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**CARDIOLOGY**

# PEDIATRIC ELECTROCARDIOGRAM - EASY STEPS TO ANALYSE

***Anita Khalil***

**Abstract:** *With the development of pediatric emergency, pediatric and neonatal intensive care units, the need for understanding ECG has tremendously increased. Many critical derangements like arrhythmia and electrolyte disturbances have to be recognized and resolved in time without any delay. ECG rhythm plays a vital role in resuscitating a child in cardiac arrest. It also has a small but important role in the initial diagnosis and management of conditions like myocarditis and scorpion sting causing myocardial involvement. A pediatrician working in acute care areas should be familiar with ECG rhythm strip, as pediatric cardiology consultation may not be available at all times and places. Hence, ECG interpretation adds strength to the skills of pediatrician.*

**Keywords:** *Electrocardiogram, Children.*

An electrocardiogram (ECG) is an investigation which records changes in the electrical activity of the heart and the information provided by the ECG is not readily obtained by any other method. ECG plays an important role in arrhythmia detection and management. It supplements the information required for diagnosis along with clinical examination and chest radiography.

## Cardiac conduction system (Fig.1)

Specialized conducting tissues in heart are sinoatrial node and atrio-ventricular node.

a) Sinoatrial (SA) node - the pacemaker, which is a cluster of automatic cells near the junction of superior vena cava (SVC) and right atrium (RA). The tissue exhibits automaticity, and the rate of impulse generation is fastest in SA node, which normally dictates the rate and rhythm of heart beat. SA node is influenced by vagus (cardio-inhibiting) and sympathetic (cardio-stimulating) nerves.

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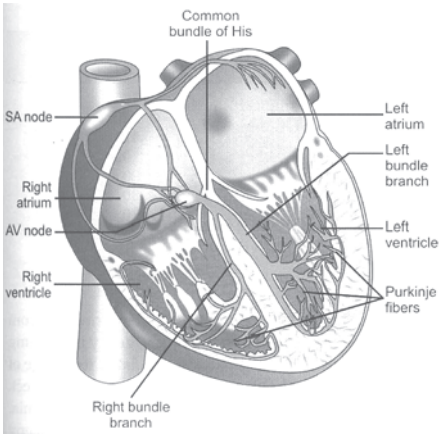



**Fig.1. Normal conduction pathway**

b) Atrio-ventricular (AV) node - situated in anteromedial portion of RA, anterior to coronary sinus. The impulse generated in SA node, spreads throughout both the atria and to AV node from where it passes via bundle of His to supply both ventricles through the Purkinje fibers.

## Basics in electrocardiogram

ECG is made up of 12 different leads giving views obtained from different directions or leads. There are six standard limb leads (I, II, III, aVL, aVR, aVF) and six chest leads (V1 to V6). (Fig.2a and b).

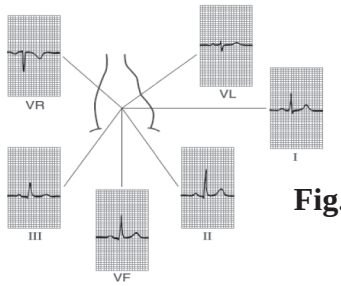



**Fig.2a. Standard limb leads**

*The relationship between the six chest leads and the heart*

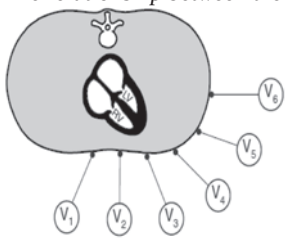



**Fig.2b. Chest leads**

*(Source: John R. Hampton. What the ECG is about? In: The ECG made easy. 8th edn, Churchill Livingstone Elsevier, London 2013; pp10-11.)*

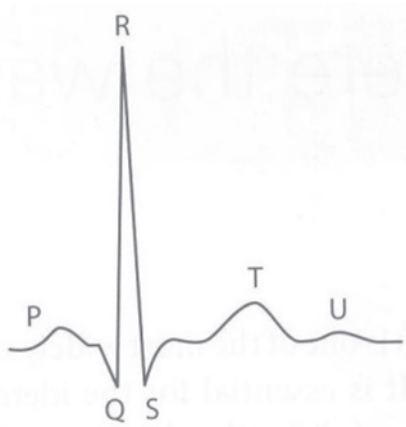



**Fig.3a. ECG - Main waves**

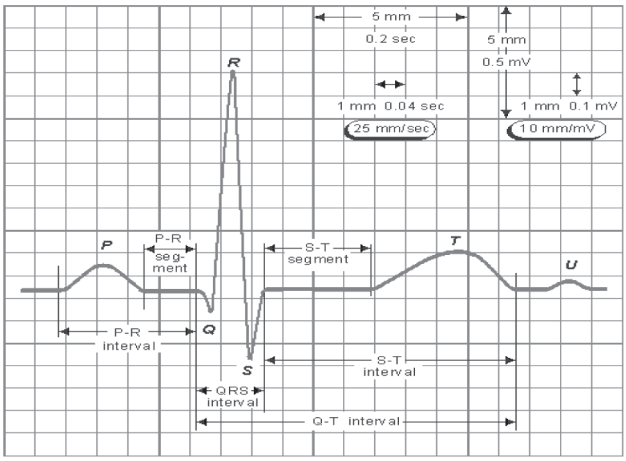
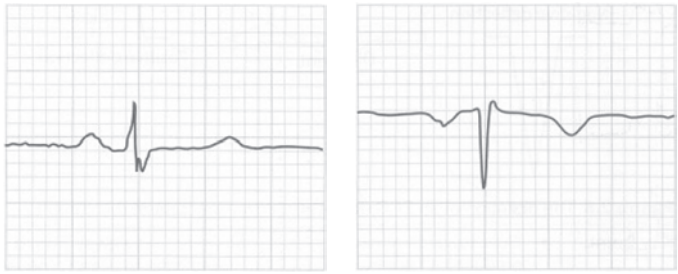



**Fig.3b. ECG – Intervals and segments**

Components of a normal ECG complex: A single ECG complex represents the electrical activity which occurs in one cardiac cycle and recorded in the ECG paper. It is made up of five waves (P,Q,R,S,T) and sometimes U (Fig.3a). The various intervals and segments are shown in Fig.3b.



Lead II Lead aVR

**Fig.4. P wave**

## Recognition of each component in ECG

### P wave

The orientation of P wave depends on the lead and is best read in lead II. P wave appears when impulse spreads from SA node to depolarize atria. Because electrical activity appears to spread towards almost all leads, the P wave will be a positive (upward) deflection except in aVR, where the electricity appears to flow away and hence the P wave is negative (Fig.4).

### P-R interval

P-R interval indicates the time taken for the depolarization wave to pass from SA node, through atria and AV node and finally to the ventricular muscle. PR interval is the interval from the beginning of the P wave to the beginning of the QRS complex and is normally between 0.12 sec to 0.20 sec (Fig.5).

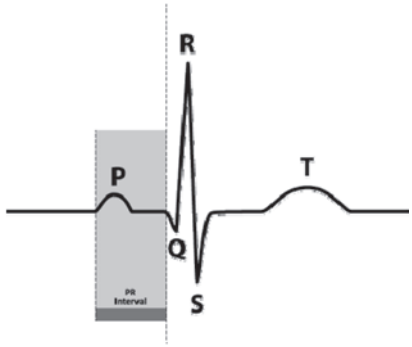



**Fig.5. P-R interval**

### QRS complex

By convention, the first deflection of QRS complex is downward - Q wave. This is followed by an upward deflection - R wave and the downward deflection following R wave - S wave. These waves are due to the depolarization of the right and left ventricles. Fig.6. shows the varieties of QRS complex.

### ST segment

It is measured from end of S wave to the beginning of T wave. It is the transient period when electrical current passes through the myocardium (Fig.7).

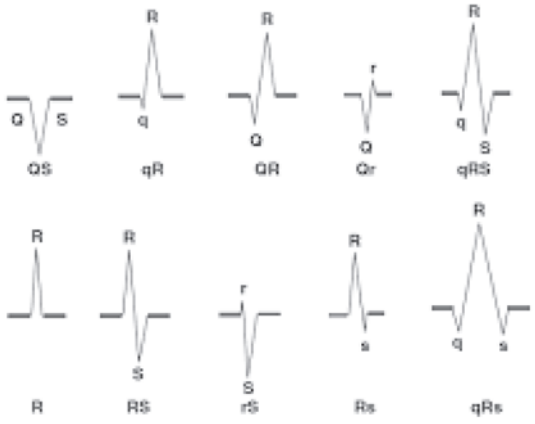



**Fig.6. Different varieties of QRS complex**

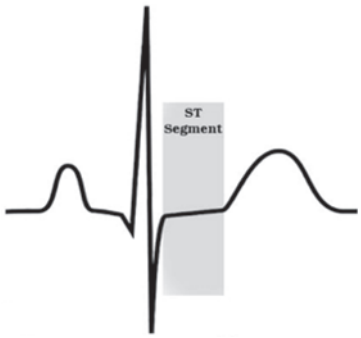



**Fig.7. ST Segment**

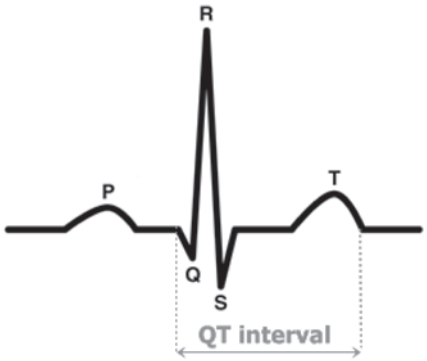



**Fig.8. QT interval**

**T wave**

It represents the repolarization (recharging) of ventricular myocardium. QT interval: measures total time for activation of the ventricles and recovery to normal resting state (Fig.8).

**U wave**

The origin is uncertain, but may represent repolarization of interventricular septum or slow repolarization of ventricles (Fig.3a).

## Stepwise interpretation of ECG

After ensuring the name age, gender, time of recording, check whether standardization curve is appropriate at 10 mms (10 small squares). ECG should be interpreted systematically in a stepwise fashion (Box 1).

**Box 1. Stepwise evaluation of ECG**

1. Rate
2. Rhythm. Is it sinus rhythm and whether it is regular?
3. QRS axis
4. P wave amplitude and duration
5. PR interval and QT intervals - Are they prolonged?
6. QRS duration
7. Any pathological Q wave?
8. Any ST segment changes - Elevation or depression
9. T wave
10. U wave
11. Atrial enlargement or ventricular hypertrophy

**Heart rate**

Measurement of heart rate and identification of cardiac rhythm go hand in hand, as many abnormalities of heart rate result from arrhythmias. When one measures the heart rate, it normally means ventricular rate, which corresponds to patient's pulse (Table I). Depolarization of ventricles produces the QRS complex in the ECG, and hence it is the rate of QRS complex that needs to be measured to determine the heart rate.

To measure heart rate: The ECG is recorded at standard paper speed of 25mm/second. Time is plotted in the X axis and voltage is recorded in the y axis. At this speed one should be aware that one minute ECG tracing covers 300 large squares and 1500 small squares. Hence each second there are five large squares, so one large square is equivalent to 0.2 secs and each small square is representing 0.04 seconds. If the rhythm is regular the number of large squares between 2 consecutive R waves is counted e.g. if there are 4 large squares between each R waves then the heart rate is 300 divided by number of large squares is 300/4 = 75. Alternately if small squares between two consecutive R waves are counted then the heart rate is 1500 divided by number of small squares which would give accurate heart rate. Normal heart rate varies with age.

**Rhythm**

Sinus rhythm implies the normal sequence of conduction originating in SA node, proceeding to ventricles via A-V node and bundle of His to Purkinje system. P wave precedes each QRS complex with regular P-R interval. P wave is better seen either in LII or V1. During inspiration, the heart rate increases, whereas during expiration it decreases. This variation is known as sinus arrhythmia. Here RR interval is varying, but PR interval is constant and P wave configuration is similar in all the complexes in the same lead. The exact relationship of PQRS complex, T waves and PR interval with shape of QRS complex has to be analyzed to indicate the type of cardiac arrhythmia.

**Axis**

The flow of electrical current through the heart normally passes along a well defined pathway. The QRS

**Table I. Pulse rate at rest**

| Age | Lower Limits of Normal | | Average | | Upper Limits of Normal | |
|---|---|---|---|---|---|---|
| Newborn | 70/min | | 125/min | | 190/min | |
| 1–11 mo | 80 | | 120 | | 160 | |
| 2 yr | 80 | | 110 | | 130 | |
| 4 yr | 80 | | 100 | | 120 | |
| 6 yr | 75 | | 100 | | 115 | |
| 8 yr | 70 | | 90 | | 110 | |
| 10 yr | 70 | | 90 | | 110 | |
| | **GIRLS** | **BOYS** | **GIRLS** | **BOYS** | **GIRLS** | **BOYS** |
| 12 yr | 70 | 65 | 90 | 85 | 110 | 105 |
| 14 yr | 65 | 60 | 85 | 80 | 105 | 100 |
| 16 yr | 60 | 55 | 80 | 75 | 100 | 95 |
| 18 yr | 55 | 50 | 75 | 70 | 95 | 90 |

*(Source: Bernstein D. History and physical examination. In: Robert M. Kliegman, Bonita F Stanton, Joseph W. St. Geme, Nina F. Schor, Richard E. Behrman (eds.), Nelson Text book of pediatrics, 1st South Asia edn, Reed Elsevier India Pvt Ltd, New Delhi 2016;pp2163-2170)*

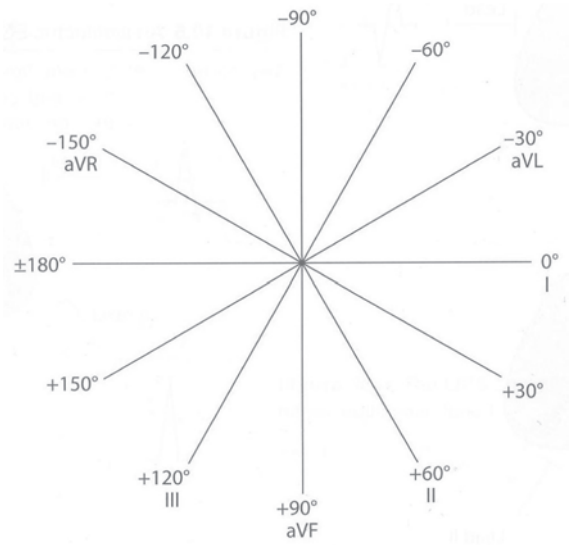



**Fig.9. Hexaxial reference system based on 6 limb leads**

axis is therefore conventionally referred to as the angle measured in degrees of the direction of electrical current passing through the ventricles. The angle from which each lead looks at the heart is represented by a hexaxial diagram which usually represents the angle from which each limb lead views the heart (Fig.9).

**Interpretation of QRS axis**

The information from limb leads is used to work out QRS axis in the frontal plane.

- Lead I - If QRS complex is positive, then axis is between -90° to +90°. Thus, predominantly positive QRS complex in Lead I rules out right axis deviation (axis beyond +90°) but does not exclude left axis deviation i.e. axis less than -30°.
- Lead II - If QRS complex is positive, then axis is between -30° to +150°. Thus predominantly positive QRS complex in lead II rules out left axis deviation (axis less than -30°) but does not exclude right axis deviation i.e. axis beyond +90°.

By looking at the QRS complex in lead I and lead II, the following interpretations can be made

(a) Positive QRS complex in both leads I and II - normal axis (- 30° to + 90°)

(b) Positive QRS in lead I and negative QRS in lead II - left axis deviation (- 30° to -90°)

(c) Negative QRS complex in lead I and positive QRS in lead II - right axis deviation (+ 90° to ± 180°)

(d) Negative QRS in lead I and II - extreme right axis deviation (- 90° to ± 180°)

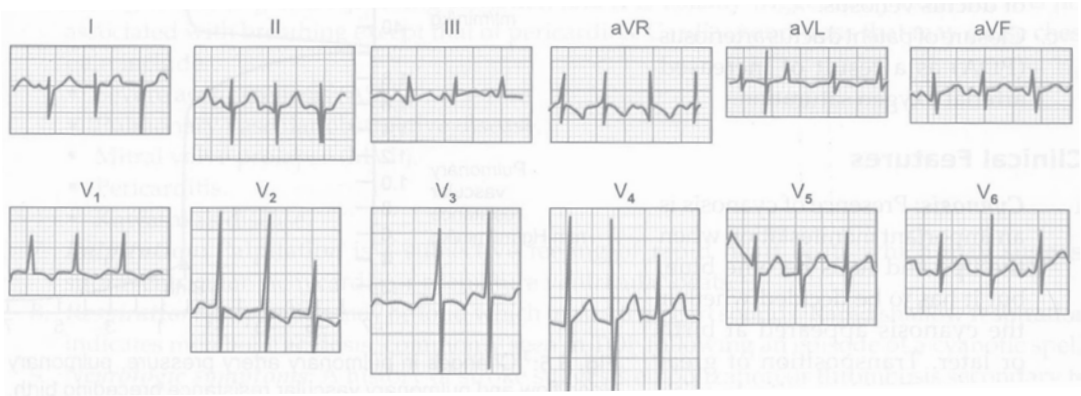



**Fig.10. Normal ECG of newborn – RV dominance**

## Newborn - ECG

The electrocardiogram of a newborn gives the picture of right axis deviation with right ventricular hypertrophy (RVH) due to increased pressure in the right side of heart (Fig.10). Normal heart rate at birth is between 120-180/ minute. Right axis deviation of mean QRS complex at birth (+125° to +180°) becomes normal by 1 year of age. R wave axis is positive in lead I and aVF. In premature babies less than 28 weeks gestation the chest leads show LV dominance and QRS axis is either normal or leftward.

## Common electrocardiographic abnormalities

### P wave

Common abnormalities can be due to right or left atrial enlargement (Fig.11a). In right atrial enlargement, tall and peaked P wave ( P "pulmonale") is seen where P wave amplitude is more than 2.5 mms with a normal P wave duration and is best seen in Lead II. Tall peaked P waves are seen in tricuspid atresia, pulmonary atresia with intact ventricular septum and severe pulmonary stenosis. In left atrial enlargement, P wave duration is prolonged ie >110 ms (>2.5 small squares in horizontal axis) and is inverted in V1. It is usually biphasic in L II and V1 (P "mitrale") (Fig.11b). It is commonly seen in mitral stenosis, post-tricuspid shunts (VSD, PDA, A-P window).

### QRS complex

QRS complex can show evidence of right, left or biventricular hypertrophy. In right ventricular hypertrophy (RVH) R/S ratio >1 in, V1, V2 and V4R with upright T wave in right precordial leads, right bundle branch block (RBBB), right axis deviation [(+135°) (except in newborn)] and Q wave (QR) in right precordial leads (Fig.12).

Right ventricular hypertrophy (RVH) due to pressure overload is shown by tall 'R' waves in aVR and right sided

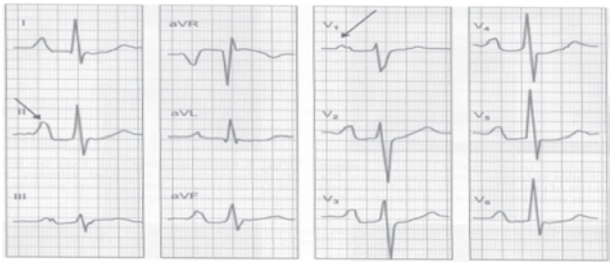


**Fig.11a. P wave - Right atrial enlargement with prolonged PR interval**

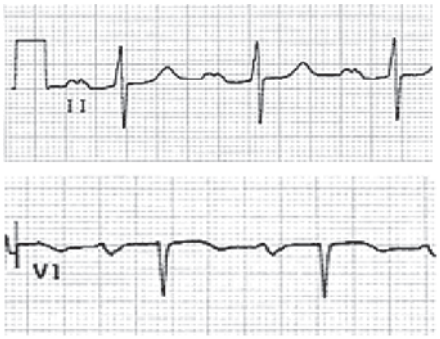



**Fig.11b. P wave-Left atrial enlargement**

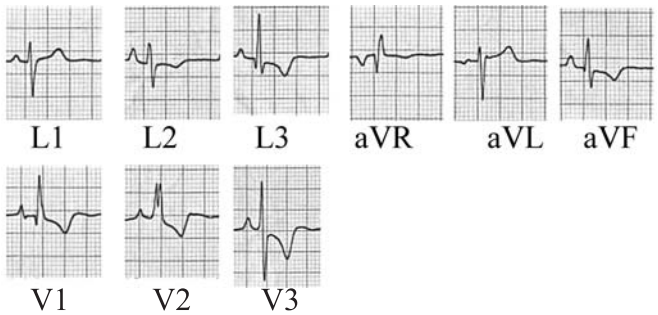



**Fig.12.ECG - RVH (QR in aVR)**

chest leads as in pulmonic stenosis while volume overload, RSR' pattern (right bundle branch block) as in atrial septal defect and in addition prolonged P-R interval may be seen because of interatrial conduction delay.

Left ventricular hypertrophy (LVH) is shown by tall 'R' waves in V5 and V6 and deep 'S' waves in V1.

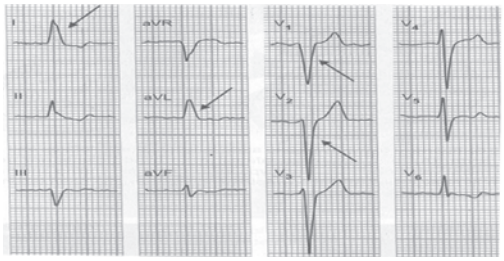


**Fig.13a. Left ventricular hypertrophy with strain**

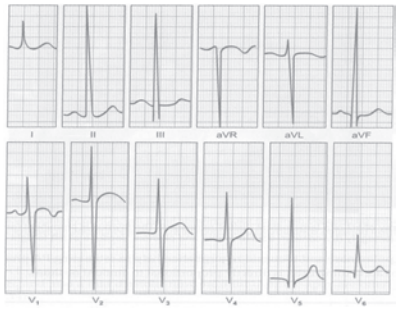


**Fig.13b. Left ventricular volume overload**

ST depression and T wave inversion in V5 and V6 are indicative of pressure overload as in aortic stenosis and coarctation of aorta. But in volume overload prominent q waves and minimal ST segment elevation with upward concavity (Fig.13a and b). Left ventricular volume overload is indicated by tall 'R' waves in V5 and V6 as in ventricular septal defect and patent ductus arteriosus (Fig.13b). In a newborn left axis deviation (LAD) (< +60°) and absence of RV dominance indicate LVH.

In combined ventricular hypertrophy criteria of RVH plus LVH, or criteria of RVH with left atrial enlargement or criteria of LVH with right axis deviation are seen (Table II).

**ST Segment**

ST segment elevation is seen in pericarditis, and hyperkalemia (Fig.14a and b). ST segment depression is seen in LVH, RVH, hypokalemia and digoxin effect (Fig.15).

