men. Often, fascicular tachycardia is triggered by physical activity or emotion.
- When it is not associated with symptoms, therapy is not necessary because the prognosis is good. When therapy is needed, verapamil is the first choice drug; betablockers, class 1C, 1B, class III drugs, or transcatheter ablation can be used.

B. Bradycardia:

- In pediatric patients, a diagnosis of bradycardia depends on the age.
- In general, bradycardia is defined, at rest and awake, as a heart rate of:
  - less than 100 bpm in children up to 3 years old,
  - less than 60 bpm in patients 3 to 9 years old,
  - less than 50 bpm in patients 9 to 16 years old,
  - and less than 40 bpm for patients older than 16 years.
- During sleep, these cutoffs are reduced by 15% to 20%. :

1. Atrioventricular Block :

- AV block is an arrhythmia owing to a disorder in AV conduction :

a. First-degree AV block is characterized by a prolongation of the AV conduction (PR interval on ECG) over 17 to 20 ms, according to the patient's age.

b. Second-degree AV block :

- (Mobitz 1) consists of a progressive prolongation of the PR interval until a P wave is blocked and not followed by a QRS.
- Second-degree AV block (Mobitz 2) is an intermittent and sudden block in the AV conduction (suddenly P waves are not followed by QRS).

c. In third-degree AV block, there is a complete interruption of the AV conduction so that P waves are independent from QRS complexes, which derive from a junctional or ventricular escape rhythm.

- AV block can be isolated or associated with a congenital heart disease (25%–50%).
- First-degree and second-degree Mobitz 1 AV block are clinically silent and are discovered occasionally.
- Second-degree Mobitz 2 and third-degree AV block can be asymptomatic, symptomatic (weakness, presyncope, or syncope), or associated with heart failure.
- Third-degree AV block can be congenital, and is sometimes associated with congenital heart disease (congenitally corrected transposition of the great arteries or univentricular heart).
- In 70% to 80% of congenital isolated AV block, maternal autoantibodies (SSA/Ro and SSB/La) cross the placenta between the 16th and 23rd weeks of gestation, damaging the fetal heart conduction system.

- Diagnosis is based on ECG, ECG Holter monitoring, event recorder devices, and implantable loop recorders. Echocardiography, exercise stress testing, and electrophysiologic study can complete the diagnostic process and prognostic stratification.

➔ Therapy :

- First-degree and second-degree AV block do not necessitate any therapy.
- Mobitz 2 and third degree AV block :
  - require pacemaker implantation in the neonate if the heart rate is less than 55 bpm in a structurally normal heart or less than 70 bpm if a congenital heart disease is present.
  - Pacemaker implantation is also recommended if a large QRS escape rhythm or ventricular dysfunction is present. In neonates, the implant is epicardial.
  - The preferred pacing site is the left ventricle apex and, if body dimension allows, dual-chamber pacing is preferred.
  - In children weighing more than 20 kg, a transvenous implant can be performed, preferably choosing as pacing sites the right atrial appendage and the right ventricle septum.

2. Sinus Atrial Node Dysfunction :

- Sinus atrial node dysfunction includes many different brady-arrhythmias, namely, sinus bradycardia, sinus pauses, and junctional bradycardia.
- ECG criteria for the diagnosis of sinus node dysfunction include sinus bradycardia, sinus pauses of greater than 3 seconds, and a slow escape rhythm.
- Some other arrhythmias may be wrongly interpreted as sinus node dysfunction include a second-degree AV block 2:1, bigeminal atrial extra beat

blocked, and a complete AV block when atrial and ventricular rate seem synchronous.

- Sinus atrial node dysfunction can be due to :

  (1) noncardiac causes (neurologic or metabolic disorders) or

  (2) intrinsic anomalies of sinus node function.
- Sinus bradycardia, sinus pauses, and junctional escape beats can occur in 20% to 90% of normal neonates, and more often in preterm or low weight babies.
- In neonates, sinus pauses of 800 to 1000 ms can be present, but pauses of longer than 2000 ms are considered pathologic.
- A junctional rhythm can be present in healthy neonates as well.
- Transient bradycardias and QT interval prolongation (470 ms) can be the result of a stressful delivery,
- but usually these forms normalize in 48 to 72 hours A secondary sinus bradycardia in a neonate can be consequence of sepsis, central nervous system anomalies, hypothermia, hypopituitarism, intracranial hypertension, meningitis, maternal assumption of drugs, obstructive icterus, hypothyroidism, electrolytes or metabolic alterations, maternal autoimmune diseases.
- Sinus atrial node dysfunction can be associated with congenital heart disease in the natural history (eg, atrial septum defect, AV canal defect, Ebstein anomaly, and a single ventricle) or, more often, after heart surgery (eg, Fontan, Mustard, and Sening operations).
- Be completely asymptomatic or may suffer from weakness, pallor, presyncope/syncope, or heart failure. Parents should be very careful to recognize symptoms that sometimes can be very sneaky.