**T wave**

T wave is normally inverted in V1-V3 between 7 days and 1 year. Upright T wave in V1 are seen in right ventricular hypertrophy (RVH). T wave inversion in lateral leads are due to pressure overload strain (ischemia) as seen in anomalous left coronary artery from pulmonary artery (ALCAPA) and coronary aneurysm in Kawasaki disease (Fig.15).

**Table II. Features of RV and LV hypertrophy**

| RV hypertrophy | LV hypertrophy |
|---|---|
| At least 2 of these changes should be present | |
| • qR pattern in right ventricular surface leads | • Deep Q wave in left precordial leads |
| • Positive T wave in leads $V_3R$-$V_4R$ and $V_1$-$V_3$ between the ages of 6 days and 6 yr | • Increased voltage of S wave in $V_3R$ and $V_1$ or R wave in $V_6$-$V_7$, or both |
| • Monophasic R wave in $V_3R$, $V_4R$, or $V_1$ | • Tall R waves, large Q wave and normal T waves over left precordium - diastolic overload |
| • rsR2 pattern in right precordial leads with 2nd R wave taller than initial one | • Depression of ST segments and inversion of T waves in left precordial leads ($V_5$, $V_6$, and $V_7$) - left ventricular strain pattern |
| • Age-corrected increased voltage of R wave in leads $V_3R$-$V_4R$ or the S wave in leads $V_6$-$V_7$, or both | |
| • Marked right axis deviation (>120 degrees in patients beyond newborn period) | |
| • Complete reversal of normal adult precordial RS pattern. | |

*(Source: Bernstein D. Laboratory evaluation. In: Robert M. Kliegman, Bonita F Stanton, Joseph W. St. Geme, Nina F. Schor, Richard E. Behrman (eds.), Nelson Text book of pediatrics, 1st South Asia edn, Reed Elsevier India Pvt Ltd, New Delhi 2016;pp2170-2182)*

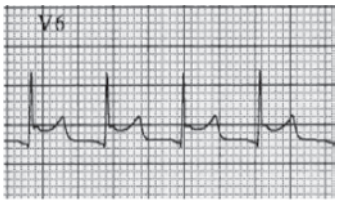



**Fig.14a. ST elevation – pericarditis**

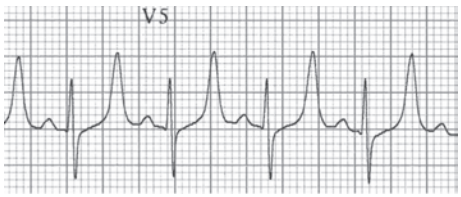



**Fig.14b. T wave - Hyperkalemia**

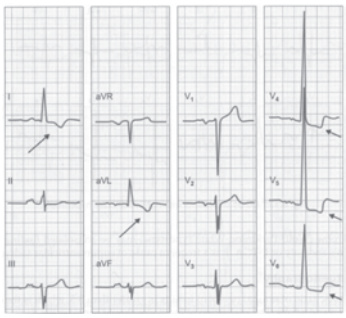


**Fig.15. ST segment depression and T wave inversion**

## Cardiac arrhythmias

Cardiac arrhythmias are rhythm disturbances due to abnormal impulse generation or abnormal impulse conduction block or delay, functional or fixed re-entry circuit (Fig.16).

Arrhythmias can be classified based on the following characteristics (Box 2). Arrhythmias can also be broadly classified into either tachyarrhythmias or bradyarrhythmias (Table III).

### Tachyarrhythmias

All the rhythms that originate in sino-atrial (SA) node is sinus rhythm and when they are faster than normal, they

**Box 2. Arrhythmia classification**

| | | |
|---|---|---|
| (i) | Heart rate | - increased/decreased |
| (ii) | Heart rhythm | - regular/irregular |
| (iii) | Site of origin | - supraventricular/ventricular |
| (iv) | ECG complexes | - narrow/broad |

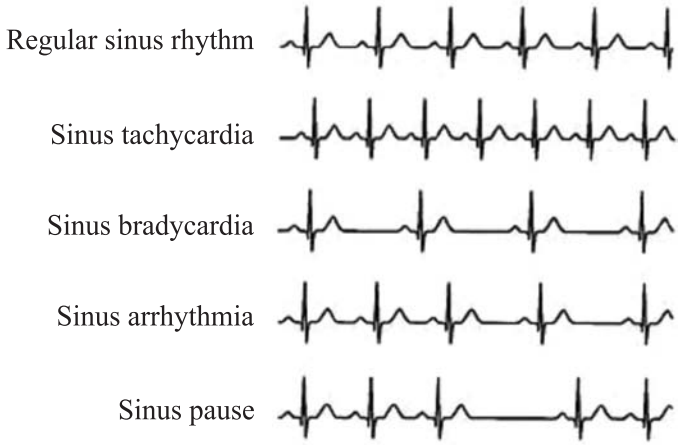



**Fig.16. Normal and abnormal rhythms originating in SA node**

are tachyarrhythmias. Tachyarrhythmias may be further classified into sinus tachycardia, premature ventricular contractions (PVCs), supraventricular tachycardia (SVT), atrial flutter, atrial fibrillation, ventricular tachycardia and ventricular fibrillation. In ventricular arrhythmia, QRS duration will be prolonged ie > 0.09 seconds.

**Sinus tachycardia:** When the heart rate is more than age appropriate range (Table I) in children with maintenance of sinus rhythm, it is called sinus tachycardia.

**Supraventricular tachycardia (SVT):** It is a pre-excitation syndrome and is an abnormally fast rhythm originating above the ventricles. SVT is the most common significant arrhythmia in children. It is most commonly caused by a re-entry mechanism that involves an accessory pathway or AV conduction system (Fig.17). ECG reveals a heart rate of more than 220/min in infants and more than 180/min in children, absent or abnormal P wave, often constant R-R interval and usually narrow QRS complex (Fig.18).

**Atrial flutter:** It is characterized by a strictly regular atrial rate (F wave with "saw tooth" configuration) at about 300 beats/minute followed by ventricular response with varying degrees of block (e.g. 2:1,3:1,4:1) and a normal QRS complex (Fig.19).

**Atrial fibrillation:** There are multiple small migratory re-entry circuits in right atrium leading to uncoordinated atrial contraction. P waves are absent. They are replaced by 'F' waves. It is characterized by fast atrial rate (F wave at rate - 350-600 beats/min) and irregular ventricular response with normal QRS complex (Fig.20).

**Table III. Identification of cardiac rhythm based on R-R interval**

| R-R Interval | | |
|---|---|---|
| **Regular** | **Irregular** | **Long pause** |
| **Slow**<br>Sinus bradycardia<br>Sinus node dysfunction or AV block with a regular escaperhythm (nodal or ventricular) | **Regularly irregular**<br>Sinus arrhythmia<br>Mobitz type 1 AV block (Wenckebach)<br>Bigeminy or trigeminy | Sinus pause or arrest<br>Complete AV block with no escape rhythm |
| **Normal**<br>Sinus rhythm<br>Ectopic atrial pacemaker<br>Accelerated escape rhythm<br>2:1 AV block with sinus node tachycardia | **Irregularly irregular**<br>Atrial fibrillation<br>Atrial flutter with variable AV conduction<br>Ventricular fibrillation | |
| **Fast**<br>Sinus tachycardia<br>Supraventricular tachycardia<br>Ventricular tachycardia | **Occasionally irregular**<br>Premature atrial contractions<br>Premature ventricular contractions<br>2nd degree AV block | |

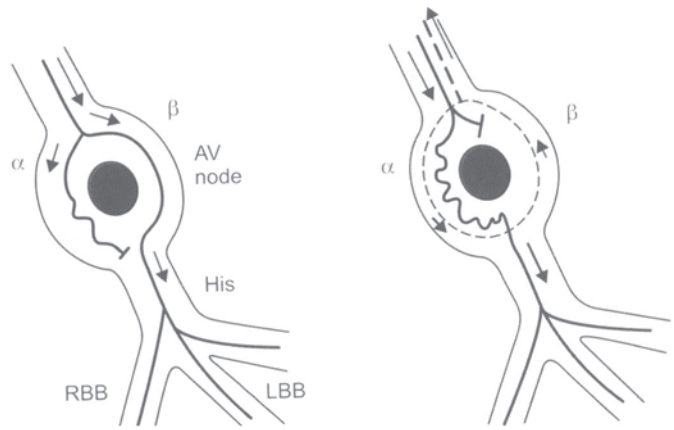



**Fig.17. Schematic diagram of dual pathways of AV node**

a – Normal conduction; b – Re-entrant circuit, resulting in AV nodal re-entrant SVT.

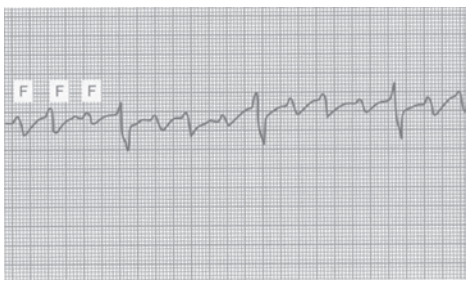



**Fig.19. Atrial flutter - "saw tooth" undulating P waves**

**Premature ventricular contraction (PVC) (Fig.21):** It is seen as a bizarre and wide QRS complex (> 0.09 secs) occurring earlier than anticipated with T wave pointing in opposite direction of the QRS complex, followed by a full compensatory pause.

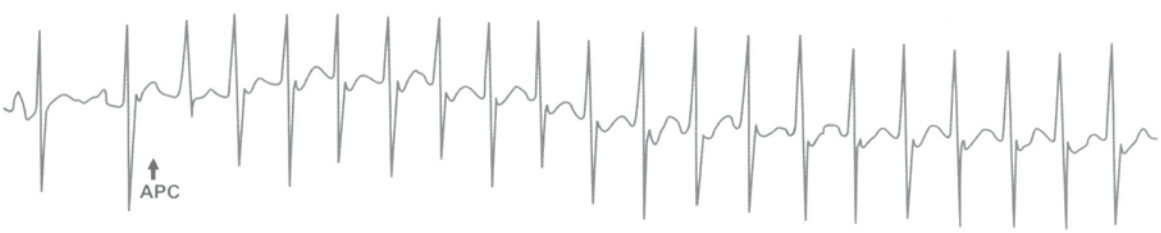



**Fig.18. Onset of SVT - Atrial premature contraction (APC) initiating re-entry circuit**

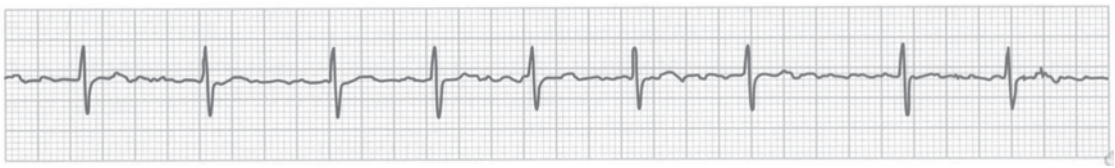


**Fig.20. Atrial fibrillation**

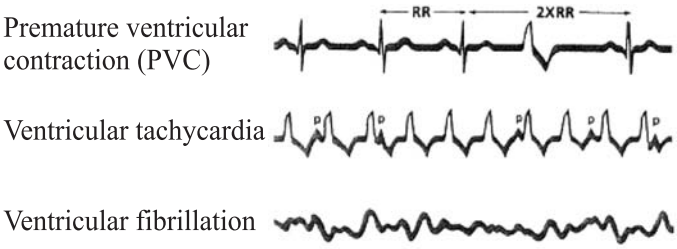



**Fig.21. Ventricular arrhythmias**

**Ventricular tachycardia (VT)** (Fig.21): VT is a series of 3 or more repetitive beats originating from the ventricle distal to bifurcation of bundle of His. It is also defined by a rate faster than 120 beats/min in children. The QRS complex is different from underlying sinus rhythm and normally shows ventriculo-atrial dissociation.

**Ventricular fibrillation (VF)** (Fig.21): It is characterized by low amplitude, rapid irregular depolarization without identifiable QRS complexes. It is an irregular rhythmic configuration and mostly terminates fatally.

**Brady arrhythmias**

Bradyarrhythmias may be classified as follows:-

1. Sinus bradycardia
2. Sinus node dysfunction
3. Atrio-ventricular conduction disturbances
   a. First degree A-V block
   b. Second degree A-V block
   c. Third degree AV block

**Sinus bradycardia:** The characteristics of this are sinus rhythm but the rate is slow. In infant it is less than 80 per minute while in older child less than 60 per minute.

**Sinus node dysfunction** (Fig.22): It is characterised by momentary absence of P wave and QRS complex (sinus pause). The causes are increased vagal tone, focal myocarditis, cardiomyopathy, drugs (digoxin, antiarrhythmics), hypoxia and hypothyroidism. In children, atrial surgery is the commonest cause of sinus bradycardia.

**Fig.22. Sinus node dysfunction**

**Atrio-ventricular block (A-V conduction disturbance):** In A-V block, there is disturbance in conduction between normal sinus impulse generation and ventricular response. First degree A-V block is when P-R interval is greater than the established norms. The norms P-R interval is shorter than 160 ms in infancy rising to a maximum of 180 ms in adolescents (Fig.23).

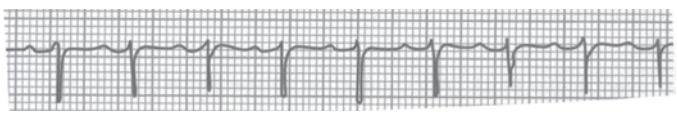


**Fig.23. First degree AV block**

Second degree A-V block- Mobitz type I (Wenckebach block) - The block at AV causes a decrease in PP interval with increasing P-R interval and subsequent QRS complex gets dropped (Fig.24a). In type II there is intermittent loss of QRS complex without preceding loss of P-R interval (Fig.24b). Block is at level of bundle of His and mostly progresses to complete heart block.

Third degree AV block: Atrial impulse cannot propagate to ventricles. P waves are regular (regular PP interval) QR complexes regular (R-R interval regular) but there is varying P-R interval (Fig.25).

**Disease specific ECG changes**

Congenital heart disease (e.g.) TOF, TAPVC, D-TGA, pulmonary atresia, truncus arteriosus, hypoplastic left heart syndrome shows right axis deviation with Q waves in Leads III and aVR and V4R (Fig.26).

Anomalous origin of left coronary artery from pulmonary artery (ALCAPA) shows deep Q waves, ST segment and T wave inversion in lateral leads I, aVL and V5-V6 in ECG (Fig.27). Tricuspid atresia has left axis deviation with Q waves in I and aVL, right atrial enlargement Indicated by tall p waves in lead II , and left ventricular hypertrophy with strain pattern (Fig.28). Ebstein's anomaly has giant 'P' waves with RBBB pattern,

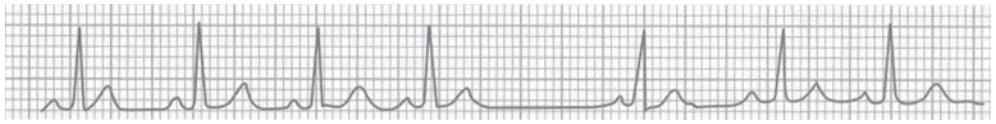


**Fig.24a. Mobitz type I - Increasing PR interval followed by dropped QRS complex**

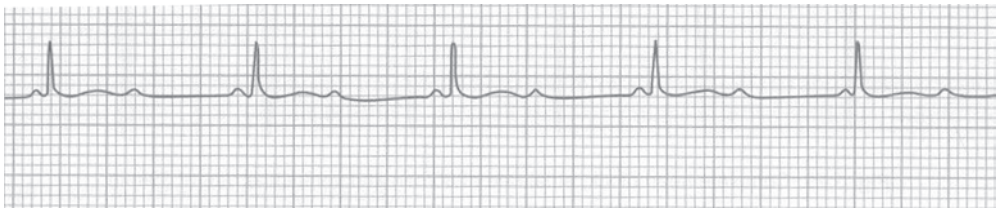


**Fig.24b. Mobitz type II - Dropped QRS complex without preceeding loss of PR interval**

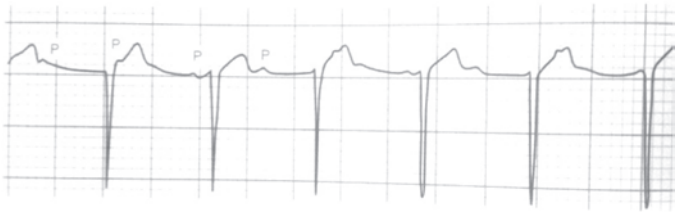



**Fig.25. Third degree heart block -
No P waves are conducted to ventricles**

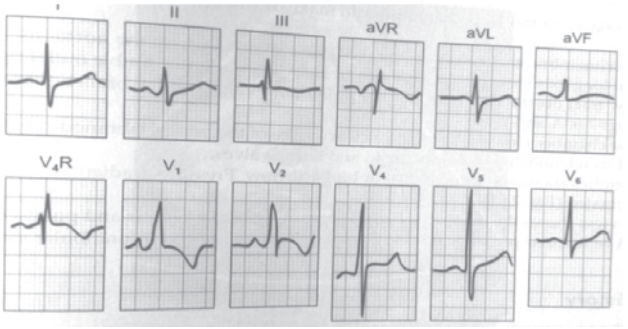



**Fig.26. ECG - TOF - RAD with Q wave in LIII, aVR and $V_4R$**

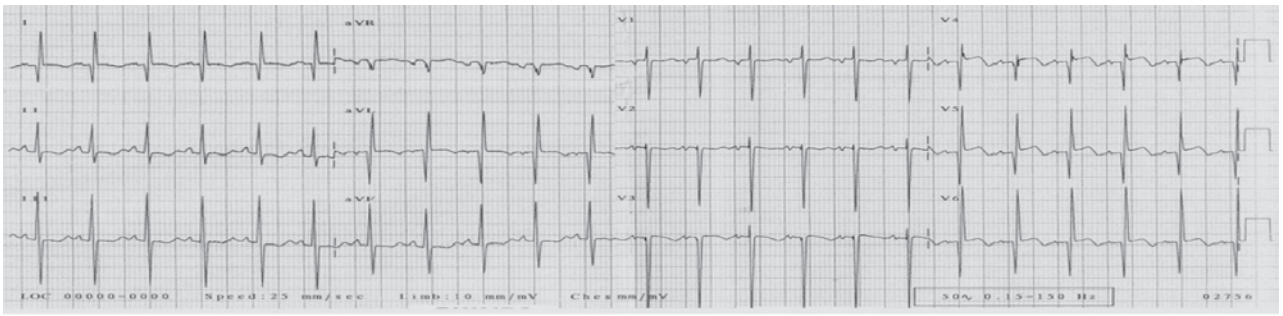


**Fig.27. ECG - ALCAPA - Deep Q waves, ST elevation, T wave inversion in LI, aVL and $V_5$ - $V_6$**

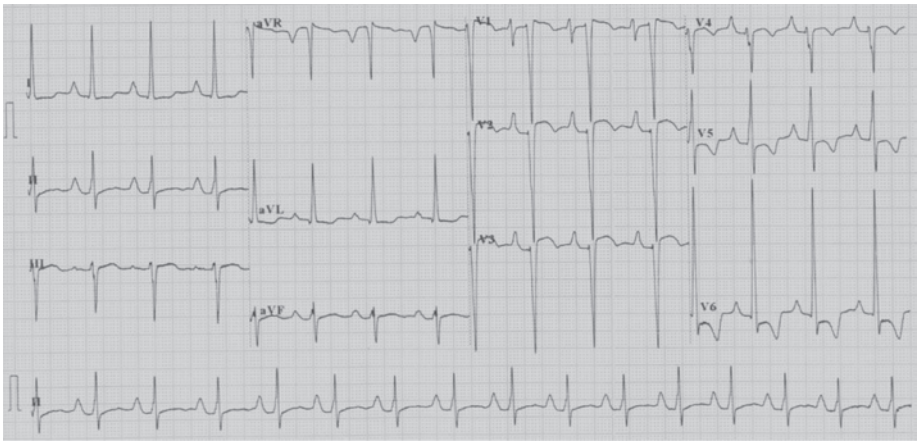



**Fig.28. ECG - Tricuspid atresia - LAD with Q waves in LI, aVL, tall P in LII**

first degree AV block and low voltage especially in limb leads (Fig.29).

Mitral stenosis has right axis deviation, left atrial hypertrophy and right ventricular hypertrophy (Fig.30). ECG changes in Wolf Parkinson White syndrome are short PR interval, delta wave (initial slurring of QRS) and wide QRS (Fig.31). In long QT syndrome, Bazett formula [(QTc) = QT/square root of the R-R interval] is used to calculate the corrected QT interval (Fig.32). QT interval is measured from the beginning of the QRS complex to the end of the T wave in LII or V5, V6. QTc more than 0.46 sec is abnormal.

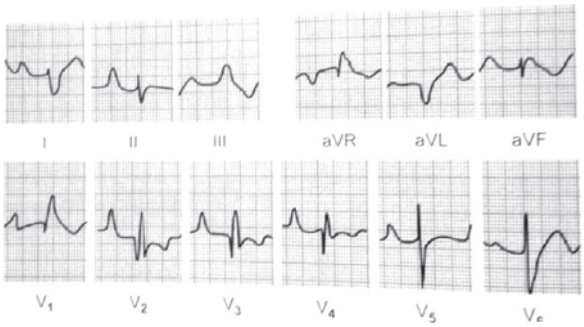



**Fig.29. Ebstein's Anomaly - Gaint P waves with RBBB**

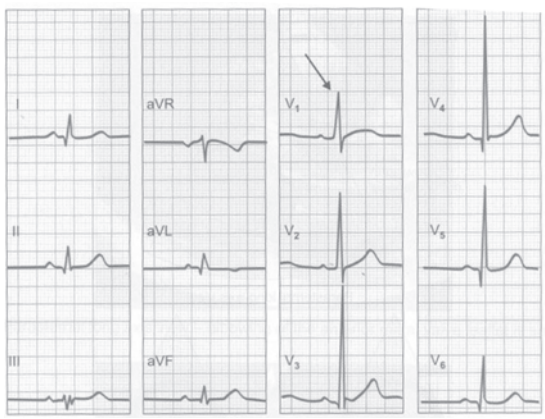



**Fig.30. ECG showing LAH & RVH due to mitral stenosis**

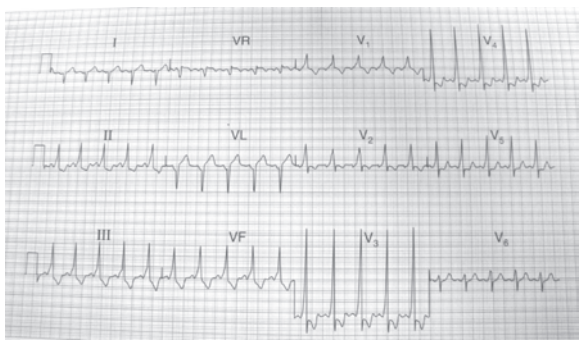



**Fig.31. ECG - Wolf Parkinson White syndrome - short PR interval, delta wave and wide QRS complex**

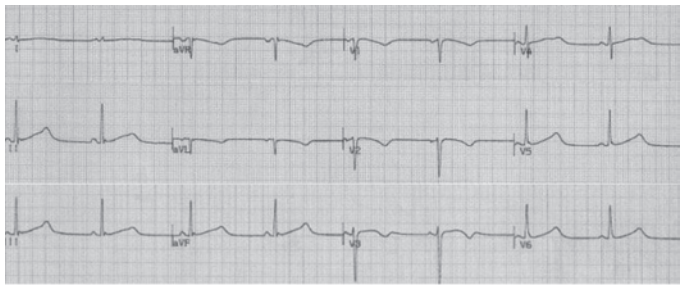


**Fig.32. Congenital long QT syndrome**

## Points to Remember

- ***An electrocardiogram (ECG) is the only investigation which records changes in the electrical activity of the heart.***
- ***Measurement of heart rate and identification of cardiac rhythm go hand in hand -abnormalities of heart rate can result in arrhythmias.***
- ***Main waves on ECGs have been named as PQRST and U. All the waves signify depolarization and repolarization of atria, ventricles and interventricular septum.***
- ***ECG of the newborn shows right ventricular dominance due to increased pressures on right side of the heart.***
- ***Common ECG abnormalities include atrial and ventricular enlargement or hypertrophy and different types of arrhythmias.***
- ***Arrhythmias are rhythm disturbances due to abnormal impulse generation, impulse conduction, block or delay.***
- ***Specific ECG changes in some congenital cardiac anomalies are diagnostic - which include TOF, anomalous origin of coronary artery from pulmonary artery, tricuspid atresia and Ebstein's anomaly.***

## References

1. Hust JW. Naming of the waves in ECG, with a brief account of their genesis. Circulation 1998; 98:1937 - 1942.
2. Davignon A Rantaharju P, Boisselle F, Soumis F, Megelas M, Choquette A. Normal ECG standards for infants and children. Pediatr cardiol 1979; 1: 123-152.
3. Goodacre S, McLeod K. ABC of clinical electrocardiography. Pediatric electrocardiography. Br Med J 2002; 324: 1382-1385.
4. Burchell HB. A centennial note on Waller and the first human electrocardiogram. Am J Cardiol 1987;59:979-983.

5. Fisch C. Evolution of clinical electro-cardiogram. J Am coll cardiol 1989; 14:1127-1138.

6. Schwartz PJ, Garson A, Paul T, Stramba-Badiale M, Vetter VL, Villain E, et al. Guidelines for the interpretation of the neonatal electrocardiogram. European Heart J 2002; 23: 1329-1344.

7. Southall DP, Johnston F, Shinebourne EA, Johnston PG. 24 hour ECG study of heart rate and rhythm patterns in a population of healthy children. Br Heart J 1981; 45: 281-291.

8. Anita Khalil. Arrhythmias. In: Essentials of Pediatric Cardiology. 1nd Edn, Jaypee Publishers. New Delhi, 2011; pp42-72.

9. Mason JW, Hancock EW, Gettes L S-AHA/ACCF/HRS recommendations and interpretation of the electrocardiogram. Part II: Electrocardiographic diagnostic statement list. J Am Coll Cardiol 2007; 49: 1128- 1135.

10. Meek S, Morri F. ABC of Clinical Electrocardiography-Introduction I-Leads ,rate, rhythm and cardiac axis. Br Med J 2002; 324:415-418.

## CLIPPINGS

**Association of short antenatal corticosteroid administration-to-birth intervals with survival and morbidity among very preterm infants**

Administration-to-birth intervals of antenatal corticosteroids (ANS) vary. The significance of this variation is unclear. Specifically, to our knowledge, the shortest effective administration-to-birth interval is unknown. The objective was to explore the associations between ANS administration-to-birth interval and survival and morbidity among very preterm infants.

The Effective Perinatal Intensive Care in Europe (EPICE) study, a population-based prospective cohort study, gathered data from 19 regions in 11 European countries in 2011 and 2012 on 4594 singleton infants with gestational ages between 24 and 31 weeks, without severe anomalies and unexposed to repeated courses of ANS. Data were analyzed November 2016. The exposure considered was time from first injection of ANS to delivery in hours and days.Three outcomes were studied: in-hospital mortality; a composite of mortality or severe neonatal morbidity, defined as an intraventricular hemorrhage grade of 3 or greater, cystic periventricular leukomalacia, surgical necrotizing enterocolitis, or stage 3 or greater retinopathy of prematurity; and severe neonatal brain injury, defined as an intraventricular hemorrhage grade of 3 or greater or cystic periventricular leukomalacia.

Mortality for the 662 infants (14.4%) unexposed to ANS was 20.6% (136 of 661). Administration of ANS was associated with an immediate and rapid decline in mortality, reaching a plateau with more than 50% risk reduction after an administration-to-birth interval of 18 to 36 hours. A similar pattern for timing was seen for the composite mortality or morbidity outcome, whereas a significant risk reduction of severe neonatal brain injury was associated with longer administration-to-birth intervals (greater than 48 hours). For all outcomes, the risk reduction associated with ANS was transient, with increasing mortality and risk for severe neonatal brain injury associated with administration-to-birth intervals exceeding 1 week. Under the assumption of a causal relationship between timing of ANS and mortality, a simulation of ANS administered 3 hours before delivery to infants who did not receive ANS showed that their estimated decline in mortality would be 26%.

Antenatal corticosteroids may be effective even if given only hours before delivery. Therefore, the infants of pregnant women at risk of imminent preterm delivery may benefit from its use.

***Norman M, Piedvache A, Børch K, Huusom LD, Bonamy AE, Howell EA, et al. For the effective perinatal intensive care in europe (EPICE) research group. Association of short antenatal corticosteroid administration-to-birth intervals with survival and morbidity among very preterm infants Results From the EPICE Cohort. JAMA Pediatr 2017; 171(7):678–686. doi:10.1001/jamapediatrics.2017.0602***

**CARDIOLOGY**

# CONGESTIVE CARDIAC FAILURE - CURRENT CONCEPTS IN MANAGEMENT

***Smita Mishra***

**Abstract**: *Clinical syndrome of pediatric heart failure is a gamut of varied etiologies and treatment options. An infant or child presenting with the cardiac dilatation and dysfunction must be proactively investigated for correctable lesions like-a structural heart disease, rhythm disorders and electrolyte imbalance. Henceforth, the traditional astuteness for clinical diagnosis remains the handy tool of a cost-effective advanced management-plan. Since research has revealed comprehensively, that HF is a catastrophic outcome of metabolic aberrations resulting into oxidative stress at the cellular level owing to the unbalanced compensatory neuro-hormonal mechanism, new therapeutic substrates are being gauged. Moreover, the solitary decongestive therapy is ousted completely and being replaced by the multipronged approach which includes pharmacotherapy, surgical or catheter intervention as well as the devices to provide mechanical support to the cardiorespiratory unit. New genetic tools are being explored through the gene or stem cell therapy as the futuristic but promising modalities. Finally, the modern management of heart failure is about presumptive, supervised target-oriented fine tuning of the available modalities for a patient, starting from the ICU and extending it upto the rehabilitation home care program.*

**Keywords:** *Heart failure, Children, Congestive, Causes, Diagnostic approach, Inotropes, Beta blockers, ECMO, Ventricular assist devices, Cardiac transplantation.*

"Heart failure (HF) is a complex clinical syndrome that can result from any structural or functional cardiac disorder that impairs the ability of the ventricle to fill with or eject".[1,2] Accordingly, HF is the product of variety of etiologies plummeting the systemic cardiac-output required to fulfill the metabolic demand of body. Arguably, can HF be transitory or curable? The answer is encouragingly affirmative for structural abnormalities, rhythm disorder and electrolyte imbalance, the three-major correctible cause of pediatric heart failure and therefore, unlike adults, pediatric HF may be controlled to the extent of cure. The terminology used in pediatric heart failure is given in Table I.

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## Epidemiology

Nonetheless, acquired disorders like myocarditis and cardiomyopathies predominate in older children while in infants and young children, correctible lesions predominate. Reported incidence of CHF is 4/1000 person years in infant and in children (<10 years of age), the prevalence is 1.3 in 1000.

## Age of onset of heart failure according to etiology

Table II gives of possible diagnosis according to the age of onset of congestive heart failure (CHF). Many congenital heart diseases (CHD) may not follow the rule and may remain asymptomatic till they have some precipitating factors like anemia or endocarditis.

## Pathophysiology – Congestive heart failure (Fig. 1)

Heart failure is a multifactorial syndrome represented by the deranged energetics and substrate metabolism of cardiac and skeletal muscles.[3] Overall, HF is compensated through three important mechanisms i) sympathetic nervous system (SNS); ii) renin angiotensin system (RAS); iii) release of vasopressin and natriuretic peptides. However, long term effects of resultant adaptive remodelling of cardiovascular system, are catastrophic which eventually, contribute to the oxidative stress at the molecular, cellular, tissue and organ levels causing myocardiocyte apoptosis, necrosis and cardiac fibrosis leading to maladaptive cardiac dilatation and hypertrophy and unwarranted fluid retention and vasoconstriction.

Obviously, these evidences have led to the efforts to reduce oxidative stress and to induce reverse remodeling by rational prescription of pharmacological agents like spironolactone, ACE inhibitors, carvedilol, optimum exercise, as well as the nutritional supplements known to have anti-oxidant property like taurine, ubiquinone (co enzyme Q10) and omega-3 fatty acid.[6]

**Table I. Pediatric heart failure – Terminology and associated features**

| Terminology | Features |
|---|---|
| Acute HF acute decompensated HF | Rapid onset of low cardiac output, dyspnea, systemic/pulmonary congestion. |
| Congestive heart failure | Volume overloading of upstream chambers leading systemic/pulmonary congestion. |
| High output failure | Normal ventricular ejection fraction, but low systemic blood flow /tissue perfusion. |
| Pretricuspid shunt | Shunt lesion at atrial level [Pulmonary arterial pressure (PAP)< Systemic blood pressure (SBP) initially] |
| Post tricuspid shunt | systolic systemic pressure and pulmonary artery pressure are same (VSD/PDA AP window) |
| Hyper kinetic pulmonary hypertension | In post-tricuspid shunt lesions- PA and aortic systolic BP remain same but PA diastolic pressure is low allowing left to right shunt and increased PBF(Qp>Qs.) |
| Obstructive pulmonary hypertension & Eisenmenger syndrome | Pulmonary veno-occlusive disease (POVD), PA systolic/Diastolic/Mean pressure = systemic or aortic pressure. CXR- oligemic lungs /no cardiomegaly (except in ASD) |
| Primary pulmonary hypertension | In absence of any shunt lesions PA systolic, diastolic and mean pressures are high. |
| Persistent pulmonary of new born | Right to left shunt across the persistent PFO and PDA (persistent fetal hypertension circulation) usually after difficult delivery and lung issues. |
| Cardiogenic pulmonary edema | Pulmonary edema (PE) with increased pulmonary capillary wedge pressure (PCWP) (>22mmHg), increased pulmonary venous hypertension (PVH) secondary to a cardiac cause. |

**Heart failure – Neonates:** Management of HF in neonates needs to be customized as they have small myocytes, less developed Frank-starling mechanism, preload dependent contractility and less intracellular calcium. They depend more on chronotropic response (heart rate dependence) to increase the cardiac output.

**Heart failure - Structural heart diseases:** Heart failure in structural heart disease is unique. In shunt lesions (VSD, PDA), surgical or cath intervention can cure the HF. Duct dependent cyanotic CHDs and acyanotic CHD with obstructive lesions may be palliated by prostaglandin (PG) infusion with or without balloon atrial septostomy (d-TGA) in early neonatal period and the corrective surgery can be done subsequently. Obstructed TAPVC needs the emergency surgery while other non-emergent admixture lesions, like unobstructed TAPVC, truncus arteriousus may wait for few weeks. End-stage myocardial dysfunction in the children with operated or unoperated complex CHD may be refractory to usual pharmacotherapy because systemic ventricle may not have left ventricular morphology.

**Heart failure - Coronary artery abnormalities:** Unlike adults, only small number of children may have coronary abnormality as the cause of HF (Box 1).

**Table II. Congestive heart failure (CHF) - Usual age of onset**

| A | B | C | D |
|---|---|---|---|
| **Fetus** | **CHF <6 weeks** | **CHF >6 weeks** | **CHF beyond infancy** |
| Supraventricular tachycardia, severe complete heart block, severe hypoglycaemia, anemia, Ebstein's anomaly or dysplastic tricuspid valve, atrioventricular septal defect with severe atrio-ventricular valve regurgitation, premature closure of ductus arteriosus or foramen ovale, fetal myocarditis | (Column A + following cardiac diseases) birth asphyxia, sepsis, hypercalcemia, critical AS/PS, duct dependent congenital heart diseases (DDCHDs), large PDA/VSD/ Atrio ventricular septal defect (AVSD) / aorto pulnmonary window (APW) in preterm neonates, admixture lesions-truncus arteriosus, unobstructed TAPVC, tricuspid atresia without PS, single ventricle, obstructed TAPVC, severe mitral regurgitation, complex congenital anomaly without pulmonary stenosis - Heterotaxy syndrome, large systemic arteriovenous fistula (Vein of Galen malformation), adrenal insufficiency/severe thyrotoxicosis | (Column A&B+ following ardiac diseases) large VSD, clarge PDA, AP window, AV canal defect etc, ALCAPA, fulminant myocarditis, dilated cardiomyopathy, atypical Kawasaki disease with coronary involvement/ myocarditis | (Column A, B, C + following cardiac diseases) severe valvular regurgitation with or without rheumatic aetiology, infective endocarditis, myocarditis, cardiomyopathy, anemia, acute systemic hypertension -primary or secondary HT, late presentation of ventricular failure in operated and unoperated cases of CHDs, cardiomyo pathy – dilated, restrictive, hypertrophic, drug induced, late presentation of HF in otherwise asymptomatic heart defect may also be due to some additional factors like anemia, infection. |

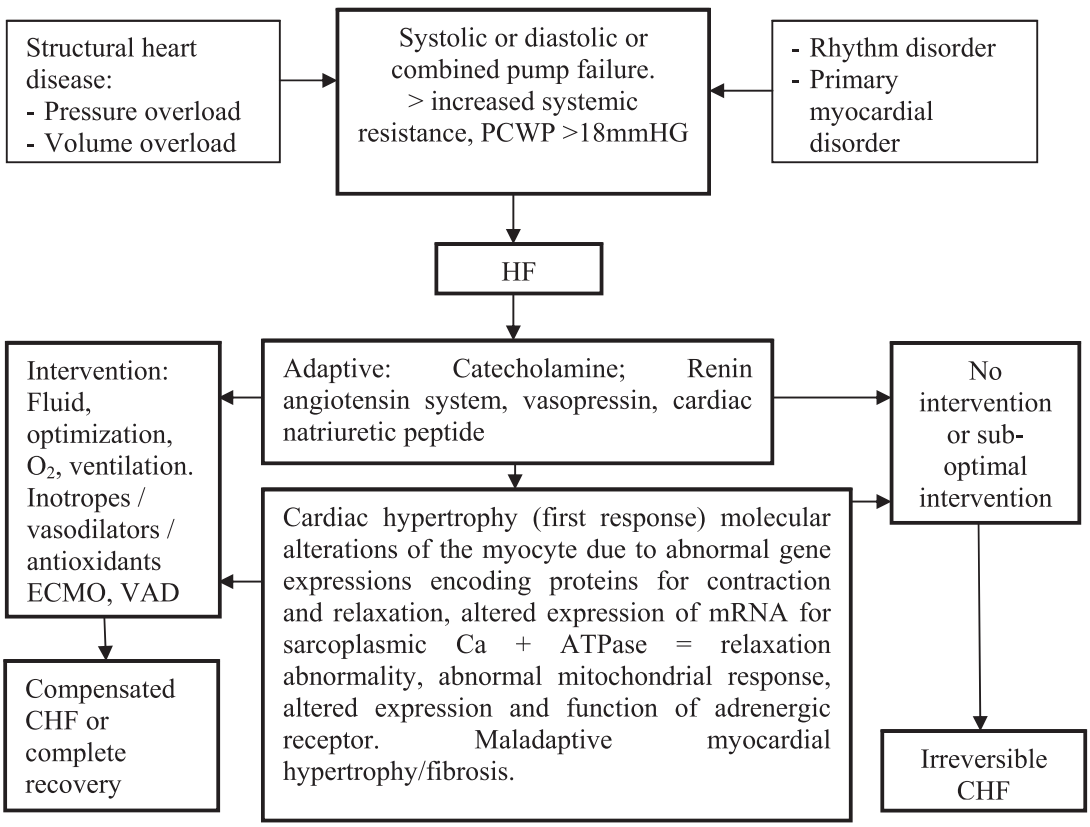


**Fig.1. Congestive heart failure - Hormonal and cellular basis**

**Box 1. Coronary abnormalities**

I. Anomalous origin of coronary artery (CA) from pulmonary artery (ALCAPA).

II. Large coronary arterio-venous fistula (AVF)

III. Post Kawasaki disease-CA aneurysm or stenosis (may present like adult with myocardial infarction).

IV. Coronary abnormalities associated with complex CHDs like pulmonary atresia/intact ventricular septum or ostial atresia (may have adult like chest-pain and ischemic pattern on ECG).

**Heart failure and rhythm disorders:** Both SVT and complete heart block are common but treatable cause of fetal, neonatal and infantile HF. Ventricular tachycardia (VT) or atrial fibrillation (AF) are usually intractable and are expression of, either the late presenting uncorrected and corrected structural heart diseases or the inheritable channelopathies. Bradycardia with CHF in fetus, infants and children may be due to complete heart block and may have underlying corrected transposition physiology.

**Heart failure and electrolyte imbalance:** Hypocalcemia particularly is a common and curable cause of secondary dilated cardiomyopathy in infants.

**Heart failure and cardiomyopathy:** CMP can be classified as dilated (mostly systolic dysfunction), hypertrophic (HOCM), restrictive (diastolic ventricular dysfunction to begin with) and non-compaction CMP. There may be a variety of genetic predisposing factors. Dilated CMP is the the major cause of pediatric cardiac transplant. Approximately 22%-25% of these children may recover spontaneously.

**Heart failure - Miscellaneous group:** There are many other causes of heart failure which include infection (particularly bacterial endocarditis), infiltrative, familial (hypercholesterolemia), vasculopathies involving coronary arteries, cardiomyopathy related to liver and kidney disorders.

## Heart failure - Functional classification (Table IIIA & B)

**1. New York Heart Association (NYHA classification)** NYHA classification is the most commonly used functional classification for adults which can be used for grown-up children.[4]

**2. Modified Ross classification -** The Ross classification for heart failure was developed for infants and subsequently was modified to accommodate the older children as well. The scoring system incorporates feeding difficulties growth issues and exercise intolerance into a comparable numeric score to that of NYHA classification.[5]

## Diagnosis

The diagnosis of HF is arrived based on the constellation of clinical signs and symptoms.[6,7] Symptoms of heart failure varies with age. HF in infants is characterized by excessive, unprovoked cry, suck-rest-suck cycle, excessive sweating, lethargy, hurried difficult breathing, failure to thrive (fall in weight for age below two percentiles from a previously noted growth pattern), +/- cyanosis. HF beyond the infancy is characterized by growth failure, respiratory distress, exercise intolerance. Older children may present with chest pain, wheezing, dependent edema and ascites.

**Table IIIA. Functional classification of heart failure (NYHA and Ross classification)**

| Class | New York Heart Association (NYHA) | Ross functional class |
|---|---|---|
| I | No limitations of physical activity | No limitations or symptoms |
| II | May experience fatigue, palpitations, dyspnea, or angina during moderate exercise but not during rest | Infants: Mild tachypnea or diaphoresis with feeding<br>Older children: Mild to moderate dyspnea on exertion |
| III | Symptoms with minimal exertion that interfere with normal daily activity | Infants: Growth failure, marked tachypnea or diaphoresis with feeding<br>Older children: Marked dyspnea on exertion |
| IV | Unable to carry out any physical activity, symptoms of HF at rest that worsen with any exertion | Symptoms at rest such as tachypnea, retractions, grunting or diaphoresis |

**Table IIIB. Modified Ross criteria - Variables**

| Age in years | 0 | +1 | +2 |
|---|---|---|---|
| **Respiratory rate ( per minute)** | | | |
| 0-1 | <50 | 50-60 | >60 |
| 1-6 | <35 | 35-45 | >45 |
| 7-10 | <25 | 25-35 | >35 |
| 11-14 | <18 | 18-28 | >28 |
| **Heart Rate (Per minute)** | | | |
| 0-1 | <160 | 160-170 | >170 |
| 1-6 | <105 | 105-115 | >115 |
| 7-10 | <90 | 90-0-100 | >100 |
| 11-14 | <80 | 80-90 | >90 |
| **Hepatomegaly (cm)** | <2 | 2-3 | >3 |

Clinical assessment of child with HF (Table IV): In triage, all critically ill children must be examined to rule out cardiovascular instability- by monitoring heart rate and HR variability, palpation of all the pulses for volume, thrill, radio-femoral delay, blood pressure in all the 4 limbs, $SPO_2$ in right upper and lower limb and core - peripheral temperature gradient. Characterization of S2 split, relationship of A2 and P2 and relative loudness of P2 are the most important auscultatory signs. RV failure is identified by triad of peripheral venous congestion, intra-cavitary and interstitial fluid collection.

## Investigations

**Chest x-ray** (Table V)**:** There are few classical chest x-ray images like 'figure of 8' in unobstructed TAPVC and cardiomegaly. Infants presenting with cardiomegaly usually labelled as myocarditis/DCMP, may have following correctible lesions: 1) ALCAPA, 2) Coarctation of aorta (LVH), 3) tachycardia induced cardiomyopathy (episodes of SVT, Accessory pathway in surface ECG), 4) Hypocalcemic CMP (Prolonged QTc).

**Electrocardiogram:** Few important abnormalities of ECG which may help in suggesting abnormality and need to be investigated are as follows:

(i) Abnormal HR, R-R interval, PR relationship, QTc interval, delta wave.