- If acute support is needed :
  - atropine (0.02– 0.04 mg/kg IV),
  - isoproterenol (0.02–0.05 mg/kg/ min),
  - adrenaline (0.01 mg/kg IV),
- or, if necessary, external transthoracic or transvenous pacing are suggested. When associated with symptoms, pacemaker implantation is among the class 1 indications.

➢ **For mor reading :**

1= Drago, F., Battipaglia, I., & Di Mambro, C. (2018). ***Neonatal and Pediatric Arrhythmias. Cardiac Electrophysiology Clinics, 10(2), 397–412***

2= **Jaeggi, E., & Öhman, A. (2016).** ***Fetal and Neonatal Arrhythmias. Clinics in Perinatology, 43(1), 99–112.***

Chapter 21 : Malaise in infants

I. Introduction :

- Le malaise : is a feeling of general discomfort, uneasiness, or pain, and often the first sign of an infection or other disease.
- the word has existed in French since at least the 12th century.
- The term is often used figuratively in other contexts.
- Malaise is a feeling of being unwell, having general discomfort, uneasiness in one's bodily health or having pain, overall weakness, and is often the first indication of an infection or the onset of an illness or disease.
- Infant with malaise is a frequent reason for consultation in pediatric emergencies.
- Infants <6 months of age are the most affected, with a predominance of male .
- A serious malaise of the infant is an unexpected and sudden accident, causing modifications of the tone and / or the coloring of the integuments and / or the respiratory rhythm, with or without loss of consciousness.
- The infant is usually hospitalized for at least 24-48 hours after a recent and authenticated severe illness.
- This makes it possible to order additional examinations on a systematic basis or even others guided by clinical data, to monitor short-term progress, and to reassure parents.

II. Diagnosis of Malaise :

a. The Malaise is defined as an unexpected and brutal accident associating to varying degrees:
   - changes in tone: hypotonia, hypertonia;

- changes in the color of the integuments: pallor, cyanosis;
- with or without modification of the respiratory rhythm: bradypneas, tachypnea , apneas;
- with or without loss of consciousness.

b. The description of the malaise is often reported by the parents, the only witnesses to the episode. It is important for the doctor to translate their verbal semiology ("it has turned all blue ... soft ..."), and to identify as such the onset of genuine malaise in the infant.

c. The functional signs reported are transient, and the first clinical examination is usually normal.

- History is essential, both to assess the severity of the malaise and its cause.
- NB: The malaise is a sometimes severe symptom of which it is important to specify the cause

III. Etiologic Diagnosis:

A. History

- **Family history :**
  - Early death, malaise , heart diseases , etc …
  - Familial vagal context .
  - Consanguinity.
- **Personal history:**
  - Course of pregnancy, prematurity;
  - Gastroesophageal reflux disease , another known pathology;
  - Psychomotor development, vaccinations.
- **Lifestyle and entourage**:

- sleeping arrangements, food.
- family environment (smoking, mistreatment), infectious contagion.

- **Sociological description of the malaise** : before / during / after :

1. Before :
   - Context: taking a bottle or changing (GERD), meals (foreign body), bedtime, sleep
   - Environment: witnesses, place, position of the child
   - Prodromes: fever and / or infectious syndrome, digestive disorders, behavior modification
2. During The malaise :
   - Functional signs of orientation
   - Possible signs of clinical severity
   - Chronology, duration of symptoms
3. After :
   - Recovery: spontaneous or assisted, fast or slow
   - Follow-up: immediate stabilization or recurrence
   - Time elapsed between the episode and the consultation

B. Clinical examination

- The clinical examination must be complete, with in particular : the search for respiratory sounds, hematomas, bruises, retrognathism, ogival palate.
- The child is observed during sleep and during a milk meal (sucking-swallowing).
- This examination is most often normal at a distance from the episode (at the time of the consultation); which does not exclude any cause, especially neurological.

C. Paraclinical investigation :

- NB: Take a capillary blood sugar level on arrival.
- Systematic paraclinical examinations :

1. Blood test (BS)
   - Capillary and then venous glycemia
   - NFS-platelets
   - CRP, PCT (if available)
   - Ionogram blood test ,+ serum creatinine, urea .
   - Calcemia , transaminases
   - ± lactates (if clinical severity)
2. Others :
   - ECG with corrected QT measurement .
   - Chest x-ray (face) .
   - Urine dipstick .
   - No additional examination (apart from examinations on the child's arrival in the emergency room) should be prescribed systematically. The etiological paraclinical investigation should be guided by anamnestic and clinical data.

⇨ In case of referral to a neurological cause, discuss:

- ammonia and blood gas + lactates (if possible upon admission);
- EEG;
- brain imaging: ETF, CT;
- fundus .
- A cardiac Holter is indicated in case of:
  - existence of ECG abnormalities (arrhythmias, conduction disturbances);
  - recurrence of malaise without a found etiology.

IV. The Causes :

- It is important to "prioritize" these causes according to their frequency and clinical data.
- Causes of severe malaise in an infant

1. Gastroesophageal reflux disease (GERD)
2. Acute pain
   - Esophagitis
   - Acute intussusception
   - Myocardial ischemia
3. High mechanical obstructive causes
   - Obstructive rhinitis
   - Vomiting, false routes (gluttonous baby, pipette medication)
   - Inhalation of foreign body (mobile)
4. Neurological causes
   - Convulsions
   - Intra- or peri-cerebral hemorrhages, shaken children syndrome
5. Infectious causes
   - Apneas: bronchiolitis (RSV), whooping cough (B. pertussis), influenza, adenovirus
   - Severe sepsis
6. Rare causes
   - Cardiac: supraventricular tachycardia, long QT syndrome, malformative heart disease
   - Metabolic: hypoglycemia, hypocalcemia, abnormality of β-oxidation of fatty acids

- Poisoning: CO, medication, vaccine
- Munchhausen syndrome
- Mechanical: asphyxia by facial burial, tracheomalacia, fistulas

V. Malaise in pediatric cardiology :

- The following causes should be searched and managed :

A. Malaise caused by acute hypoxia:

1. Fallot Malaise
   - They occur in an infant, between 2 and 12 months, with cyanogenic heart disease with pulmonary stenosis, most often tetralogy of Fallot.
   - Their appearance does not depend on the degree of cyanosis. They are due to an extreme infundibular reaction, most often during exertion, responsible for a sudden drop in pulmonary flow and as a consequence of a decrease in left ventricular filling and deactivation of the heart pump.
   - Anything that promotes tachycardia or increases oxygen demand can trigger malaise :
     - fever, anger, agitation, pain ...
   - Most often resolving without sequelae, they can sometimes be responsible for death or a neurological accident.
   - Most of the time, the malaise takes place in two phases, one prodromal tonic, quite quickly followed by a hypotonic phase, constituting the real malaise :
     - tonic phase: restlessness, crying, cyanosis and tachycardia;
     - hypotonic phase: gray complexion with cyanosis and pallor, polypnea (com-thought metabolic acidosis), tachycardia with attenuation or

disappearance of the breath, hypotonia with decreased vigilance and moaning, sometimes convulsions.

- Recovery is gradual, with the child falling asleep and remaining abnormally calm.
- The malaise is an indication for surgery; in the meantime, the child is usually placed on oral beta-blockers (Avlocardyl'i ": approximately 3 mg / kg in 3 doses, for an infant).

2. Malaise on exertion :

- A malaise in an adrenergic context must always be the subject of the most complete assessment possible.
- Examinations to be performed:
  - ECG
  - Cardiac ultrasound
  - Holter ECG
  - Stress test
- Etiology :

  a) Electric:
  - Long QT syndrome
  - Catecholergic Ventricular Tachycardia
  - Syndrome Brugda

  b) Mechanical causes:
  - obstructive cardiomyopathy;
  - aortic or pulmonary obstacles

  c) Ischemic causes:
  - birth defect of coronary artery;
  - sequela of Kawasaki disease.

B. Malaise at rest

- It is most often vagal malaise , usually triggered by emotion, heat, pain or digestive problems.
- The ECG will look for sinus variability suggestive of vagal hypertonia.
- A Holter recording will confirm the alternation of phases of acceleration and slowing down of the heart rate.
- A tilt test will look for orthostatic hypotension.

VI. Management :

A. Hospitalization:

⇨ Any infant with an authenticated and recent malaise (≤ 24 hours) must be hospitalized for at least 24–48 hours.

⇨ This maintenance in observation, even for a short period, aims to:

- treat urgently a cause of vital distress (exceptionally);
- continue the etiological investigations;
- monitor the infant with cardiorespiratory monitoring;
- ensure good clinical progress and reassure parents.

B. Preventive measures :

1- Identifying and treating the cause of the malaise is of major prognostic interest.

2- The prognosis for malaise is that of the underlying condition, which should be treated to prevent recurrence.

3- In all cases, parents should have understood the pathophysiological mechanisms of the event, the cause retained and the treatment prescribed.

4- The sleeping conditions of the child will also be checked (supine).

5- Support from parents is essential.

6- They must be reassured in the event of a benign and / or treatable pathology .

7- . Support measures are essential in the event of notification of a rare but severe pathology (eg: heart rhythm disturbances).

8- When the causal condition has not been identified, the indication for cardiorespiratory monitoring at home should be discussed on a case-by-case basis, the current indications of which are exceptional:

- severe malaise occurring without an identified cause, particularly if it recurs;
- family anxiety related to a history of NID.