(ii) Low voltage ECG (limb leads < 5 mV; Chest leads: <10mV )

(iii) The pure R, rR' or QR pattern in V1; upright T in lead V1 beyond 72 hours of age;

(iv) Broad and deep Q wave in lead I and aVL (ALCAPA)

(v) QRS axis beyond 120 or a superior axis (S wave dominance in aVF, R dominance in aVR or aVL)

**Table IV. Heart failure: Clinical evaluation**

| Clinical evaluation | Findings |
|---|---|
| **Abnormality of pulse/systemic blood pressure** | Low cardiac output: Weak, thready pulse no carotid thrill, low BP; Coarctation of aorta, Supravalvar AS, Aortic stenosis. SVT/AV block: Disproportionate tachycardia or bradycardia, Aortic regurgitation/PDA: Collapsing pulse. Systemic hypertension. |
| **Systemic venous congestion** | Dependent site edema, puffy eyelids, ascites, raised JVP (difficult to appreciate in infants) soft, tender hepatomegaly, positive hepato-jugular reflex. |
| **$SpO_2$** | Cyanotic CHD with increased PBF :CHF with $SpO_2$<95%, duct dependent systemic circulation right upper and lower $SpO_2$ difference >3%; Acyanotic CHD:$SpO_2$ >95% |
| **Cardiac evaluation** | Cardiomegaly and changed intensity and timing of cardiac sound: ASD/TAPVC abnormal S2 (wide and fixed); VSD: wide and variable, loud P2; PS-wide and variable, soft P2 with ejection murmur/ click; PDA-narrow split/continuous murmur-; AS:paradoxical split ESM/Constant click. split and intensity) Significant murmur: present with thrill, parasternal heave, systolic murmurs (>3/6) and diastolic murmurs, associated with aforesaid findings. pericarditis rheumatic fever: Pericardial rub; IE: changing murmur with fever, peripheral signs. |
| **Respiratory system** | Pulmonary congestion: left sided obstructive or regurgitant valvar lesions or in severe LV dysfunction; crackles in lungs: in shunt lesions: respiratory infection |
| **Other system** | Hepatomegaly: post-tricuspid shunt lesions and right sided obstructive lesions, in infants; (in neonates left sided obstructive lesions -AS/coarctation of aorta). Hepato-splenomegaly: storage or metabolic disorder, dysmorphism: chromosomal anomalies. Migratory arthritis or chorea: rheumatic carditis. Fever and hematuria, changes in nails and skin, neurological complication: IE, tumors, renal dysfunction. |

**Table V. Chest x-ray and pediatric heart failure**

| Variables on X-Ray chest | Details |
|---|---|
| Cardiac size | Cardiomegaly: Cardiothoracic ratio>60% (neonates); >55% (older infants) |
| Cardiac apex, Stomach bubble, Hepatic shadow | Cardiac apex and right lobe of liver on same and stomach bubble on opposite side - complex congenital heart disease. Central liver - heterotaxy syndrome. |
| Cardiac base or pedicle | Acyanotic CHD - Normal or dilated. Cyanotic CHD - Usually narrow due to small branch PA (TOF), anteroposterior great vessels (d-TGA) or absent thymus. |
| Cardiac contour | Boot shaped – TOF; egg on side - d-TGA; Snowman sign -Supracardiac TAPVC; Box like heart - TR with Ebstein's anomaly/Uhl's anomaly; Cardiomegaly with LV apex- DCM; broad apex - Tricuspid atresia; Double shadow sign-LA enlargement; third mogul sign-LA enlargement, coronary AVF, dilated RVOT |
| Pulmonary blood flow | Increased PBF: end-on vascular shadow (>4 per lung field) beyond the peri-hilar area, end-on vessel>bronchial shadow, increased vascularity in lateral 1/3rd of lung field. Dilated pulmonary arteries and enlarged cardiac shadow.Decreased PBF: translucent lungs, small-streaky pulmonary arteries end on arteriole smaller than bronchus. Special pattern of cardiac shadow like boot shaped heart of TOF.Pulmonary venous hypertension: Cephalization, redistribution of vascular markings (grade I) curley's A,B, C lines (Grade II -Pulmonary capillary wedge pressure<23mmHg), ground glass opacity, bat-wing pulmonary edema, pleural effusion (Grade III-PCWP->23mmHg).Eisenmenger syndrome: dilated proximal pulmonary arteries and tapering or pruning of distal pulmonary arteries as well as diffuse oligemia of lungs. |

**Table VI. Laboratory work-up**

| Variables | Comments |
|---|---|
| Serum electrolytes | Sodium: (Rule out hyponatremia/hypernatremia; 1/4$^{th}$ patients have Na<135 mEq/L); Potassium, calcium (Hypercalcemic cardiomyopathy) |
| Renal function test Liver function test | For drug -doses adjustment; hepatic and renal dysfunction may be associated with cardiomyopathy and pulmonary edema(renal). |
| Hematological test | Complete blood count, platelets, Hb to rule out anemia, infection etc |
| Inflammatory markers | CRP to rule out infection, D- Dimer to rule out pulmonary embolism. ASO titres, ESR must be sent in a case of suspected acute rheumatic fever. |
| Blood cultures | Three blood culture from different sites at the interval of half to one hour, must be taken in a case of suspected IE. |
| Bio-markers | Natriuretic Peptides -BNP, NT-pro-BNP, ANP |
| ABG/VBG | Arterial/venous gas analysis: to know the saturation, $PO_2$, $PCO_2$, pH. $HCO3^-$ , base deficit access. Additionally, the values for blood sugar lactate and electrolytes like sodium, potassium and calcium can also be obtained. |
| Cardiac enzymes | Biomarkers of myocardial injury: Serial measurements of CPK, CPK-MB and cardiac troponin T have prognostic significance. In children presenting with LV dysfunction, an elevated level may suggest acute myocarditis. |
| Miscellaneous | Other lab studies: Anti-nuclear antibodies, serum carnitine levels, urine organic acids and serum amino acid profile (metabolic cardiomyopathy), blood and urine viral assays for Epstein-Barr, Coxsackie, cytomegalovirus, Lyme disease etc. |

**Table VII. Special investigations**

| | |
|---|---|
| Echocardiography | Segmental analysis, LV mass, wall thickness, LVEF, FS, TAPSE (Tricuspid annular plane systolic excursion) RV Fractional area shortening, IVC collapsibility index |
| Angiography | Diagnostic and cath interventions like device closure for appropriated shunt lesions, Ballooning procedures for stenotic valves, coarctation of aorta |
| CT angiography | For anatomical details of various congenital anomaly, pericardial thickening. |
| Magnetic resonance Imaging | For structural details, differentiates inflammatory myocarditis from other reasons of myocardial dysfunction, diagnosis of cardiac tumours, also for Qp:Qs calculations |
| Genetic testing | In children having dysmophism along with CHD, cardiomyopathies (30% may have genetic predisposition) |

**Laboratory work-up** (Table VI): As per protocol, child with HF must undergo various laboratory test to know about the functional status of other organs, electrolyte imbalance, endocrinal disorders, infection or collagen disorders. Arterial/venous blood gas analysis are essential. B-type natriuretic peptide-BNP (>300pg/ml) is a biomarker which can differentiate between infection and heart failure in a sick child.[8] Cardiac enzymes must be measured in cases of myocarditis and CAD.[9]

**Special investigation** (Table VII): Point of care (POCUS) echocardiography on day today basis, is now essential for every intensive care unit to assess structural abnormality; functional abnormality, left/right ventricular ejection fraction and fluid status. It also helps in long term follow-up and family screening in genetically predisposed cardiac abnormalities. Cath interventions are therapeutic in structural heart disease.[10] CT angio and magnetic resonance imaging provide additional modalities to make diagnosis.[11] In cases with possibilities of underlying genetic etiology, genetic testing must be done.[12]

## Management of heart failure[13-18]

The children with CHF may be grouped as follows: 1.Decompensated heart failure and cardiogenic shock; 2. Compensated heart failure and 3. Cardiac arrest: when ACLS/PAL protocols must be followed for the resuscitation and revival followed by the intensive care management.[16] Compensated heart failure has to be differentiated from decompensated heart failure as management varies (Table VIII). Asthma, pericarditis, electrolyte imbalance, cardiac tamponade, acute anemia, pneumothorax, sepsis have to be differentiated from heart failure.

**Table VIII. Compensated vs decompensated heart failure**

| Findings | Compensated HF | Decompensated HF |
|---|---|---|
| HR | Tachycardia | Tachycardia |
| CFT | Prolonged | Prolonged |
| Peripheral pulse | Weak | Weak imperceptible |
| Systolic BP | Normal | Low |
| Mottling skin, peripheral cyanosis | No | Yes |
| Metabolic acidosis | No | Yes |
| Altered Sensorium | No | Yes |
| Systolic BP | Normal | Low |

**Management of decompensated heart failure (Fig.2)** Goals of management are as follows :

i. Adequate oxygenation must be ensured with oxygen by prong or high flow cannula or with invasive or noninvasive mechanical ventilatory support. High frequency jet ventilation may optimize lung volumes at minimum mean airway pressures (Table IX).

ii. Rationalized volume replacement (5-10ml/kg) is recommended under monitoring with echo/invasive CVP monitoring or clinical evaluation of JVP and hepatomegaly. CVP/JVP>10 mmHg (if no cardiac or lung disease) correlates well with high left atrial filling pressure (PCWP=22mmHg). Echo-guided evaluation of the IVC size, collapsibility index, stroke volume and ejection fraction are more specific parameters for critical evaluation. The crystalloids are good choice for volume supplement but colloids, Plasma and blood can be given if required.

iii. Use of vasodilators and inotropes : In cardiogenic shock, combination of low dose epinephrine or dobutamine and low dose milrinone is one of the

effective combinations.[17-21] Levosimendan, a Ca+ sensitizer drug may help in tackling catecholamine receptor's down-regulation.[20] The ABP/VBG monitoring is required to strategize the use of inotropes, vasodilators and diuretics (Table X).

iv. Decongestion and judicious use of diuretics and vasodilators are recommended once the optimal systolic BP is achieved. Mostly a SBP of >80 mmHg and pulse pressure of more than 25% suggests adequate cardiac output in older children.

v. Timely drainage of significant pericardial effusion, pleural effusion, ascites not responding to conservative management, is required.

vi. Rhythm control: Heart rate and HR variability must be verified. Monotonous rhythm suggests for the arrhythmia or autonomic dysfunction particularly in a child with altered sensorium. IV administration of adenosine remains the first drug of choice in a hemodynamically stable patient. In an unstable patient, electrical cardioversion is recommended. The junctional tachycardia, common in post-op patients, can be treated with core cooling, amiodarone infusion and by reducing the doses of the inotropes. IV amiodarone is an obvious choice of most of the tachyarrhythmias barring polymorphic VT, due to its efficacy, relative safety and availability.

vii. There is role of identifying viral markers. Intravenous immunoglobulin is an established mode of therapy for Kawasaki disease but not yet in myocarditis and post inflammatory dilated cardiomyopathy (DCMP). However, cases of myocarditis where certain viral etiology (adeno or parvovirus B) is identified, success has been reported. In such cases, interferon B and immunosuppressant therapy with prednisolone with or without azathioprine or cyclosporine may also be valuable.[21]

viii. Pulmonary artery banding: PAB is regularly used in those CHDs with increased PBF where total correction is not possible. Recently it is used successfully in the cases of dilated cardiomyopathy also.

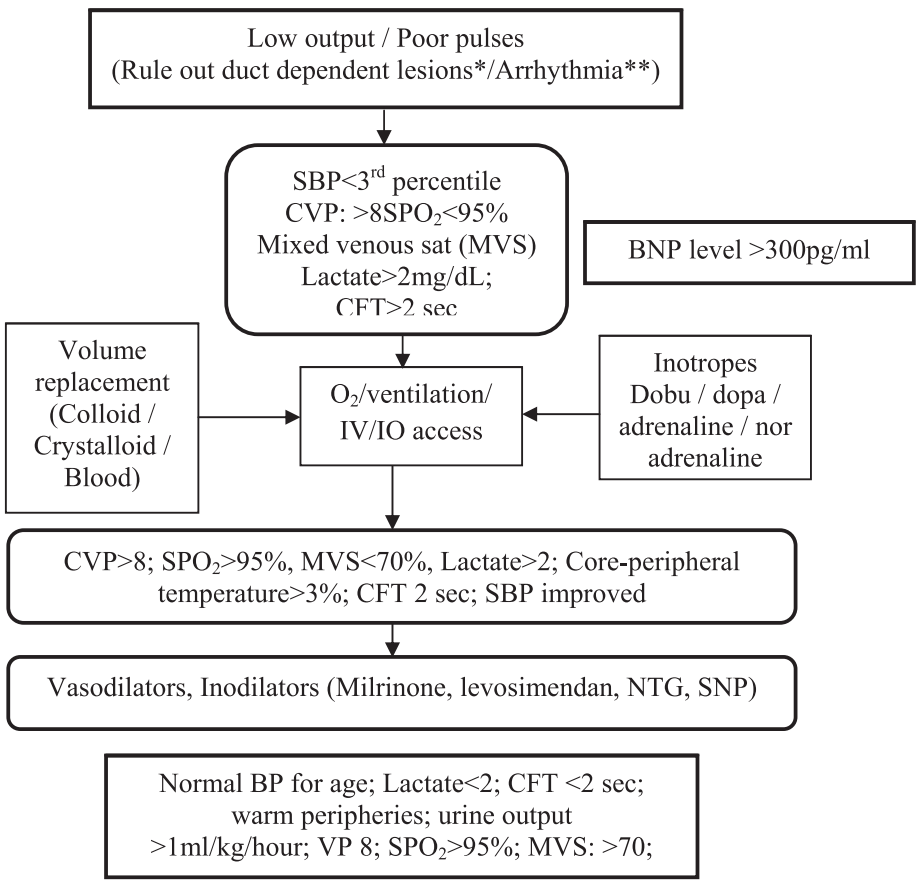


**Fig.2. Acute decompensated heart failure - Algorithm**

*SBP: Systolic blood pressure; CVP: central venous pressure; CFT: capillary filling time; B-NP: B-type natriuretic peptide; Dobu: Dobutamine; Dopa: Dopamine: NTG: Nitroglycerine; SNP: Sodium nitroprusside;**

ix. The correction of acidosis, hypo/hyperglycemia, hypo or hyperkalemia, hypocalcemia and hypomagnesemia, is paramount.

x. There may be a need of mechanical support (ECMO/ VAD) or a heart or heart-lung transplantation.

xi. Moderate hypothermia (33°C) in patients with cardiogenic shock and post resuscitation patients has been found to be neuro-protective.

xii. If endocarditis is suspected, antibiotics must be started after taking 3 cultures.

xiii. Endocrine agents like arginine vasopressin, tri-iodothyronine, angiotensin and hydrocortisone are being used to improve the outcome of HF presenting with shock.

xiv. Pulmonary vasodilators (sildenafil, bosentan) are recommended primary pulmonary hypertension. In children with RVF and not responding to pharmacotherapy, cath (balloon atrial septostomy) or surgical intervention (Pott's shunt) can be done.

xv. Primary or secondary systemic hypertension may also cause heart failure in children. They may present as hypertensive emergency. The normalization of blood pressure must be achieved in 24 to 48 hours.

**Management of heart diseases presenting with heart failure (Table XI)**

Usually babies with CHDs presenting with heart failure can be grouped as:

a. Cyanotic CHDs presenting with CHF: TGA/admixture physiology[22] and b. Acyanotic CHDs presenting with CHF: Valvular/vascular obstruction/anomalous origin of coronary artery from pulmonary artery.

**Transport of sick neonate**

Before planning transport of a neonate the diagnosis must be ascertained by clinical evaluation and all available diagnostic modalities. If prostaglandin infusion is required, mechanical ventilation must be kept handy. One must not try to give high oxygen to escalate $SpO_2$ above 90% in a baby with cyanotic CHD. Appropriate investigations and sepsis screening must be done and clinical summary must be sent to the targeted tertiary care centre. Also the financial burden must be explained to the family before transport.

**Assessment of therapeutic efficacy**

The useful indicators of successful correction are[13-18]

1. Reduced CRT (<2 sec), decreased core and peripheral temperature gap <2 degrees; improved color of skin, mental status, breathing pattern and pulse volume.
2. Improved systemic blood pressure (defined as - >60 mm Hg in term neonates; >70 mm Hg -in infants; >70 mm Hg + (2 × age in years) in 1-10 years; >90 mm Hg in age group >10years; mean arterial BP> gestational age or 30 mm Hg in preterm neonates)
3. Decrease in shock index (HR/SBP) - Shock Index Pediatric adjusted (SIPA)

**Table IX: Oxygen and ventilation in CHF**

| Strategies | Comments: |
|---|---|
| Spontaneous breathing | Spontaneous breathing helps diastolic flow across the pulmonary bed, hence good for restrictive RV physiology (example post op TOF) and Fontan repair. It can be supported with nasal prongs or high flow nasal cannula (0.5-2 L/min) |
| Non-invasive positive pressure ventilation (NIIPV)* | 1.: continuous positive airway pressure (CPAP) : Helpful in avoiding tracheal intubation in few cases. Also, it helps in weaning from mechanical ventilation. 2. bilevel positive airway pressure (BiPAP)BiPAP provides 2 levels of positive pressure: inspiratory positive airway pressure (IPAP) and expiratory positive airway pressure (EPAP). This is highly beneficial in patients with respiratory fatigue or failure. |
| Positive pressure Ventilation | Improves lung recruitment and interaction between cardio-pulmonary unit. It decreases the work of breathing, ventricular filling, ventricular transmural pressure and afterload in patients with LV dysfunction. In conditions with increased PBF helps in controlling PBF/pH/PVRI. Beneficial in conditions like myocarditis, post op structural heart diseases. |

*Non-invasive ventilation delivers mechanically assisted breaths without the placement of an artificial airway; includes continuous positive airway pressure (CPAP) and bilevel positive airway pressure (BiPAP)

**Table X. Antiarrhythmic drugs in emergency management of a child presenting with heart failure**

| Drugs | Dose |
|---|---|
| Lidocaine (IB) | Ventricular arrhythmia: 0.5-1 mg/kg q5-10 min. Loading dose: 1 mg/kg Maintenance: 10-50 mcg/kg/min by infusion |
| Esmolol | 50-100mcg/kg/min loading; maintenance:50-300mcgkg/min (max dose1000mcg) |
| Metoprolol | PO: 0.5-1 mg/kg/d, divided in 12 hourly doses; IV 0.1 mg/kg/dose; Infusion:3-5mcg/kg/min |
| Amiodarone (III) | 5 mg/kg IV/IO; bolus for VF/pulseless VT infuse over 20–60 min for perfusing tachycardias (25mcg/kg/min for 3-4 hours), Maintenance: 5-15 mcg/kg/min for 4-6 hour. PO: <1 year: 600-800mg/1.73$^2$ once a day 4-15 days. >1 year:2.5-5.mg/kg once a day. 4-15 days |
| Adenosine | First dose: 0.1 mg (100mcg)/kg IV (Max 6 mg) ; Second dose: 0.2 mg (200mcg)/kg IV (Max 12 mg); Third dose : 0.3 mg(300 mcg) IV (Max 18mg) |
| Digoxin | Initial digitalization dose 10-12 mcg/kg IV, q8h X3doses; 8-10mcg/kg PO in twice a day |

**Table XI. Timing and mode of intervention in various heart diseases**

| CHDS | Management |
|---|---|
| Acyanotic CHDs Severe PS/AS/coarctation of aorta (Card emergency)/ aortoarteritis | Prostaglandins for neonates. Infant and children: Emergency ballooning or surgery. COA, aorto-arteritis: Management of SBP, Ballooning, stenting, anti-inflammatory management of aortoarteritis |
| ALCAPA (Cardiac emergency) | Classical ECG (Figure 9) Management: ICU care, surgery-re-implantation of coronary artery into the aorta |
| Obstructed TAPVC (Card emergency) | Mechanical ventilation and urgent cardiac surgery. |
| Preterms with large PDA (Card. emergency) | Fluid restriction, decongestive medications, medical closure (indomethacin, ibuprofen, paracetamol). surgial closure or coiling. |
| Transposition of great vessels (Cardiac emergency) | Intact IVS-Prostaglandin infusion, BAS, Arterial switch operation within 2 weeks. TGA+VSD/PDA-decongestive therapy, Surgery 2-4 months. |
| Infants with admixture lesions (truncus arteriosus, TAPVC) | Decongestive therapy, nutritional support, elective Surgery: 4-8 weeks. |
| Ebstein's anomaly of TV, Uhl's Anomaly | Surgery is delayed till patients are symptomatic, depending on functional RV biventricular or univentricular repair is done. |
| Hypoplastic left heart syndrome | Modified Norwood surgery or hybrid PA banding +PDA stenting in neonates followed by Glenn (6 months) and later Fontan surgery. |
| VSD,PDA, AP Window | Decongestive therapy, nutritional support, Surgery-2- 6months of age |
| ASD/PAPVC | Intervention around 2 years of age. |
| Rheumatic valvular heart disease | Conservative management for ADHF and if it fails then for pure MS : BMV; Valve repair or replacement for the rest. |
| Pericardial diseases | Antibiotics, anti-inflammatory drugs, pericardial drainage, pericardiectomy for CP |
| Arrhythmia | Pharmacotherapy. DC conversion for tachyarrhythmia and temporary or permanent pacemaker for bradyarrhythmia |

A. 1.2 (4-6 years); B. 1 (6-12 years); C. 0.9 (>12 years)

4. Urine output more than 1 mL/kg per hour in infants and children or more than 30 mL/h in adolescents)
5. Mixed venous saturation more than 70% and blood lactate less than 2mmol/L.
6. Cardiac Index (CI) measured between more than 3.3 and less than 6 L/min/m2 (if measurement is possible).

## Outpatient management of pediatric heart failure

**Goals** - Patient who have compensated HF or those who have been treated successfully for ADHF are treated outside the hospital to maintain the successful outcome of in-house management with pharmaco-therapy and nutritional support, bridge to corrective (CHD) / transplant therapy and to rehabilitate the patients.

**General Measures:** The special care for children with HF includes feeding, nutritional support, home oxygen therapy.

### Pharmacologic therapy-to improve cardiac function

The drugs may be broadly grouped into three classes: a) to combat neuro-hormonal activation, oxidative stress and to induce reverse cardiac remodeling (eg: β blockers, ACE Inhibitors, ARBs (angiotensin receptor blockers), aldosterone antagonists (spironolactone and eplerenone). b) to keep the fluid balance (loop diuretics and thiazides) and c) To treat the precipitating cause like antihypertensive drugs, antiarrhythmic drugs, thyroxin, steroids.

### Angiotensin converting enzyme inhibitors (ACEi), angiotensin receptor blockers (ARBs), Neprilysin inhibitors

ACE inhibitors block the conversion of angiotensin I to Angiotensin II and hence they prevent RAS mediated catastrophic cardiovascular remodeling. They are contraindicated in azotemia and may cause hyperkalemia, hypotension, neutropenia, cough, altered taste and drug interactions. Primarily they are recommended for acyanotic and cyanotic CHD with increased PBF, systemic hypertension, DCMP as frontline drugs.

ARBs are a related class of drugs that act directly on Angiotensin II AT1 receptor. In practice, a beneficial effect is mitigation of cough due to unopposed actions of bradykinin, an effect of ACE inhibition. Sacubitril (neprilysin inhibitor) and valsartan (ARBS) combination is another promising new drug. Losartan is also useful in preventing aortic root dilatation in Marfan syndrome and alike diseases.

### β blockers

Beta-blockers antagonize catecholamine to decrease the heart rate, oxygen consumption, arrhythmogenicity, ventricular after-load by bringing down blood pressure. In due course, they improve the ejection fraction and promote ventricular remodeling. The metoprolol and bisoprolol are β1 selective drugs used for hypertension, tachyarrhythmia and HF. Carvedilol is a most widely used, non-selective β blocker for the HF in children, which has shown the beneficial effect on the cytosolic and mitochondrial calcium regulation during oxidative stress-induced apoptosis of cardiac myocytes.

### Digitalis

Despite the extensive debate against its use, digoxin stays in the list of the drugs recommended for HF. It increases sarcoplasmic calcium concentrations via inhibition of myocardial sodium-potassium ATPase pump. It increases diastolic time and is useful in controlling stress related sympathomimetic response generating disproportionate tachycardia. It has many side effects like-nausea, vomiting visual disturbances and rhythm disturbances. The dose of digoxin is reduced to less than two third, in those with DCMP particularly when combined with the carvedilol.

### Diuretics

Diuretics are best tool to optimize preload to counter the fluid overload and sodium retention. Use of loop diuretics requires careful monitoring of electrolytes, hypovolemia, renal function and urine output. Loop diuretics have been associated with toxicity like ototoxicity, dehydration, electrolyte imbalance and renal stones. Usually, aldosterone inhibitors or ACE inhibitors rather than oral potassium preparations are used, to overcome the hypokalemia associated with the administration of the loop diuretics in pediatric practice. Resistance to diuretics is known. It is defined as failure to reduce extravascular volume despite of adequate doses of diuretics. Excess intake of sodium may be one of the causes. Switching over to IV diuretics, use of AVP receptor antagonists or addition of metolazone (a thiazide like diuretic) can be a useful way to tackle it.

The aldosterone antagonists like spironolactone and eplerenone, are potassium sparing and they help in cardiac remodeling by inhibiting cardiac fibrosis.

**Arginine vasopressin receptor antagonist:** AVP level rises in patients with CHF and may be a cause of hyponatremia co-existing with CHF. Hence, AVP receptor antagonist-veptans like tolvaptan are potential adjunct in HF therapy.

**Inotropes in outpatient setting**

To optimize the cost, intermittent inotrope administration has been advocated as outpatient therapy. Some studies have shown some benefit of oral low dose milrinone and pulsed levosimendan.

**Anti-platelet, anticoagulation in HF**

Patients with severe LV dysfunction, atrial fibrillation and those with prosthetic implants need to be put on anticoagulation/antiplatelet therapy to avoid thrombosis.

**Nutrition in HF**

Failure to thrive is an important feature of CHF. Following are the factors responsible for the malnutrition. (a). Increased work of breathing and cardiac stress due to tachycardia, (b) Loss of appetite and recurrent chest infection, (c) altered microcirculation and permeability of intestine, (d) absorption of bacterial endotoxins by the GIT, triggering release of cytokines which then act as cardio suppressors. (e) Unplanned diet plan. Diet needs to be supplemented for Increased requirement of calories, protein, omega 3fatty acids and micronutrients: including thymine, l-carnitine, Vit D, Ca, Mg, taurine, co-enzyme Q 10. These micronutrients may also help in combating oxidative stress and mitochondrial function..There may be resistance to growth hormone, testosterone as well as appetite-stimulating peptide ghrelin, contributing to the failure to thrive.

## Advanced therapies for refractory HF

The patients with severe symptoms despite maximum pharmacotherapy, are designated as refractory, end stage (stage D) heart failure. Mechanical circulatory support is offered to these patients (Fig.3). They are not advised when long term outcome is poor because of other reasons like neurological or chromosomal disorders. A conceptual extension from the cardio-pulmonary bypass, used during the open heart surgery, the extracorporeal membrane oxygenation (ECMO) provides a window-period for spontaneous recovery of cardio-pulmonary unit (Fig.11). Intra-aortic balloon pump in pediatrics is only useful in bigger children. The ventricular assist devices (VAD) are artificial device with a life of 4-5 years, used as “bridge to transplant” in patients with refractory CHF, but are hugely expensive.

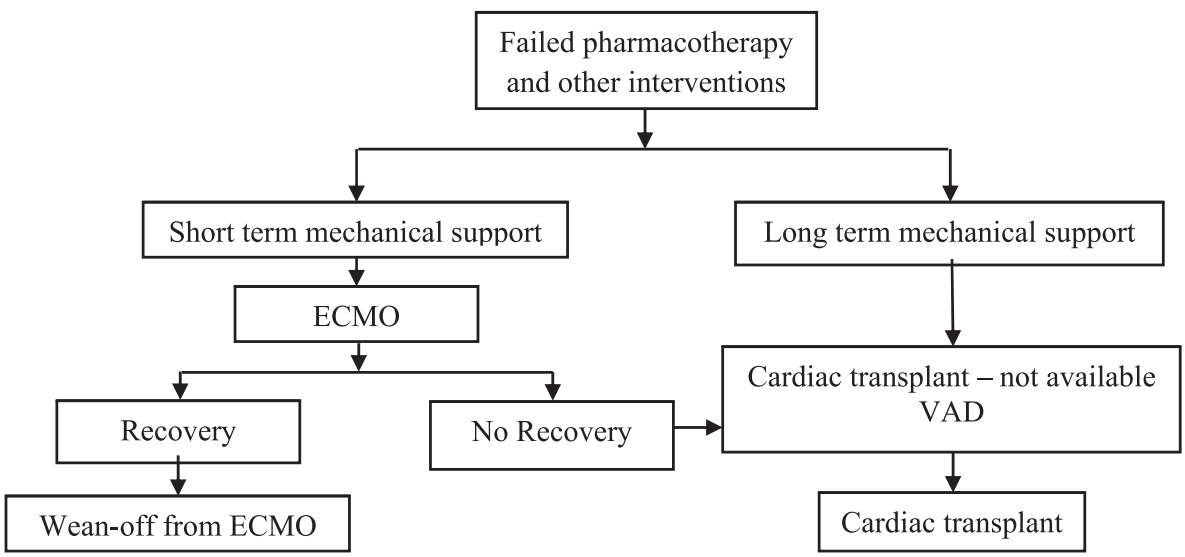


**Fig.3. Algorithm of mechanical support in heart failure**

**Electrophysiology considerations**

Intractable supraventricular and ventricular arrhythmia needs more definitive intervention. The important modalities to control arrhythmias are 1) pharmaco-therapy; 2) radiofrequency ablation; 3) modified mazeprocedure during cardiac surgery 4) intra ventricular device/ cardiac resynchronization therapy for recurrent VT;[23] 5) temporary or permanent pacemaker for patients with severe bradycardia(neonate: <55/min; children <40/min; in patients with CHD <70/min ) or bradycardia dependent VT.

**Cardiac transplantation for heart failure in children**

Cardiac transplantation is done for end stage HF or for complex congenital heart diseases –like HLHS, failed Fontan surgery.[24] This surgery is contraindicated in patients with primary or secondary PPH (PVRI more than 6 woods unit), HIV infection, chronic liver and kidney diseases.

The over-all survival 20 years after transplantation is 40%. The pediatric survival rate is 80% after 1 year and about 70% after 5 years. Late survival is limited by graft rejection, coronary allograft vasculopathy and infections.[25]

**Stem cell therapy**

Much hyped**,** cardiac specific **s**tem cell therapy is the most attractive butfuturistic modality, in present. It would be an ideal alternative to cardiac transplant for those patients who are suffering from end-stage heart diseases. Potential indications for stem cell use in pediatric heart failure include creation of biological heart valves, tissue, engineered vessels, and biological pacemakers.[8,14]

## Points to Rembember

- ***The clinical syndrome of HF may result from congenital or acquired disorders of the pericardium, myocardium, endocardium, heart valves, or great vessels or from certain metabolic abnormalities.***
- ***The traditional decongestive and ionotropy-based management has been replaced by pharmacotherapy based on neurohumoral model of HF bringing in ACEi/ARBs/betablockers/levosimendan as the preferential drugs. The micro and macro-nutritional factors with anti-oxidant property are also related to better outcome.***
- ***Very high doses of dopamine and dobutamine must be avoided and rather combination of inotropes must be preferred. Fluid challenges and diuretics must be used with monitoring of CVP and input and output charting.***
- ***A meticulous effort has to be made to identify a correctable etiology a timely intervention may lead to complete recovery.***
- ***Pulmonary artery banding in DCM is a new modality promised to be an effective alternative therapy.***
- ***IVIG and immunosuppressant therapy have limited but beneficial use in some subsets of patients.***
- ***Mechanical support and cardiac transplant therapy, are now available in India but cost is an issue and family counselling is very important.***

## References


1. Hsu DT, Pearson GD. Heart Failure in Children: Part I history, etiology, and Pathophysiology. Circ Heart Fail 2009; 2:63-70.
2. Sommers C, Nagel BH, Neudorf U, Schmaltz AA. Congestive heart failure in childhood. An epidemiologic study. Herz 2005; 30:652– 662.
3. Kaludercic N, Carpi A, Paolocci N; Monoamine oxidases (MAO) in the pathogenesis of heart failure and ischemia/ reperfusion injury; Advances in monitoring and management of shock. Ped Clin North Am 2013; 60(3); 641-654.
4. Connolly D, Rutkowski M, Auslender M, Artman M. The New York University Pediatric Heart Failure Index: a new method of quantifying chronic heart failure severity in children. J Pediatr 2001; 138:644–648.
5. Ross RD, Bollinger RO, Pinsky WW. Grading the severity of congestive heart failure in infants. Pediatr Cardiol 1992; 13:72–75.
6. Tandon R; Bedside approach in the diagnosis of congenital heart diseases; second edition; published by Sitaram Bharatiya institute o science and research 2009.
7. Talner N. Heart failure. In: Heart Disease in Infants, Children, and Adolescents. 1995:1746-1773.
8. Auerbach SR, Richmond ME, Lamour JM, Blume ED, Addonizio LJ, Shaddy RE, et al. BNP levels predict outcome in pediatric heart failure patients: post hoc analysis of the pediatric carvedilol trial. Circ Heart Fail 2010; 3:606-611.
9. Soongswang J, Durongpisitkul K, Nana A, Laohaprasittiporn D, Kangkagate C, Punlee K, et al. Cardiac Troponin T: a marker in the diagnosis of acute myocarditis in children. Pediatr Cardiol 2005; 26:45-49.
10. Srinivasan S, Cornell TT; Bedside ultrasound in pediatric critical care: a review. Pediatr Crit Care Med 2011; 12(6):667–674.
11. Laissy JP, Messin B, Varenne O, Iuag B, Karila-Cohen D, Schouman-Claeys E, et al. MRI of acute myocarditis: a comprehensive approach based on various imaging sequences. Chest 2002; 122: 1638–1648.

12. Pierpont ME, Basson CT, Benson DW Jr, Gelb BD, Giglia TM, Goldmuntz, et al. Genetic basis for congenital heart defects: Current Knowledge; a Scientific Statement from the American Heart Association Congenital Cardiac Defects Committee, Council on Cardiovascular Disease in the Young: endorsed by the American Academy of Pediatrics. Circulation 2007; 115: 3015-3038.
13. Shekerdemian L. Acute circulatory failure: Pharmacological and mechanical support. Chapter 14, Pediatric cardiology, Third Edition. Editors- Anderson RH, Baker EJ, Penny DJ, Redington AN, Rigby ML, Wernovsky G. Churchil Livingstone. Elsevier 2010.
14. Cotter G, Moshkovitz Y, Milovanov O, Salah A, Blatt A, Krakover R, et al: Acute heart failure: a novel approach to its pathogenesis and treatment. Eur J Heart Fail 2002; 4:227-234.
15. Andrews RE, Fenton MJ, Ridout DA, Burch M. New-onset heart failuredue to heart muscle disease in childhood: a prospective study in the United kingdom and Ireland. Circulation 2008; 117:79–84.
16. Part 12: Pediatric Advanced Life Support2005 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. Circulation 2005; 112: IV-167-IV-187.
17. Clifford M. Inotropes in Children. Australasian Anaesthesia 2005:129-134.
18. Mtaweh H, Trakas EV, Su E, Carcillo JA, Aneja RK. Advances in Monitoring and Management of Shock. Pediatr Clin North Am 2013; 60:641–654.
19. Beekman RH, Rocchini AP, Dick M II, Crowley DC, Rosenthal A. Vasodilator therapy in children: acute and chronic effects in children with left ventricular dysfunction or mitral regurgitation. Pediatrics 1984; 73:43-51.
20. Braun JP, Schneider M, Kastrup M, Liu J. Treatment of acute heart failure in an infant after cardiac surgery using levosimendan. Eur J Cardiothorac Surg 2004; 26:228-230.
21. Magnani JW, William G, Myocarditis: current trends in diagnosis and treatment. Circulation 2006; 113:876-890.
22. Mishra S. Khatri S. Congenital heart diseases and duct dependent circulation; chapter 5,84-97; in An comprehensive approach to congenital heart diseases; Editor in Chief-Dr IB Vijaylaxmi; Jaypee Publishers, 2013.
23. Cecchin F, Frangini PA, Brown DW, Fynn-Thompson F, Alexander ME, Triedman JK, et al. Cardiac resynchronization therapy (and multisite pacing) in pediatrics and congenital heart disease: five years experience in a single institution. J Cardiovasc Electrophysiol 2009; 20:58–65.
24. Blume ED, Naftel DC, Bastardi HJ, Duncan BW, Kirklin JK, Webber SA. Outcomes of children bridged to heart transplantation with ventricular assist devices: a multi-institutional study. Circulation 2006; 113:2313–2319.
25. Caspi O, Lesman A, Basevitch Y, Gepstein A, Arbel G, Habib IH, et al. Tissue engineering of vascularized cardiac muscle from human embryonic stem cells. Circ Res 2007; 100:263–272.

## CLIPPINGS

***Effectiveness of Vaccination During Pregnancy to Prevent Infant Pertussis.***

Immunization with the tetanus, diphtheria, and acellular pertussis (Tdap) vaccine is recommended for women during each pregnancy. This provides passive protection against pertussis to their infants. Although passive transfer of maternal antibodies can blunt the infant's own immune response to infant doses of the diphtheria, tetanus toxoids, and acellular pertussis (DTaP) vaccine, it does not appear to interfere with clinical vaccine efficacy. In a retrospective study of nearly 150,000 infants at every level of DTaP vaccine exposure, infants exposed in utero to Tdap vaccine were better protected against pertussis during the first year of life than infants not exposed in utero. This study strongly supports the current recommendation to administer Tdap during each pregnancy.

***Baxter R, Bartlett J, Fireman B, Lewis E, Klein NP. Effectiveness of Vaccination During Pregnancy to Prevent Infant Pertussis. Pediatrics 2017; 139(5) Epub 2017 Apr 3.***

**CARDIOLOGY**

# CONGENITAL HEART DEFECTS - NONSURGICAL MANAGEMENT

***Snehal Kulkarni**
****Tanuja Karande**

**Abstract:** *Structural heart defects in children are the most common congenital anomalies. Surgery was the only option until few years back. Today, therapeutic catheterization techniques have replaced conventional surgery for many lesions. The percutaneous transcatheter procedures may be broadly grouped as dilations (septostomy, valvuloplasty, angioplasty and endovascular stenting) or as closures (vascular embolization and device closure of defects). With improving hardware and increasing experience and expertise, more and more procedures are being performed with great degree of safety and efficacy. The major advantages of non surgical procedures are avoidance of thoracotomy, cardiopulmonary bypass and scar, along with a shortened period of hospitalization, less post-operative pain and recuperation period.*

**Keywords:** *Nonsurgical management, Cardiac defect, Congenital.*

Most of the congenital heart defects are structural heart defects and need treatment to repair these defects. Previously cardiac surgery was the only option. Over the past decade, some of these defects can be repaired with nonsurgical or transcatheter treatment. These procedures are performed in cardiac catheterization laboratory under fluoroscopic guidance.

The field of catheter based interventions for congenital heart lesions spans nearly half a century with the Rashkind balloon atrial septostomy first performed in 1966. Interventional pediatric cardiology since then has come a long way and several lesions are now treated by minimally invasive transcutaneous route. These procedures are carried out on a beating heart under fluoroscopic guidance via transfemoral route and patient can be discharged the following day of the procedure without any scar. The pediatric cardiac interventions are given in Box 1.

**Box 1. Pediatric cardiac interventions**

1) Balloon atrial septostomy
2) Closure of shunt lesions:
   - Atrial level - ASD device closure
   - Ventricular level - VSD device closure
   - Great vessel level - PDA closure, AP window device closure
3) Balloon dilatation of stenosed valves /
   - Valvuloplasties
   - Balloon aortic valvuloplasty
   - Balloon pulmonary valvuloplasty
4) Balloon dilatation of (Angioplasties) / Stent placement in stenosed vessels
   - For coarctation of aorta
   - Branch pulmonary arteries
   - Stenting patent ductus arteriosus in duct dependent lesions
5) Miscellaneous procedures
   - Closure of coronary AV fistulae
   - Hybrid procedures in operation theatre

*ASD - Atrial septal defect; VSD - Ventricular septal defect; PDA - Patent ductus arteriosus; AP window - Aortopulmonary window*

## Balloon atrial septostomy (BAS)

The commonest neonatal intervention performed in the cardiac catheterisation laboratory still remains to be atrial septostomy. It is a life saving procedure and is classically required in babies with transposition of great vessels with intact inter ventricular septum. Most often the ductus arteriosus is inadequate for mixing of the oxygenated blood and an additional shunt in the form of atrial communication is necessary.

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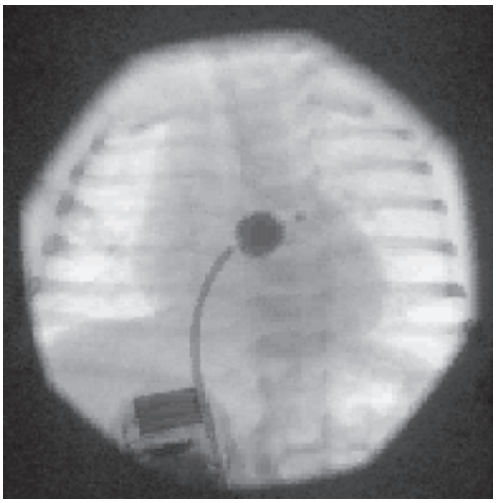

**Fig.1. Balloon atrial septostomy - Inflated balloon in left atrium**

The procedure requires a venous access (femoral / umbilical vein) and an uninflated balloon is passed into the left atrium through patent foramen ovale. Then the balloon is inflated in the left atrium and pulled back into the right atrium with a controlled force. This forceful "jerk" allows an inflated balloon to open the restrictive atrial septum optimally (Fig.1). Conventionally, the procedure is performed in the catheterization laboratory under fluoroscopic guidance although, it can be safely performed in the neonatal intensive care unit under echocardiographic guidance. Because septal thickness increases with age, balloon atrial septostomy is effective only in infants less than 1 to 2 months of age. Complications are very less. Minor complications include rhythm disturbances.

## Closure of shunt lesions

**Atrial septal defect (ASD) device closure:** Percutaneous closure is now the procedure of choice over surgical closure for majority of ostium secundum atrial septal defects in both children and adults, with experienced centres successfully closing over 80% of all ASDs in selected cases.[1] It is carried out under general anesthesia mainly under transesophageal echocardiographic guidance. There are many devices currently available, and Amplatzer septal occluder was the first to receive FDA approval in December 2001. The device is made of nitinol (a metal alloy of nickel and titanium) wire mesh and consists of two discs with a connecting waist (Fig.2). Class I indication of ASD device closure as per AHA guidelines is ostium secundum ASD causing volume overload on the right side of the heart (RA and RV enlargement) with suitable anatomic features (adequate margins).[2]

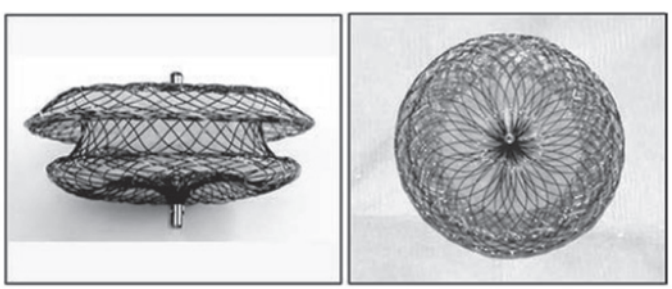

**Fig.2. Amplatzer septal occluder**

Contraindications for device closure includes ostium primum ASD, sinus venosus defects, very large ASDs with insufficient rims, active infection, contraindication to aspirin and associated other cardiac lesions which need surgical intervention. The limitations of the procedure is that it can be carried out only in select patients of secundum ASD with good rim margins. Complications of this procedure are device migration, device malposition, embolization, cardiac erosion leading to cardiac tamponade and rhythm disturbances.[3]

**Ventricular septal defect closure (VSD):** VSDs account for 20- 30% of all forms of CHD.[4] The septum can be divided into 4 regions: membranous, inlet, trabecular and outlet. VSDs can be single in any of the mentioned regions or multiple ("Swiss cheese") in the muscular part of the septum. Only small to moderate sized VSDs which are either muscular or perimembranous can be closed by

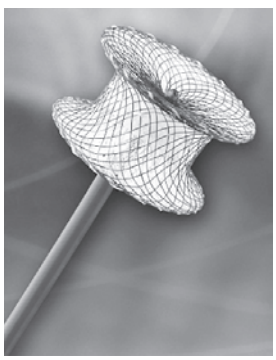

**Fig.3. Muscular VSD closure device with double discs**

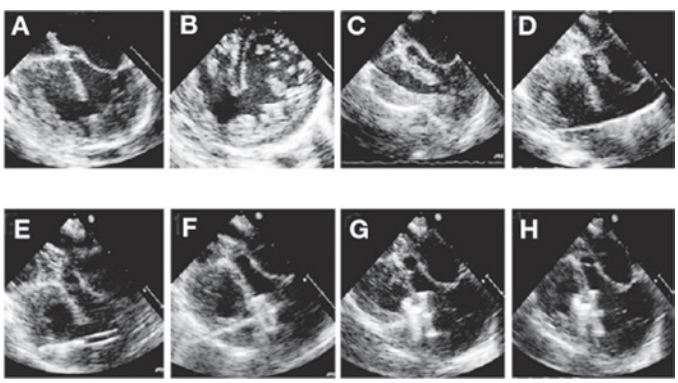


**Fig.4. VSD device closure under transesophageal guidance**

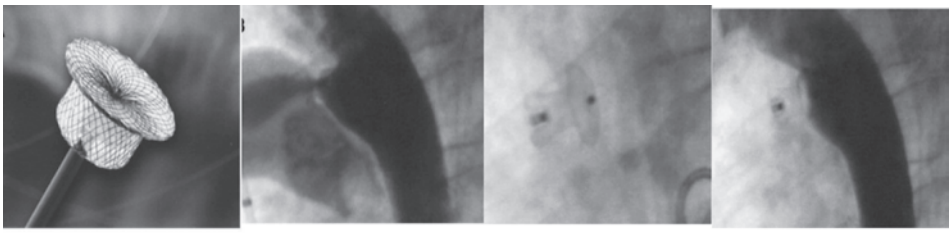


**Fig. 5. Procedure of PDA closure with device**

transcatheter techniques. Most of the VSDs which are in the inlet or outlet location cannot be closed by this technique (Fig.3 and 4).