- **For more reading :**
  1 :http://campus.cerimes.fr/media/campus/deploiement/pediatrie/enseignement/malaise_grave/site/html/1.html
  2 : https://en.wikipedia.org/wiki/Malaise
  3 : https://me-pedia.org/wiki/Malaise
  4: "Alain Batisse, Marilyn Lévy "; " Practical pediatric cardiology";" 3rd edition"; (2008): Pages: 7 – 8 ; "

SUMMARY :

Introduction:

- Cardio-pediatric therapy takes a very important place in daily pediatric practice.
- Its therapeutic modalities are well codified with precise indications for each heart disease, with the objective of healing and preserving the functional integrity of the heart.

Materials and methods :

- Our work is concerned with therapeutics in cardio-pediatrics.
- This is a manual and Android guide to the following heart disease therapy:

1. Cyanotic Neonate.
2. The Child with Chest Pain
3. Common Arterial Trunk
4. Ebstein's anomaly
5. Tetralogy of Fallot
6. COMPLETE TRANSPOSITION OF THE GREAT ARTERIES
7. Coarctation of the aorta
8. Atrial Septal Defect
9. Ventricular Septal Defects
10. Patent ductus arteriosus
11. Patent Ductus Arteriosus in Preterm Neonates
12. Atrioventricular canal
13. Pulmonary stenosis
14. Infective Endocarditis
15. MYOCARDITIS

16. ACUTE PERICARDITIS
17. Acute Rheumatic Fever
18. Pediatrics hypertension
19. Pulmonary Hypertension
20. Neonatal and Pediatric Arrhythmias
21. Malaise in infants

Objectives :

The aim of this work is:

- Guide and facilitate therapeutic prescription in cardio-pediatrics.
- Avoid possible therapeutic errors during prescription by using our Android application.

RÉSUMÉ :

Introduction:

- Les thérapeutiques en cardio-pédiatrie prend une place très important dans le pratique quotidien pédiatrique
- Ses modalités thérapeutiques sont bien codifiés avec des indications précises pour chacune de cardiopathie , avec pour objectif la guérison et la préservation de l'intégrité fonctionnel de cœur

Matériels et méthodes :

- Notre travail s'intéresse les thérapeutique en cardio-pédiatrie .
- Il s'agit d'une guide manuel , et Android des thérapeutique des cardiopathies suivant :

1. Cyanotic Neonate .
2. The Child with Chest Pain
3. Common Arterial Trunk
4. Ebstein's anomaly
5. Tetralogy of Fallot
6. COMPLETE TRANSPOSITION OF THE GREAT ARTERIES
7. Coarctation of the aorta
8. Atrial Septal Defect
9. Ventricular Septal Defects
10. Patent ductus arteriosus
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15. MYOCARDITIS
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19. Pulmonary Hypertension
20. Neonatal and Pediatric Arrhythmias
21. Malaise in infants

Objectif :

Le but de ce travail est :

- Orienter et faciliter la prescription thérapeutique en cardio-pédiatrie .
- Éviter les éventuels erreurs thérapeutiques pendant la prescription par l'utilisation de notre application Android .

The Link to download our application Therapeutic in Cardio pediatrie :

https://play.google.com/store/apps/details?id=com.husam.cardiopediatrie

Royaume du Maroc المملكة المغربية

كلية الطب والصيدلة
ⵜⴰⵖⵍⵓⵍⵉⵜ ⵏ ⵜⵓⵙⵙⵉⵔⵉⵜ ⴰ ⵜⵓⴰⵅⵅⵓⵜ
FACULTÉ DE MÉDECINE ET DE PHARMACIE

ⵜⴰⵙⴷⴰⵡⵉⵜ ⵙⵉⴷⵉ ⵎⵓⵃⴰⵎⴻⴷ ⴱⵏ ⵄⴱⴷⵍⵍⴰⵀ
Université Sidi Mohamed Ben Abdellah

سنـــة 2021

أطروحة رقم 21/257

العلاجات في طب الاطفال القلبي في كتيب يدوي وتطبيق اندرويد

الأطروحة

قدمت و نوقشت علانية يوم 2021/07/06

من طرف

السيد حسام دراغمة

المزداد في 1993/06/05 بفلسطين

لنيل شهادة الدكتوراه في الطب

الكلمات الأساسية

امراض القلب - طب الاطفال - العلاجات - الوصفات الطبية

اللجنة

السيد سمير عثماني..... الرئيس و المشرف
أستاذ في علم أمراض الأطفال

الأعضاء

السيدة سناء شوكي.....
أستاذة في علم أمراض الأطفال

السيدة سناء أبورزاق.....
أستاذة في علم أمراض الأطفال

السيدة فاطمة الزهراء السويلمي.....
أستاذة في علم أمراض الأطفال