Indications for VSD device closure: Children more than 5kg in weight and with favorable anatomy are considered candidates for percutaneous closure and adolescents with muscular small VSDs producing left heart volume overload. Some of VSDs can be closed in the operation theatre by hybrid technique (Fig.4). Complications include device migration and embolization. There is a long term risk of complete heart block and aortic regurgitation after closure of perimembranous VSD and hence long term follow up is required to monitor these complications.

**Patent ductus arteriosus closure:** The incidence of isolated patent arterial duct in full-term infants is about 1 in 2000 live births, accounting for approximately 10% of all types of congenital heart disease. Occlusion of the PDA was first described in 1971 with an Ivalon plug.[5] Transcatheter closure of PDA has become a standard practice of closure of PDA in children. Surgery is required in very small neonates and very large PDAs. Small PDAs (<2mm) are easily closed with stainless-steel Gianturco coils. Larger PDAs are closed with the duct occluder devices, which are mushroom-shaped devices with a nitinol frame and filled with an occlusive polyester fabric mesh. This device is delivered from the venous approach placing the 'hat' in the aortic ampulla and the 'stem' in the PDA itself (Fig.5). Closure rates are virtually 100% for PDAs up to 10mm and complications are rare.

**Indications for PDA device closure:** Transcatheter PDA occlusion is indicated for the treatment of a moderate-sized or large PDA with left-to-right shunt that results in any of the following - congestive heart failure, failure to thrive, pulmonary over circulation (with or without pulmonary hypertension), or an enlarged left atrium or left ventricle, provided the anatomy and patient size are suitable.

## Balloon dilatation of stenosed valve

**Balloon aortic valvuloplasty:** Bicuspid aortic valve with severe valvular stenosis is a common emergency in neonates and small infants. Valvular aortic stenosis is a progressive disease usually requiring multiple interventions. Balloon aortic valvuloplasty is the procedure of choice in severe valvular aortic stenosis. The procedure is usually performed from a retrograde approach via a femoral artery. Detailed echocardiography is required prior to the procedure for measurement of aortic valve annulus, assessment of left ventricular function and associated lesions like coarctation of aorta.

Indications are based on the gradients across the valve and ventricular function. But it is indicated regardless of valve gradient in the newborn with isolated critical valvular AS who is ductal dependent or in children with isolated valvular AS and depressed left ventricular systolic function. In children it is indicated with isolated valvular AS who have a resting peak systolic valve gradient (by catheter) of >50 mm Hg or peak systolic valve gradient (by catheter) of >40 mm Hg if there are symptoms.

Balloon dilation provides excellent palliation for most children with congenital valvular AS though it cannot be considered curative as valve restenosis or significant valve regurgitation eventually necessitates the need for reballooning or surgical intervention in 20-30% of cases. Complications include possibility of injury to femoral artery and with use of larger sized balloon aortic regurgitation can happen.

**Balloon pulmonary valvuloplasty:** Balloon valvuloplasty remains the treatment of choice for valvular pulmonary stenosis in patients of all ages and has almost replaced surgery. Restenosis after balloon dilation is rare, with few children ever requiring repeat dilation. The indications for balloon therapy is a transvalvular echocardiographically determined gradient of ≥50 mmHg with normal cardiac output. The subgroup of patients with thickened, dysplastic pulmonary valves, as commonly seen in Noonan syndrome, has however shown a lower success rate with balloon valvuloplasty.[6]

Pulmonary regurgitation after dilation is common, occurring in 10% to 40% of patients. Balloon pulmonary valvuloplasty is a relatively safe procedure and is the first

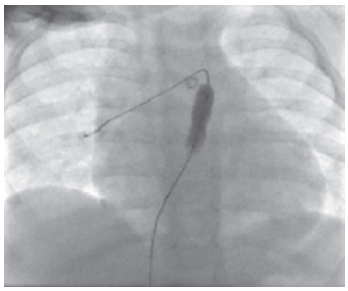

**Fig.6. Balloon pulmonary valvotomy - shows inflated balloon across pulmonary valve**

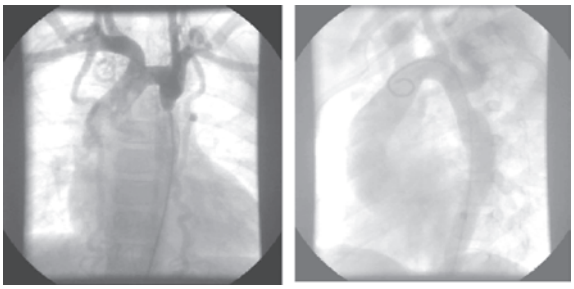

**Fig.7.Stent implantation for coarctation of aorta**

line of management in cases with severe valvular PS (Fig.6). Recently, modified catheterization techniques have been developed for treatment of newborns with pulmonary atresia and intact ventricular septum. The atretic membranous valve can be perforated with a wire or with a hot tipped catheter using laser or radiofrequency energy. Once perforated, the valve is balloon dilated to create unobstructed continuity between the right ventricle and pulmonary artery.[7]

## Balloon dilatation/stent placement of stenosed vessels

**Balloon dilatation of coarctation of aorta:** Coarctation of the aorta (CoA) is a common form of CHD, accounting for 6% to 8% of all cardiac defects. The prevalence of coarctation is increased in certain disorders, such as Turner syndrome.[8] The most common associated cardiac anomaly is bicuspid aortic valve, which is present in 30% to 40% of all cases. The usual location of coarctation is juxtaductal, just distal to the left subclavian artery. Neonates with coarctation of the aorta may present with signs and symptoms of low cardiac output and shock once the ductus arteriosus closes. Older infants and children may present with hypertension, headaches and claudication. For native coarctation of the aorta, initially, surgical repair (extended resection with an end-to-end anastomosis) has been the primary treatment at most centers and remains the "gold standard" therapeutic option especially for neonates and small infants. Balloon angioplasty is usually indicated in older children above the age of one year and for restenosis after surgical repair.

**Balloon dilatation with stent implantation:** Common indications for stent deployment in CHD[9] include treatment of obstructive lesions of the branch and peripheral pulmonary arteries, systemic veins, aorta and its branches, right ventricular outflow tract (RVOT) conduits and maintenance of patency of the arterial duct in duct-dependent circulation. Most of these vessels are elastic structures and there is a tendency of recoil after balloon dilatation. Stents keep the narrowed vessels open.

The largest pediatric experience is with stenting of congenital or postoperative branch pulmonary artery stenoses. These lesions are difficult if to access surgically and the rate of restenosis after attempted surgery has been high. Stent repair of CoA may be useful in preventing restenosis and aneurysm formation seen after surgery or balloon angioplasty (Fig.7). A large delivery sheath is required for implanting the majority of stent diameters. This may cause vascular complications, which is of major concern when implanting a stent (via the femoral artery) to treat CoA.

## Hybrid procedures

Hybrid pediatric cardiac surgery is an emerging field that combines skills and techniques used by pediatric cardiac surgeons and interventional pediatric cardiologists. Both surgery and transcatheter approaches have limitations if performed independently. The invasive nature of surgery and long cardiopulmonary bypass time have potential developmental implications when done at a very young age. Transcatheter approaches may be limited by access, patient size, and related issues. It is often not physically possible to deliver the required devices intravascularly through relatively large delivery sheaths that are difficult to negotiate around the curves of the heart. Therefore, it is not surprising that surgeons and interventionalists have increasingly started working together to maximize the potentials and minimize the limitations of their respective approaches. It is in this setting that the "hybrid" approach to CHD has evolved. This type of collaboration provides the interventionalist and surgeon with direct access to the heart and may help patients avoid the need for cardiopulmonary bypass.[10] Currently hybrid approach is used in hypoplastic left heart syndromes, periventricular VSD closure and pulmonary valve implantation.

## Conclusion

Pediatric cardiac intervention is a rapidly advancing field with several new procedures replacing some of the simpler surgeries. Advances in interventional hardware has improved the potential of interventions in neonates.

## Points to Remember

- ***Pediatric cardiac intervention is a rapidly advancing field with several new procedures replacing some of the simpler surgeries in congeital heart defects.***
- ***A mainstay of interventional congenital cardiology is the use of transcatheter balloon dilation and stenting to relieve vascular stenoses and closure of shunts using various FDA approved devices.***
- ***Hybrid pediatric cardiac surgery is an emerging field that combines skills of pediatric cardiac surgeons and interventional pediatric cardiologists.***

## References


1. Butera G, Romagnoli E, Carminati M, Chessa M, Piazza L, Negura D, et al. Treatment of isolated secundum atrial septal defects: impact of age and defect morphology in 1013 consecutive patients. Am Heart J 2008; 156(4): 706 -712.
2. Feltes TF, Bacha E, Beekman RH III, Cheatham JP, Feinstein JA, Gomes AS, et al. Indications for cardiac catheterization and intervention in pediatric cardiac disease: a scientific statement from the American Heart Association. American Heart Association Congenital Cardiac Defects Committee of the Council on Cardiovascular Disease in the Young; Council on Cardiovascular Radiology and Intervention. Circulation 2011; 123(22):2607-2652.
3. Dibardino DJ. Clarification of statements made regarding investigation into Amplatzer device complication incidence and comparison with the Society of Thoracic Surgery database. J Thorac Cardiovasc Surg 2009; 138: 784 –785.
4. Rudolph AM. Ventricular septal defect. In: Rudolph AM. Congenital Diseases of the Heart: Clinical-Physiological Considerations. Armonk, NY: Futura Publishing; 2001;pp197–244.
5. Porstmann W, Wierny L, Warnke H, Gerstberger G, Romaniuk PA. Catheter closure of patent ductus arteriosus: 62 cases treated without thoracotomy. Radiol Clin North Am 1971; 9:203–218.
6. Witsenburg M, Talsma M, Rohmer J, Hess J. Balloon valvuloplasty for valvular pulmonary stenosis in children over 6 months of age: initial results and long-term follow-up. Eur Heart J 1993; 14:1657–1660.
7. Justo RN, Nykanen D, Williams WG, Freedom RM, Benson LN. Transcatheter perforation of the right ventricular outflow tract as initial therapy for pulmonary valve atresia and intact ventricular septum in the newborn. Cathet Cardiovasc Diagn 1997; 40:408-413.
8. Gotzsche CO, Krag-Olsen B, Nielsen J, Sørensen KE, Kristensen BO. Prevalence of cardiovascular malformations and association with karyotypes in Turner's syndrome. Arch Dis Child 1994; 71:433–436.
9. Peters B, Ewert P, Berger F. The role of stents in the treatment of congenital heart disease: Current status and future perspectives. Ann Pediatr Cardiol 2009; 2(1):3-23. doi:10.4103/0974-2069.52802.
10. Holoshitz N, Kenny D, Hijazi ZM. Hybrid Interventional Procedures in Congenital Heart Disease. Methodist DeBakey Cardiovasc J 2014; 10(2):93-98.


## NEWS AND NOTES

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**CARDIOLOGY**

# CARDIOGENIC SHOCK

***Arpita Chattopadhyay**
****Rakesh Lodha**

**Abstract:** *Cardiogenic shock is defined as a state of acute circulatory failure, leading to reduced cardiac output that is unable to meet the metabolic demands of the body. Apart from congenital heart diseases, other causes of acute heart failure such as primary or secondary cardiomyopathy, several metabolic, infectious and medications or toxin related etiologies may present as cardiogenic shock. Management involves fine tuning oxygen consumption and delivery variables by titrating inotropes, vasopressors, mechanical ventilation and in some cases extra corporeal membrane oxygenation. This article summarizes the pathophysiology, diagnosis and management of a pediatric patient presenting with cardiogenic shock.*

**Keywords:** *Cardiogenic shock, Myocarditis, Cardiac output, Systolic heart failure.*

Cardiogenic shock is a state of acute circulatory failure with end organ hypoperfusion due to low cardiac output. The diagnosis is established mainly on clinical examination with the following features:

i) Sustained hypotension (<5$^{th}$ percentile for age) or need of vasopressors to maintain blood pressure above 5$^{th}$ percentile for age.

ii) Signs of pulmonary congestion – due to elevated left ventricular end diastolic pressure.

iii) Evidence of end organ hypoperfusion - cold and clammy peripheries, altered mental status, oliguria and elevated serum lactate.[1]

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## Epidemiology

Population studies from the United States reported admission rates for pediatric heart failure of 17.9 per 100,000 children in 2006. Of these, congenital heart diseases (CHD) comprised 69.3% of total admissions for heart failure, while cardiomyopathy, myocarditis and arrhythmias comprised admission rates of 13.6, 2.1 and 15.2%, respectively. Further 2.8% of patients admitted with heart failure underwent extra corporeal membrane oxygenation (ECMO), while 0.8% required ventricular assist device (VAD).[2] Studies from India on prevalence of cardiogenic shock among children presenting with shock are few. Of the few studies, a study conducted in Punjab in 2006,[3] showed that cardiogenic shock constituted 17% of the total cases of shock. Among these cases, CHD was most common cause (53%) followed by cardiomyopathy (23.5%) and heart rate abnormalities (23.5%). Mortality in patients with cardiogenic shock was 57%. Although mortality depends upon the etiology of shock, it increases in the presence of co-morbidities (acute kidney injury, liver failure or sepsis) by up to five times.[4]

## Etiology

Etiology of cardiogenic shock in children is given in Box 1.

## Pathophysiology

Depending on the underlying etiology, patients in cardiogenic shock have low cardiac output either due to impaired filling/diastolic dysfunction or impaired emptying / systolic dysfunction or both.[5]

Infants and children with heart failure primarily increase cardiac output by increasing heart rate due to small ventricular mass resulting in inability to make appreciable changes in contractility [Cardiac output (CO) = Heart rate (HR) X Stroke volume (SV)]. Determinants of stroke volume are preload, afterload and contractility. The clinical application of Frank Starling's relationship, which describes how with an increased ventricular filling during diastole (venous return), the ventricular fiber length increases, which in turn increases the ventricular contraction and thus the stroke volume helps to titrate preload.[6]

**Box 1. Cardiogenic shock - Etiology**

| | |
|---|---|
| **Congenital heart disease** | **Cardiomyopathy** |
| Hypoplastic left heart syndrome | Glycogen storage disease |
| Aortic stenosis | Carnitine deficiency |
| Coarctation of Aorta | Hypothyroidism |
| Anomalous left coronary artery from | Mucopolysaccharidosis |
| pulmonary artery (ALCAPA)) | Disorder of fatty acid metabolism |
| | Infectious agents – bacterial, viral, fungal, protozoal. |
| **Rhythm abnormalities** | **Metabolic** |
| Supraventricular tachycardia | Hypocalcemia |
| Ventricular tachycardia | Acidosis |
| Bradyarrhythmias | Hypothermia |
| **Drug induced** | **Neuromuscular disorders** |
| Anthracyclines | Duchenne muscular dystrophy |
| | Myotonic dystrophy |
| **Ischemia re-perfusion injury** | Spinal muscular dystrophy |
| Post-operative state | Friedreich's ataxia |
| Post cardiac arrest state | **Cardiac tamponade** |

Impaired myocardial relaxation due to diastolic dysfunction leads to increased ventricular diastolic pressure which is transmitted to the lung and results in pulmonary edema and dyspnea. Such children are in heart failure often with normal systolic ventricular function.[7] Subendocardial ischemia may also develop due to decreased myocardial perfusion pressure as a result of elevated left ventricular end diastolic pressure (e.g. left ventricular hypertrophy due to long standing hypertension).[7]

The goal of treatment is by manipulating Frank Starling law physiology so as to titrate preload and afterload, such that ventricle remains on the flat portion of its pressure-stroke volume (SV) curve. If it falls on the steep portion of its function curve, SV and CO will decrease, patient will be preload responsive (with a stroke volume deficit) or have excessive LV end diastolic volume (myocytes stretched beyond their ability to generate force) culminating in heart failure. Thus, an adequate ventricular filling pressure is essential so as to maintain SV and CO.[5]

## Clinical signs

According to Dr. Lynne Warner Stevenson's concept,[8] patients in cardiogenic shock may present either with signs of congestion at rest such as orthopnea, raised jugular venous pressure (JVP), edema and basal crepitations and or signs of hypoperfusion at rest (cold clammy extremities, tachycardia, narrow pulse pressure, altered mental status and reduced urine output). Children in cardiogenic shock often enter a vicious cycle of neurohormonal activation to compensate for poor cardiac output, leading to increase in systemic vascular resistance, further deteriorating contractility and pump function. Based on the findings they may fit in any of the four categories (Fig.1).

**Cold and wet:** Presence of evidence of hypoperfusion due to impaired myocardial contractility and congestion due to increased left ventricular filling pressure (systolic and diastolic dysfunction).[10]

**Cold and dry:** Critical hypoperfusion with impaired myocardial contractility and low left ventricular filling pressure (systolic dysfunction).[10]

**Warm and wet:** Normal myocardial contractility but high left ventricular filling pressure due to impaired myocardial relaxation (diastolic dysfunction).[10]

**Warm and dry:** Normal state or seen in compensated heart failure.

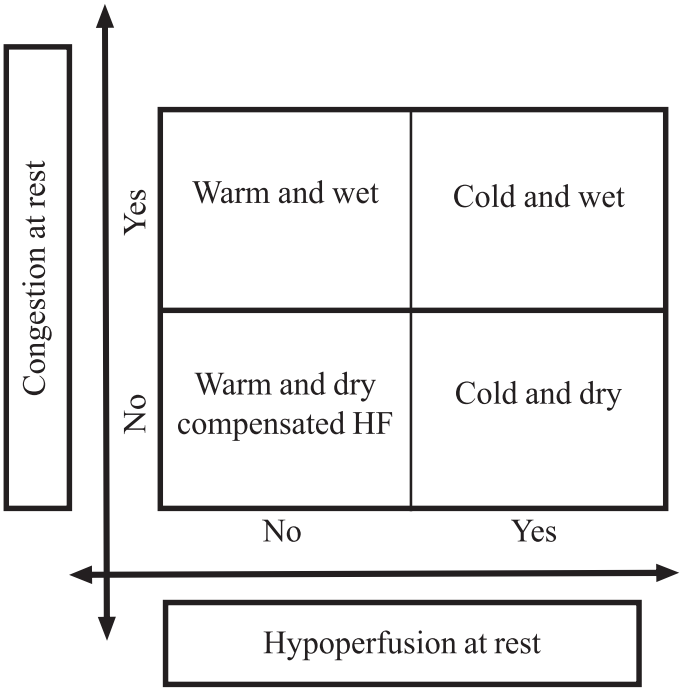


**Fig.1. Table for bedside assessment and early recognition of pathophysiological state in cardiogenic shock[9]**

## Monitoring

**Heart rate and rhythm:** Continuous monitoring of heart rate and rhythm is essential as it gives valuable clues to patient's preload, ventricular function and cardiac output. A thorough knowledge of rhythm disturbances expected to be seen with certain cardiac surgeries, congenital heart lesions or drug toxicity helps guide treatment.

**Systemic arterial blood pressure:** Indwelling arterial catheters are considered as part of essential monitoring in patients with cardiogenic shock. A wide pulse pressure points to aortic run off lesions (aortic regurgitation) while a narrow pulse pressure suggests low stroke volume or increased tone of vessels. Also arterial lines are used to guide titration of vasopressors in patients with cardiogenic shock.

**Central venous pressure (CVP):** This is an index of preload reserve in a patient and can be used to titrate fluid therapy. Monitoring CVP is also a standard of care in patients with right heart failure or in those having episodes of pulmonary hypertensive crises.

**End tidal $CO_2$ monitoring:** Monitoring the concentration of expired $CO_2$ as a measure of tissue $CO_2$ production, alveolar ventilation and state of pulmonary blood flow, is a helpful adjunct to standard monitoring in patients with cardiogenic shock. Usually there is a negligible difference between sampled arterial $CO_2$ ($PaCO_2$) and the end tidal $CO_2$ level ($ETCO_2$) in capnography in normal subjects. However, in states of ventilation perfusion mismatch, wasted ventilation leads to creation of a significant arterial to end tidal $CO_2$ gradient and is a reliable marker of reduced venous return, pulmonary blood flow and thus cardiac output.[11]

**Serum lactate:** Serial lactate levels are reflective of metabolic demand- oxygen delivery balance and evidence of cellular hypoxia. Both hypoxic and non-hypoxic causes of hyperlactatemia (post cardiac bypass, liver dysfunction) need to be considered while interpreting the results. A normal lactate level is taken as 1- 2 mmol/L.

**Venous oximetry:** Venous oximetry is an earlier marker of a fall in cardiac output and oxygen delivery than serum lactate levels. According to the Fick principle, with a decrease in oxygen delivery to the tissues, the arterio-venous oxygen content difference increases due to an increase in oxygen extraction. When oxygen delivery drops below a critical threshold, such that an increase in oxygen extraction can no longer fully compensate for decreased oxygen delivery, anaerobic metabolism results with elevated serum lactate levels.[12]

[Oxygen extraction ratio ($O_2ER$) = $SaO_2$ – $ScvO_2$/ $SaO_2$] where $SaO_2$ and $ScvO_2$ are arterial and central venous oxygen saturations, respectively. The normal $O_2ER$ is 25%-30% and as it rises above 50-60%, anaerobic metabolism begins.[13]

**Near-infrared spectroscopy (NIRS):** NIRS provides continuous noninvasive organ-specific perfusion monitoring by analyzing the absorption and scatter of near infrared light.[14] It measures regional tissue oxygenation and perfusion by approximating regional venous saturation and in combination with arterial oxygen saturation allows for the estimation of regional oxygen balance. Thus, NIRS guides titration of organ-specific goal-directed treatments.[15]

**Fluid balance:** Patients in shock, irrespective of etiology, present with both global hemodynamic derangement as well as microcirculatory abnormalities. This is further amplified in cardiogenic shock patients who develop a systemic inflammatory response syndrome (SIRS) due to SIRS-related vasodilatation and the resulting hypotension. Fluid resuscitation which may lead to restoration of global circulation; does not correct the microcirculatory abnormalities. In fact, excessive administration of fluids to restore global circulation can lead to edema which causes further deterioration of microcirculatory function.

**Biomarkers:** Serial values of Troponin I, CPK-MB, BNP, ProBNP may be monitored.[10]

## Echocardiography

**Assessment of cardiac output:** CO is calculated by multiplying the stroke volume (SV) by the heart rate (HR). The measurement of stroke volume (SV) and thus cardiac output (CO) is conventionally, made at the left ventricle outflow tract (LVOT). From the parasternal long axis (PLAX) view, the LVOT diameter is measured immediately below the hinge point of the aortic valve leaflets. The cross sectional LVOT area ($cm^2$) is calculated from this diameter measurement using the formula:[16]

$$\text{LVOT area } (cm^2) = (\text{LVOT diameter}/2)^2 \times 3.14$$

Next, the pulse wave doppler (PWD) sample volume is placed in the LVOT to measure the systolic velocity envelope of blood flow in the LVOT, using the five chamber apical view. The velocity time integral (VTI) can be derived from the PWD measured at the LVOT. This allows measurement of SV by formula:[16]

$$\text{SV } (cm^3 \text{ or mL}) = \text{LVOT area } (cm^2) \times \text{VTI (cm)}$$

**Assessment of LV function:** Measurement technique: LV function can be assessed both qualitatively and quantitatively. Qualitative measurement is a visual estimate (simply 'eyeballing') of overall LV function by the clinician who examines the global and focal contractile function of the LV in the parasternal long-axis (PLAX), parasternal short-axis (PSS) views, the apical four chamber (AP4) view, or the subcostal (SC) view using 2D echocardiography. It is usually graded as mildly, moderately and severely reduced or normal.[16] Depending upon the experience of the clinician, these estimations are fairly reliable. For quantitative assessment several methods are used namely:

a. The biplane Simpson's method – It is a 2D method and calculates a volume by delineating the end systolic and end diastolic area by careful tracing and perfect long axis orientation in apical four chamber or two chamber views.[17]

b. Fractional shortening method (FS Method) – Measurements of the LV end systolic (ESD) and end diastolic diameter (EDD) in the M mode, right below the mitral valve leaflet perpendicular to long axis of heart, in the parasternal short or long-axis views to obtain the fractional shortening, which is calculated using the formula.[17]

$$FS = (EDD - ESD)/(EDD) \times 100$$

**Assessment of RV Function:** LV dimensions are larger than RV dimensions typically. Hence by observing a 'D – shaped' LV where RV is larger than LV with leftward shift of interventricular septum points toward RV volume/ pressure overload. Paradoxical motion of the septum visualized as a bounce of the septum or movement of the septum toward the left ventricle during ventricular contraction is also a feature of RV pressure/volume overload.[16]

## Treatment of acute heart failure syndromes (Fig.2)

Mainstay of treatment is a careful balance of oxygen delivery and consumption variables. Treatable causes should be urgently addressed such as pericardial tamponade, pneumothorax, arrhythmias, dyselectrolytemia, or fluid overload. The broad principles of management of acute heart failure syndromes (AHFS) are given below.

1.Oxygen delivery optimization is done by ensuring adequate gas exchange, supporting ventilation mechanically, preload restoration, afterload relaxation. Oxygen consumption optimization is ensured by taking charge of work of breathing, fever control, pain /anxiety control.

2. Fluid resuscitation should preferably be done after echocardiographic evaluation. If patient appears fluid overloaded, gentle loop diuretic infusion may be started once the patient is out of shock.

3. Systolic heart failure – Drugs.

Dobutamine: By acting on the beta-1 receptors, increases cardiac contractility thus increasing cardiac output (CO) and decreases the pulmonary capillary wedge pressure (PCWP) by vasodilating arterial resistance and venous capacitance vessels (a beta 2 receptor effect).[18]

Dopamine: It also has beta-1 and beta-2 receptor activity, also acts on alpha 1 receptors increasing systemic vascular resistance (SVR) and CO. But the PCWP increases significantly.[19] Hence, dopamine is not preferred in patients with cardiogenic shock.

Epinephrine: In low doses (< 0.05–0.10 μg/kg/min) reduces SVR, while at higher doses, SVR increases considerably. At all doses, epinephrine causes venoconstriction, and provides greater inotropic support than dopamine or dobutamine.[19]

Inotropic agents are arrhythmogenic and should be used at the lowest possible dose and for the shortest

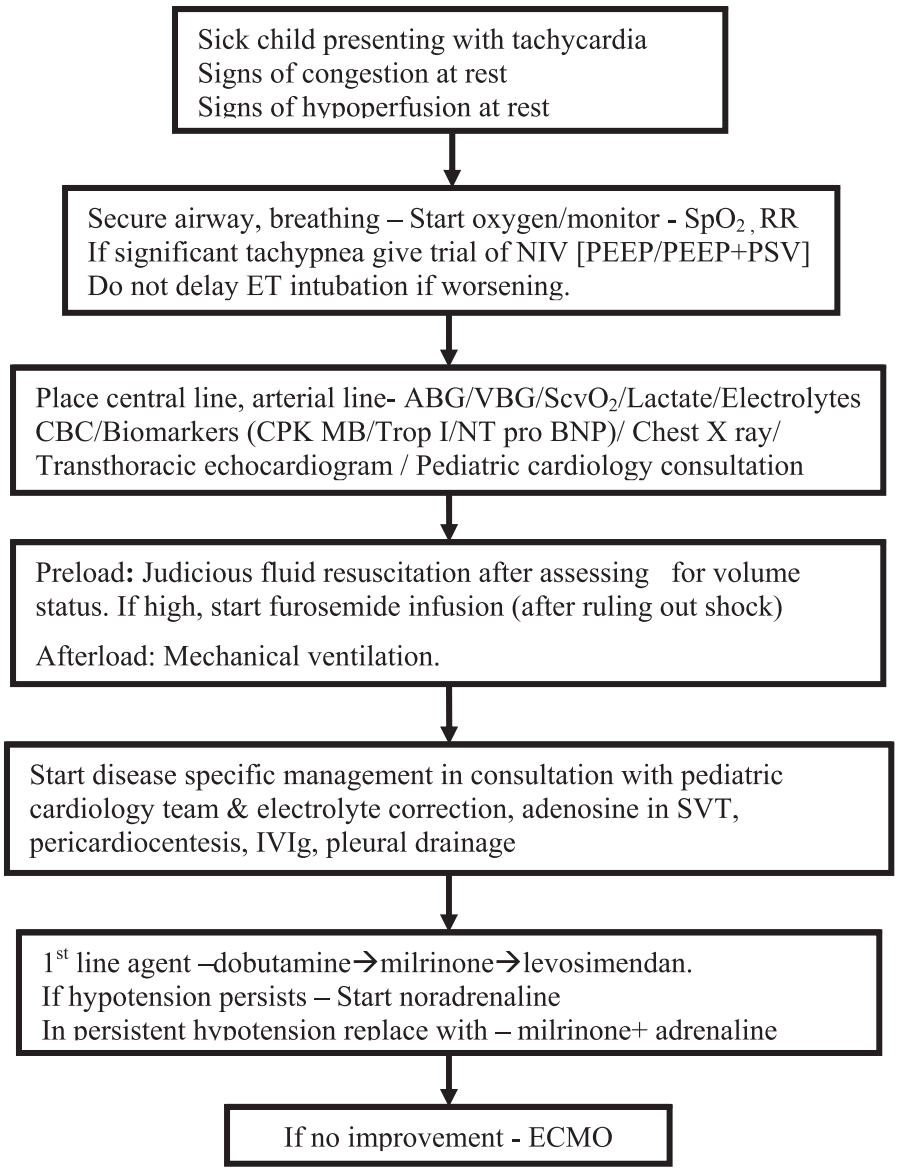


**Fig.2. Approach to management of cardiogenic shock**

duration, given that all increase myocardial oxygen consumption, except levosimendan, and milrinone.

Milrinone: An inodilator, is commonly administered to children with acutely decompensated heart failure with the aim of decreasing SVR, PVR, lusitropy and augmenting myocardial systolic and diastolic function. Milrinone increases intracellular cyclic adenosine monophosphate levels by inhibiting phosphodiesterase III. It also enhances coronary venous flow thus favoring myocardial energetics reflected by a decrease in the myocardial arteriovenous oxygen content difference.[20]

Norepinephrine: Increases SVR even at very low doses and is used to maintain perfusion pressure. It is the preferred vasopressor in combination with inotropes to increase SVR, perfusion pressure and to maintain blood pressure. However, it should be replaced with epinephrine in cases of inotrope resistant shock.

Dobutamine is still considered preferred drug, followed by Milrinone (dose range – 0.5 -0.75 µg/kg/min) especially in patients who have undergone cardiac surgery, cases of impaired right ventricle function and/or pulmonary hypertension.[10]

Newer inotropic agent: Levosimendan, which is a calcium sensitizer causes enhanced inotropy without increasing myocardial oxygen consumption. Experience in children is still limited. Nitrated derivatives and â blockers are not recommended in patients with cardiogenic shock.

4. Immunomodulatory treatment in myocarditis: Myocarditis is an inflammation of myocardium due to varied causes resulting in degenerative/necrotic changes manifesting as varying levels of myocardial dysfunction.[21] The most common etiology is viral mediated, but may also be caused by bacteria, protozoa, autoimmune disorders or drug reactions.[21] The various treatment options are as follows:

Corticosteroids: Eight RCTs (including both adult and pediatric studies, n = 719) analysed in a Cochrane review of corticosteroid use, found no difference in mortality in the corticosteroid groups and the control groups. Notably, the corticosteroid group had a higher left ventricular ejection fraction (LVEF) and a decrease in cardiac biomarker (creatinine kinase MB) but these studies were considered as low quality with small sample size.[22] Corticosteroids have been used in patients with myocarditis in doses of 0.5-2 mg/kg/d divided 1-4 times per day.[22]

IV Immunoglobulin: Though none of the studies show a mortality benefit, some studies did show an improvement in left ventricle end diastolic volume and ejection fraction. A dose of 2 g/kg/day has been used most commonly in all studies.[23]

5. Mechanical circulatory support (MCS) is indicated in refractory low cardiac output state not responding to conventional therapy. It is practically not feasible to prolong ECMO support beyond 2 weeks and hence, MCS devices help as bridge to transplantation.[24] The various ventricular assist devices available are pulsatile pump (Berlin Heart EXCOR) and continuous flow pump (SynCardia, Thoratec). There are several device selection strategies depending upon whether MCS is temporary or for long term, also depending on weight of the baby. The discussion of VAD is beyond the scope of this chapter.

6. ECMO: This is indicated in cardiac arrest persisting for 15 minutes or beyond but less than 60 minutes.[10] In patients refractory to conventional management, ECMO is indicated as a bridge to transplant.

## Conclusion

Children presenting with cardiogenic shock require intensive monitoring and titration of therapy to optimize stroke volume, contractility and reduce afterload. In the patients with severely reduced cardiac output refractory to medical management, ECMO and ventricular assist devices are available options.

## Points to Rembember

- ***Cardiogenic shock is a state of acute circulatory failure due to low cardiac output.***
- ***Diagnosis is mainly based on hypotension, signs of pulmonary congestion and features of end organ hypoperfusion.***
- ***Management is by optimising oxygen consumption and by titrating inotropes and vasopressors.***

## References


1. Reynolds HR, Hochman JS. Cardiogenic shock: current concepts and improving outcomes. Circulation 2008; 117:686–697.
2. Rossano JW, Kim JJ, Decker JA, Price JF, Zafar F, Graves DE, et al. Prevalence, morbidity, and mortality of heart failure-related hospitalizations in children in the United States: a population-based study. J Card Fail 2012; 18:459–470.
3. Singh D, Chopra A, Pooni PA, Bhatia RC. A clinical profile of shock in children in Punjab, India. Indian Pediatr 2006; 43:619–623.
4. Webster G, Zhang J, Rosenthal D. Comparison of the epidemiology and co-morbidities of heart failure in the pediatric and adult populations: a retrospective, cross-sectional study. BMC Cardiovasc Disord 2006; 6:23.
5. Tume SC, Schwartz SM, Bronicki RA. Pediatric Cardiac Intensive Care Society 2014 Consensus Statement: Pharmacotherapies in Cardiac Critical Care Treatment of Acute Heart Failure. Pediatr Crit Care Med 2016; 17:S16 –19.
6. Katz AM. Ernest Henry Starling, his Predecessors, and the "Law of the Heart". Circulation 2002; 106:2986–2992.
7. Smith LS, Hernan LJ. Shock states. In: Fuhrman B, Zimmerman J (Eds). Pediatric Critical Care, 4th edn. Elsevier, Philadelphia 2011; pp364-378.
8. Stevenson LW, Massie BM, Francis GS. Optimizing therapy for complex or refractory heart failure: a management algorithm. Am Heart J 1998; 135:S293-S309.
9. Nohria A, Lewis E, Stevenson LW. Medical management of advanced heart failure. JAMA 2002; 287:628-640.
10. Brissaud O, Botte A, Cambonie G, Dauger S, de Saint Blanquat L, Durand P, et al. Experts' recommendations for the management of cardiogenic shock in children. Ann Intensive Care 2016; 6:14.
11. Isserles SA, Breen PH. Can changes in end-tidal PCO2 measure changes in cardiac output? Anesth Analg 1991; 73:808-814.

12. Bronicki RA. Venous oximetry and the assessment of oxygen transport balance. Pediatr Crit Care Med 2011; 12(4 Suppl): S21-S26.
13. Tsang R, Checchia P, Bronicki RA. Hemodynamic monitoring in the acute management of pediatric heart failure. Curr Cardiol Rev 2016; 12:112-116.
14. McQuillen PS, Nishimoto MS, Bottrell CL, Fineman LD, Hamrick SE, Glidden DV, et al. Regional and central venous oxygen saturation monitoring following pediatric cardiac surgery: concordance and association with clinical variables. Pediatr Crit Care Med 2007; 8:154–160.
15. Li J, Zhang G, Holtby H, Guerguerian AM, Cai S, Humpl T, et al. The influence of systemic hemodynamics and oxygen transport on cerebral oxygen saturation in neonates after the Norwood procedure. J Thorac Cardiovasc Surg 2008; 135: 83-90.
16. Pershad J, Myers S, Plouman C, Rosson C, Elam K, Wan J, et al. Bedside limited echocardiography by the emergency physician is accurate during evaluation of the critically ill patient. Pediatrics 2004; 114:e667–671.
17. Gaspar HA, Morhy SS. The Role of Focused Echocardiography in Pediatric Intensive Care: A Critical Appraisal," BioMed Res Int 2015, Article ID 596451, 7 pages, 2015. doi:10.1155/2015/596451.
18. Overgaard CB, Dzavik V. Inotropes and vasopressors: review of physiology and clinical use in cardiovascular disease. Circulation 2008; 118:1047-1056.
19. Herbert P, Tinker J. Inotropic drugs in acute circulatory failure. Intensive Care Med 1980; 6:101–111.
20. Bailey JM, Miller BE, Lu W, Tosone SR, Kanter KR, Tam VK. The pharmacokinetics of milrinone in pediatric patients after cardiac surgery. Anesthesiology 1999; 90:1012-1018.
21. Levine MC, Klugman D, Teach SJ. Update on myocarditis in children. Curr Opin Pediatr 2010; 22:278–283.
22. Chen HS, Wang W, Wu SN, Liu JP. Corticosteroids for viral myocarditis. Cochrane Database Syst Rev 2013 Oct 18; (10):CD004471. doi: 10.1002/14651858. CD004471.pub3.
23. Robinson J, Hartling L, Vandermeer B, Crumley E, Klassen TP. Intravenous immunoglobulin for presumed viral myocarditis in children and adults. Cochrane Database Syst Rev 2005 Jan 25; (1):CD004370.
24. Jeffries JL, Price JF, Morales DL. Mechanical support in childhood heart failure. Heart Fail Clin 2010; 6(4): 559–573.

## CLIPPINGS

***Early, Goal-Directed Therapy for Septic Shock - A Patient-Level Meta-Analysis.***

After a single-center trial and observational studies suggesting that early, goal-directed therapy (EGDT) reduced mortality from septic shock, three multicenter trials (ProCESS, ARISE, and ProMISe) showed no benefit. This meta-analysis of individual patient data from the three recent trials was designed prospectively to improve statistical power and explore heterogeneity of treatment effect of EGDT.

This meta-analysis harmonized entry criteria, intervention protocols, outcomes, resource-use measures and data collection across the trials and specified all analyses before unblinding. After completion of the trials, we pooled data, excluding the protocol-based standard-therapy group from the ProCESS trial, and resolved residual differences. The primary outcome was 90-day mortality. Secondary outcomes included 1-year survival, organ support and hospitalization costs. We tested for treatment-by-subgroup interactions for 16 patient characteristics and 6 care-delivery characteristics.

In this meta-analysis, 3723 patients at 138 hospitals in seven countries were studied. Mortality at 90 days was similar for EGDT (462 of 1852 patients [24.9%]) and usual care (475 of 1871 patients [25.4%]); the adjusted odds ratio was 0.97 (95% confidence interval, 0.82 to 1.14; P=0.68). EGDT was associated with greater mean (±SD) use of intensive care (5.3±7.1 vs. 4.9±7.0 days, P=0.04) and cardiovascular support (1.9±3.7 vs. 1.6±2.9 days, P=0.01) than was usual care; other outcomes did not differ significantly, although average costs were higher with EGDT. Subgroup analyses showed no benefit from EGDT for patients with worse shock (higher serum lactate level, combined hypotension and hyperlactatemia, or higher predicted risk of death) or for hospitals with a lower propensity to use vasopressors or fluids during usual resuscitation.

In this meta-analysis of individual patient data, EGDT did not result in better outcomes than usual care and was associated with higher hospitalization costs across a broad range of patient and hospital characteristics.

***The PRISM Investigators. Early, Goal-Directed Therapy for Septic Shock - A Patient-Level Meta-Analysis. N Engl J Med 2017; 376:2223-2234.***

**CARDIOLOGY**

# EXTRA CORPOREAL MEMBRANE OXYGENATION

***Rajakumar PS***

**Abstract:** *Extracorporeal membrane oxygenation (ECMO) is a modified cardiopulmonary bypass technique which provides temporary support in severe respiratory and/or cardiac failure due to any reversible cause. Venoarterial ECMO supports both heart and lung function while venovenous ECMO supports lung function alone. Different methods and sites of cannulation are available. Anticoagulation, good intensive care focusing on lung and heart rest, specific therapy for the underlying disease, prevention of infection and meticulous monitoring are essential for the organs to recover before weaning and decannulation are done. Awareness of indications and contraindications is important as patient selection and timing of initiation are crucial for success.*

**Keywords:** *Extra corporeal membrane oxygenation, Veno venous ECMO,Veno arterial ECMO, Extra corporeal life support.*

Extra corporeal membrane oxygenation (ECMO) is a modified form of cardiopulmonary bypass technique to temporarily support lung and/ or heart function and ensure adequate oxygen delivery in severe reversible respiratory and/ or cardiac failure due to any etiology. Patient selection and timing of initiation are very crucial since ECMO is only a supportive therapy to sustain life while waiting for various therapeutic interventions and natural course to help the organs to recover and the disease to resolve.

The first successful neonatal ECMO was reported by Robert Barlett from University of Michigan, USA in 1975 in a baby with severe meconium aspiration syndrome and primary pulmonary hypertension (PPHN).[1] Soon this technology was extended to other indications and older children as ultimate rescue therapy. This was supported by studies in newborns in both USA and UK. Extracorporeal Life Support Organisation (ELSO) was established in 1989 to propagate the knowledge, collect epidemiological data on use and outcome of ECMO across the world.[2-5] The growth of ECMO in India has been slow due to the high cost involved and the need for both good cardiothoracic surgery unit and intensive care expertise. The number of centres in India offering ECMO in children and newborns have increased significantly in the recent years due to availability and affordability, with simultaneous improvements in technology.

## Basic technology

ECMO technology was developed by modifying the cardio pulmonary bypass (CPB) machine and circuit to suit prolonged extracorporeal therapy and minimize the complications.

### ECMO components (Fig.1)

1) Drainage (Access) cannula - Large cannula for draining blood from one of major veins or right atrium.

2) ECMO circuit - Special circuit for blood circulation outside body with safety mechanism to prevent air embolism and minimise activation of clotting and systemic inflammatory responses. It is primed with crystalloid, colloid or blood.

3) Pump (Heart) - To drain blood via access cannula and pump it through the ECMO circuit and back to body via another cannula (return Cannula). The most common type used now is centrifugal pump while roller pump is used in CPB machine. The centrifugal pump consists of mechanism of spinning impellar blades or rotating cones which have a vortex like action to create negative pressure on one side (pre-pump) to draw blood from patient and positive pressure on other side (post-pump) to propel blood via membrane back to patiet.[6]

4) Membrane oxygenator (Lung) - A special gas permeable membrane separating blood and gas flow which adds oxygen to blood and removes carbon dioxide from blood by diffusion before returning it to the patient. The most common type used now is microporous membrane with hollow fibres made of polymethylpentene (PMP).

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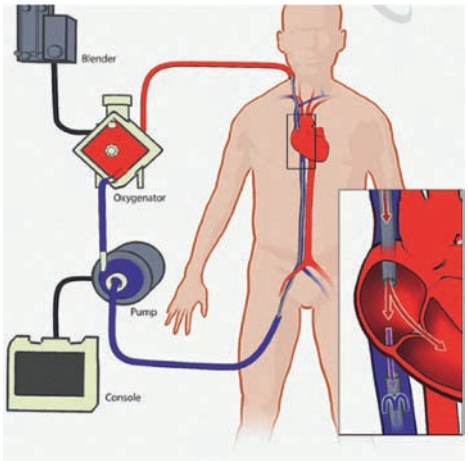


**Fig.1. ECMO components and basics**

- Venous blood is drained from a central vein via a drainage cannula, pumped through an oxygenator, and returned to a central vein through a separate reinfusion cannula *(Source: Abrams D, Brodie D. Extracorporeal circulatory approaches to treat ARDS. Clin Chest Med 2014; 35(4): 765-779).*

5) Blender with oxygen and air supply and flow meter - To supply gas flow to oxygenator.

6) Heater unit - With water hose which helps to maintain blood temperature to set value of 37° C or lower (for therapeutic hypothermia) by heat exchange across membrane.

7) Return cannula - To return blood to great vein or right atrium (Veno Venous ECMO) or any great artery (Veno Arterial ECMO). Sometimes large double lumen cannula (eg Avalon) are used for both drainage from vena cava and return into right atrium.

8) Monitoring devices - Help to detect any problems in circuit flow, membrane function and mechanical kinks. They include (a) Inlet pressure monitoring at inflow limb of circuit (pre-pump) to detect preload, (b) pre membrane and post membrane pressure monitoring transducers (post pump) - To detect oxygenator clots and return cannula kinks/ increased afterload and (c) mixed venous saturation and blood flow monitoring devices - to monitor oxygenator and pump function.

## Types of ECMO

**1. Veno venous ECMO (VV ECMO)** - Venous blood is accessed from the large central veins, pumped through the oxygenator and returned to the venous system near the right atrium. It provides support for severe respiratory failure (eg. ARDS) where the circulation is driven entirely by native cardiac function.

**2. Veno arterial ECMO (VA ECMO)** - Venous blood is accessed from the large central veins, pumped through the oxygenator and returned to the systemic arterial system in

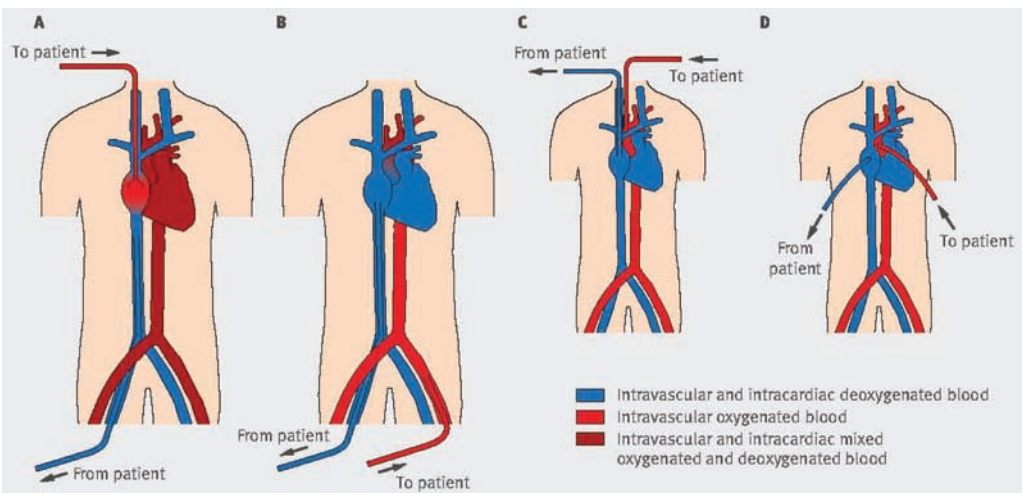


**Fig.2. Different ECMO configurations**

A: venous-venous cannulation - deoxygenated blood drained from femoral vein and oxygenated blood returned to right atrium, B-D: various venous-arterial configurations

Blue: intravascular and intracardiac deoxygenated blood

Red: intravascular oxygenated blood

Dark red: intravascular and intracardiac mixed oxygenated and deoxygenated blood

*(Source: Gaffney AM, Wildhirt SM, Griffin MJ, Annich GM, Radomski MW. Extracorporeal life support. Br Med J 2010; 341(2):c5317)*

the aorta. It provides support for severe cardiac failure (with or without associated respiratory failure) due to heart disease or post cardiac arrest.

## Types of cannulation/configurations

Central cannulation - Superior vena cava/ right atrium and ascending aorta are directly cannulated for VA ECMO with chest kept open. This is usually done following open heart surgery when there is difficulty in weaning off bypass or other situation where peripheral cannulation is not possible or very large blood (ECMO) flow is required.

Peripheral cannulation - Internal jugular vein (IJV) or femoral vein and carotid artery or femoral artery are used for cannulation.[7] Femoro-femoral VV ECMO and VA ECMO are commonly used in older children, Femoral vein - IJV VV ECMO in smaller children and IJV-carotid VA ECMO in newborns and infants (Fig.2). Cannulation of the femoral vessels in infants is not possible because the small size of the vessels does not allow implantation of cannulae large enough to achieve full ECMO flow. A heparin bolus of 50-100 IU/kg and one dose of prophylactic antibiotic (cefazolin) is administered prior to inserting the cannulae.

## Method of cannulation

There are three methods of cannulation (a) Percutaneous cannulation - Done in older children under ultrasound guidance via Seldinger technique, (b) Open surgical cannulation - Done in smaller children and in difficult cases by exposing the vessel, making an incision in vessel and directly cannulating and (c) Semi Seldinger cannulation - Where incision is made in skin to expose the vessel which is then cannulated by Seldinger technique without incision in vessel.

The indications for initiating ECMO is given in Box 1 while the contraindications are given in Box 2.

## Criteria for initiating ECMO

1. The clinical condition should be a potentially reversible cardiac or respiratory failure or both. Mechanical ventilation with high pressures and FiO2 for more than 7 to 10 days is considered a relative contraindication as injury may be irreversible.

2. The patient should be sufficiently sick with high expected mortality with conventional therapy.[8] This can be assessed by following objective parameters:

i) Respiratory failure:

- Oxygenation index (OI) > 40 for > 4 hours

**Box 1. ECMO indications**

**i) Respiratory (VV ECMO, neonates sometimes VA ECMO)**

**Neonatal**

Meconium aspiration syndrome

PPHN

Diaphragmatic hernia

RDS

Pneumonia

**Pediatric**

Viral pneumonia

Bacterial pneumonia

ARDS

Aspiration pneumonia

Asthma

**ii) Cardiac (VA ECMO) - Neonatal and pediatric**

Failure to wean from cardiopulmonary bypass (after congenital heart surgery)

Myocarditis

Cardiomyopathy (bridge to transplant or Left Ventricular Assist Device (LVAD)

Refractory sepsis with profound cardiac depression

Refractory cardiac arrhythmias

Cardiac arrest from any treatable cause (Extracorporeal cardiopulmonary resuscitation - ECPR*)

Elective peri-procedural support (Airway surgery)

**ECPR is defined as the provision of an artificial circulation using the pumping of blood from a femoral venous catheter through an oxygenator in to a femoral arterial catheter as an alternative to ventilation and external cardiac massage.*

**Box 2. Contraindications for ECMO**

1. End-stage disease
2. Untreatable underlying disease and congenital malformations
3. Significant neurological impairment, genetic abnormalities (e.g. trisomy 13 and 18)
4. Severe, irreversible organ dysfunction
5. Prematurity (gestational age <34 weeks), weight <2 kg
6. Severe coagulopathy or contraindication for anticoagulation

- Oxygenation index >20 (or P/F ratio < 100) with lack of improvement despite prolonged (>24 hour) maximal medical therapy or persistent episodes of decompensation

- Progressive respiratory failure and/or pulmonary hypertension with evidence of right ventricular dysfunction or continued high inotropic requirement

ii) Cardiac failure:

- Significant shock despite adequate inotropes
- Post cardiac arrest (ECPR: ECMO application during CPR)
- Failure to wean of cardiopulmonary bypass (CPB)

3. The neurologic status and other organ function should be consistent with possibility of reasonable recovery.

4. There should be no contraindication for limited heparinization. Prematurity less than 35 weeks, intracranial bleed or refractory coagulopathy are contraindications.

## Patient management on ECMO (Table I)

Ventilation - kept at lung protective rest settings with PEEP 10, pressure control 10, rate 10 with inspiratory time of 1 sec with FiO2 21% to 50%. This ensures lung is kept open without exposure to high pressure and oxygen so that ventilator induced lung injury is minimized.

Circulation - In VA ECMO, inotropes can be tapered off quickly and restarted only before weaning off ECMO. Hemodynamics is maintained by adjusting ECMO flow. In VV ECMO on patient with secondary cardiac dysfunction, inotropes can be tapered slowly as myocardium recovers with improvements in oxygenation. As centrifugal ECMO pump is non-occlusive, preload and afterload dependent, adequate blood volume and good vasodilation and absence of circuit/ cannula kinking are required for achieving good blood flow and oxygenation.

Fluid management - Initially more fluids may be needed as there is systemic inflammatory response syndrome (SIRS) response due to ECMO circuit. Later it will be necessary to get the child dry with diuretics or filtration to facilitate weaning.

Analgesia and sedation - Should be adequate with usually a combination of opioids and benzodiazepine for patient comfort and prevention of accidental decannulation.

Nutrition - Enteral nutrition with nasogastric tube can usually be initiated and maximised, if there is no contraindication.

Renal support - Can be initiated with continuous renal replacement therapy via ECMO circuit for fluid management or overt renal failure.

**Table I. ECMO settings and monitoring**

| | |
|---|---|
| ECMO blood flow | Newborn 100 ml/kg/min; Children 80 ml/kg/min; 50-80% of the flow may be enough; Determines hemodynamics in VA ECMO and oxygenation in both |
| ECMO $FiO_2$ | 50-100% |
| Sweep gas flow | Usually 1:1 as ECMO flow; determines carbon dioxide removal |
| ECMO monitoring | Inlet pressure, pre and post membrane pressure, mixed venous saturation and ECMO blood flow |
| Patient monitoring | ECG, $SPO_2$, invasive BP (Pulsatility), temperature, urine |
| Anticoagulation | Hourly activated clotting time (ACT) to keep 160-180 sec (Older children APTT 4 hourly); if heparin need is high, anti-thrombin levels |
| Oxygen delivery | Mixed venous saturation and lactate (Blood gas) |
| Limbs/Cannula | Distal perfusion of limb, cannula position and clots in the circuit |
| Blood tests | CBC, electrolytes, LFT, blood gas, calcium |
| Hemolysis | Plasma free hemoglobin daily (> 50 mg/dL significant) |
| Imaging | Daily CXR; In neonates daily USG cranium for IC bleed |

Anticoagulation - Continuous heparin infusion is titrated using a goal of activated clotting time (ACT) in the range of 160-180 seconds. The platelet count is maintained at or above 1 lakh/$mm^3$.

## Weaning and decannulation

### VV ECMO

Lung recovery on VV ECMO is indicated by constant need to reduce ECMO settings and improvement in chest x-ray. Weaning process is simple. Sweep gas flow is gradually reduced and turned off with increase in ventilator settings. If child has stable blood gases for few hours (2 to 12 hours), decannulation is done in ICU itself with firm pressure after decannulation.

### VA ECMO

Cardiac recovery on VA ECMO support is indicated by an increase in pulse pressure and by improved contractility on echocardiography. Weaning process is more complex. The ECMO flow is gradually decreased upto 1 l/min (or clamped), inotropes and ventilator settings are increased and hemodynamics assessed clinically and by echocardiograph. If stable for few hours on minimum flow, decannulation is done surgically with vessel repair in theatre.

## Complications

Infection - An important cause of mortality and prolonged ECMO run and ICU stay. Fever may be absent as temperature is controlled by ECMO machine. ECMO circuit can cause SIRS without sepsis. High index of suspicion and routine surveillance culture has a role in early identification of sepsis.

Bleeding - Can be life threatening and an indication for coming off ECMO. All invasive procedures should be avoided while on ECMO due to risk of bleeding, unless absolutely essential. Blood products should always be readily available all the time.

Thrombosis - Can occur in the circuit, oxygenator or pump head especially in prolonged ECMO run as ECMO circuit activates clotting cascade. Thrombus in pump head or oxygenator may necessitate emergency change of ECMO circuit.

Hemolysis - Falling Hb and platelets with DIC like blood picture can occur. Plasma free hemoglobin can be monitored.

Air embolism, decannulation and circuit disconnection are rare but catastrophic complications which should be prevented by meticulous nursing care.

Recirculation (VV ECMO) can occur between drainage and return cannula. This can be detected by bright red appearance of blood in drainage cannula similar to arterial blood. This is best prevented by placing both cannula tips wide apart and draining blood from vena cava and returning to right atrium.

Differential hypoxia (North-South syndrome or Harlequin syndrome) causes upper body appears blue hypoxemia while lower body appears pink. This happens in femoro-femoral VA ECMO in children with poor lung function and adequate heart function. The deoxygenated native blood supplies upper body while oxygenated ECMO blood supplies lower body. This is addressed by increasing ventilatory settings or ECMO flow or by changing to VV ECMO.

## Outcome

The UK Collaborative ECMO trial group publications prove that ECMO was effective in both reducing mortality and severe disability at 7 years, compared to conventional therapy.[9,10] The underlying disease processes appear to be the major influencing factor on morbidity as reported to

**Table II. Overall survival after ECMO**

| Neonates | | Children | |
|---|---|---|---|
| CDH | 50% | Viral pneumonia | 60-80% |
| MAS | 90-97% | Bacterial pneumonia | 60% |
| PPHN | 75-85% | Aspiration pneumonia | 75% |
| RDS | >70% | ARDS | 50-60% |
| Sepsis | 50-70% | Non-ARDS respiratory failure | 50-70% |

**Box 3. ECMO - Referral criteria**

1. A neonate with any respiratory problem e.g. Meconium aspiration with an oxygenation index (OI) of >40 on optimal treatment for four hours, (unresponsive to nitric oxide if severe Pulmonary hypertension is present).
2. An infant or child with a pneumonia/air leak/ARDS and an OI of 25.
3. An arterial pCO2 of > 90 for more than three hours despite optimal treatment.

Extracorporeal Life Support Organization (ELSO) (Table II).

## Referral to ECMO centre

Early discussion of a potential ECMO patient with the ECMO service provider will help in deciding the need, timing and mode of transfer and pre-transfer optimisation of patient. The criteria for an ECMO referral is given in Box 3.

## Conclusion

With the advances in the technology and expertise, ECMO complications have reduced and outcomes improved. Advent of "Mobile ECMO" and "E-CPR" have the potential to increase the number of lives saved by ECMO.[11] It is important that pediatricians taking care of sick children are familiar with indications and refer early to ECMO service as patient selection and timing are the key to success.

## Points to Remember

- ***ECMO provides lifesaving temporary lung and/or heart support in severe respiratory and cardiac failure due to any reversible cause.***
- ***Patient selection and timing of initiation are crucial for successful outcomes.***
- ***There is increase in the availability of the service in India and there is good evidence to support the use of ECMO.***
- ***Awareness of indications and early discussion with ECMO service provider is very important.***

## References


1. Bartlett RH, Gazzaniga AB, Jefferies MR, Huxtable RF, Haiduc NJ, Fong SW. Extracorporeal membrane oxygenation (ECMO) cardiopulmonary support in infancy. ASAIO J 1976; 22(1):80-92.
2. Rehder KJ, Turner DA, Cheifetz IM. Extracorporeal membrane oxygenation for neonatal and pediatric respiratory failure: an evidence-based review of the past decade (2002-2012). Pediatr Crit Care Med 2013; 14(9): 851-861.
3. Mugford M, Elbourne D, Field D. Extracorporeal membrane oxygenation for severe respiratory failure in newborn infants. Cochrane Database Syst Rev 2008;16 (3):CD001340. Accessed on 31st May, 2017.
4. Green TP, Timmons OD, Fackler JC, Moler FW, Thompson AE, Sweeney MF. The impact of extracorporeal membrane oxygenation on survival in pediatric patients with acute respiratory failure. Pediatric Critical Care Study Group. Crit Care Med 1996 Feb; 24(2):323-329.
5. Peek GJ, Mugford M, Tiruvoipati R, Wilson A, Allen E, Thalanany MM, Hibbert CL, Truesdale A, Clemens F, Cooper N, Firmin RK, Elbourne D; CESAR trial collaboration. Efficacy and economic assessment of conventional ventilatory support versus extracorporeal membrane oxygenation for severe adult respiratory failure (CESAR): a multi centre randomised controlled trial. Lancet 2009; 374(9698):1351-1363.
6. Toomasian JM, Lawson S, Harris WE. The Circuit. In: Annich GM, Lynch WR, MacLaren G, Wilson JM, Bartlett RH, eds. Extracorporeal Cardiopulmonary Support in Critical Care. 4th edn, Extracorporeal Life Support Organization, Ann Arbor, MI, 2012; pp107-132.
7. Gaffney AM, Wildhirt SM, Griffin MJ, Annich GM, Randomski MW. Extracorporeal life support. Br Med J 2010; 341:982-986.
8. Robinson S, Peek G, The role of ECMO in neonatal & paediatric patients, Paediatrics and Child Health (2015), http://dx.doi.org/10.1016/j.paed.2015.03.005.
9. Mehta A, Ibsen LM. Neurologic complications and neurodevelopmental outcome with extracorporeal life support. World J Crit Care Med 2013; 2(4):40-47.
10. McNally H, Bennett CC, Elbourne D, Field DJ: UK Collaborative ECMO Trial Group. UK collaborative randomized trial of neonatal extracorporeal membrane oxygenation: follow-up to age 7 years. Pediatrics 2006; 117(5): e845-854.
11. Thiagarajan RR, Laussen PC, Rycus PT, Bartlett RH, Bratton SL. Extracorporeal membrane oxygenation to aid cardiopulmonary resuscitation in infants and children. Circulation 2007; 116(15):1693-700.


## NEWS AND NOTES

**South PEDICON 2017**
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Rajendra Prasad : Chairman
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**CARDIOLOGY**

# ACUTE MYOCARDITIS AND CARDIOMYOPATHY

***Zulfikar Ahamed M**

**Abstract:** *Viral Myocarditis continues to be a major cause of mortality and morbidity in children among acquired cardiac causes. Myocardial cell necrosis and inflammation of myocardium, due to both viral invasion and immune mimicry leads to myocarditis. The clinical manifestations range from nearly asymptomatic presentation to fulminant myocarditis. Evaluation includes acute phase reactants, cardiac biomarkers, chest x-ray, ECG and echo-cardiography. Radionuclide scan, cardiac MRI and endomyocardial biopsy are utilized in selected situations. Treatment of myocarditis is essentially supportive-treatment of heart failure, using diuretic, ACE inhibitors, IV inotropes and mechanical support by mechanical ventilation, ECMO and LVAD. Antiviral agents and immune suppressants have limited role only in treating viral myocarditis. IVIG could be useful in children. The newer vistas in viral myocarditis encompass immunopathology in EMB, use of cardiac MRI in early detection and possible use of drugs which prevent biotransformation to DCM. The prognosis of viral myocarditis is guarded, due to both short term and long term mortality and morbidity.*

**Keywords:** *Myocarditis, Cardiomyopathy, Management, Children.*

Myocarditis is an inflammatory disease of the heart muscle. WHO / International Society and Federation of Cardiology (ISFC) in 1995 defined myocarditis as "an inflammatory disease of the heart muscle, diagnosed by established histological, immunological and immune histological evidence". Dallas criteria (1987) offers a pathological definition. "It is the presence of inflammatory infiltrate within the myocardium with myocyte degeneration or necrosis of non-ischemic origin". There are two more related terms which are closely linked to myocarditis: (a) Inflammatory cardiomyopathy (WHO/ ISFC) where myocarditis occurs in association with left ventricular dysfunction and (b) dilated cardiomyopathy (WHO/ISFC) a clinical diagnosis which is characterized by dilatation and impaired contraction of left ventricle or both ventricles that is not explained by abnormal loading conditions or coronary artery disease.

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Acute myocarditis and cardiomyopathy, although uncommon, continue to contribute to significant mortality and morbidity in children. Myocarditis can be a lethal disease in children when it presents as a fulminant myocarditis. It is also the major causative substrate for dilated cardiomyopathy, the latter contributing much morbidity and consequent mortality and hence myocarditis can be said to bite the myocardium causing mortality and maim the muscle, causing DCM. Grist and Bell proposed that virus can cause myocardial disease in 1974. After the advent of endomyocardial biopsy (EMB) and later the regular use of biopsy in myocarditis, virus genome was isolated in the myocardium, which proved the virus theory. Dallas criteria which, for the first time characterized the pathology was published in 1986. The link between myocarditis and DCM was clearly established in 1983.

## Epidemiology

The estimated annual incidence of myocarditis is 1/100,000. The incidence could be an underestimation as many myocarditis could be presenting with minor, non-specific symptoms. The autopsy data reveals an incidence of 0.5 to 1.8%. From Texas Heart Institute, the incidence of myocarditis among children admitted was 0.3%. There is a clear bimodal incidence of myocarditis. It peaks around infancy and mid teenage. There is a distinct male predominance. The age and gender factors may depend on genetic and environmental influences. At least 8%-10% of sudden cardiac death in infants and children is attributed to myocarditis.

## Etiology

Myocarditis could be due to varying etiology (Box 1). The most common cause is viral infection. Virus genome was present in 38% of EMB specimens in a large study of 624 patients with myocarditis / DCM. The most prominent viruses implicated are Coxsackie B, adeno virus and human parvo virus. Other viruses involved are Epstein

**Box 1.Etiology - Myocarditis**

**A. Infectious**

- Viral
- Bacterial
- Spirochetal
- Mycotic
- Rickettsial
- Protozoal
- Helminthic

**B. Non Infectious**

- Toxins: Anthracyclines
- Hypersensitivity
- Systemic diseases e.g. Kawasaki Disease

Barr, cytomegalovirus (CMV), enteric cytopathic human orphan (ECHO) virus, hepatitis C, human immuno-deficiency virus (HIV), herpes, influenza, mumps, measles, rubella, polio, varicella and yellow fever. Recently there has been a shift of etiologic profile, with human parvovirus B19 (HPV) being increasingly implicated in infant with myocarditis.

HIV also is an important cause of myocarditis as also dengue and H1N1, the latter presenting in epidemic form in southern states of India. While HPV myocarditis could be usually mild, causing only lymphocytic infiltration, H1N1 myocarditis can be fulminant, resulting in high acute mortality. Dengue myocarditis is well known to produce both LV dysfunction and heart blocks in addition to pericardial effusion. Of the non-viral etiologies, leptospirosis, Lyme disease, Chagas disease and anthracycline toxicity assume enhanced importance in current clinical practice.

## Pathogenesis

As the most common etiology of acute myocarditis is viral, the pathogenesis will be centered on viral myocarditis (Fig.1). There are 3 reasonably well defined phases in the pathogenesis of viral myocarditis. Most of the information is derived from murine models of enteroviral myocarditis.

**Stage I -** Acute viral invasion and multiplication (0-7 days): Virus invades myocytes and cause cell necrosis, apoptosis and inflammation. Myocyte necrosis exposes cellular antigens like myosin.

**Stage II -** Sub acute phase - Immune response (1-6 weeks): There is an acute immune reaction which activates T cell immune system. T cells, natural killer (NK) cells and macrophages are released. NK cells are protective, while T cells damage cardiac tissue by immune mimicry by T cell activation, cytokine production and auto antibody release. The T cells attack both virus and infected myocytes. Virus elimination follows. This will be usually accompanied by decline in immune response. If immune response persists despite virus elimination, it will lead to chronic inflammatory cardiomyopathy and later to dilated cardiomyopathy.

**Stage III -** Chronic phase (DCM): This phase involves healing by fibrosis and remodeling but sometimes associated with inflammation and viral persistence. LV dilatation and remodeling occur, leading to DCM.

If immune response presents with or without the presence of virus, an inflammatory cardiomyopathy occurs which later leads to DCM, by further LV dysfunction, LV dilation and remodeling.

## Pathology

Macroscopic appearance of the heart shows pale and flabby myocardium. LV is predominantly dilated along with RV. There is thinning of ventricular walls and LV dilatation. Pericardial effusion is often present. Thrombus may be present in the cavities. Three major microscopic findings are cell necrosis / degeneration, inflammatory infiltrate and interstitial edema. Dallas criteria in 1987 characterized the pathology of viral myocarditis (Box 2).

**Box 2. Dallas criteria**

i. Cell death and inflammation – Active myocarditis

ii. No cell death and inflammation is present – Borderline myocarditis

iii. No cell death and no inflammation – Resolved myocarditis

iv. No cell death and inflammation is present (on repeat EMB) – Resolving

## Clinical presentation

Viral myocarditis presents clinically as a spectrum of manifestations. It can be asymptomatic to fulminant and can cause sudden cardiac death in infants and children. It is often heralded by flu like illness. The clinical presentation varies with age (Box 3). It could be sepsis like presentation in neonate and young infant, SIDS in infants, stroke due to embolic episode and acute abdomen.

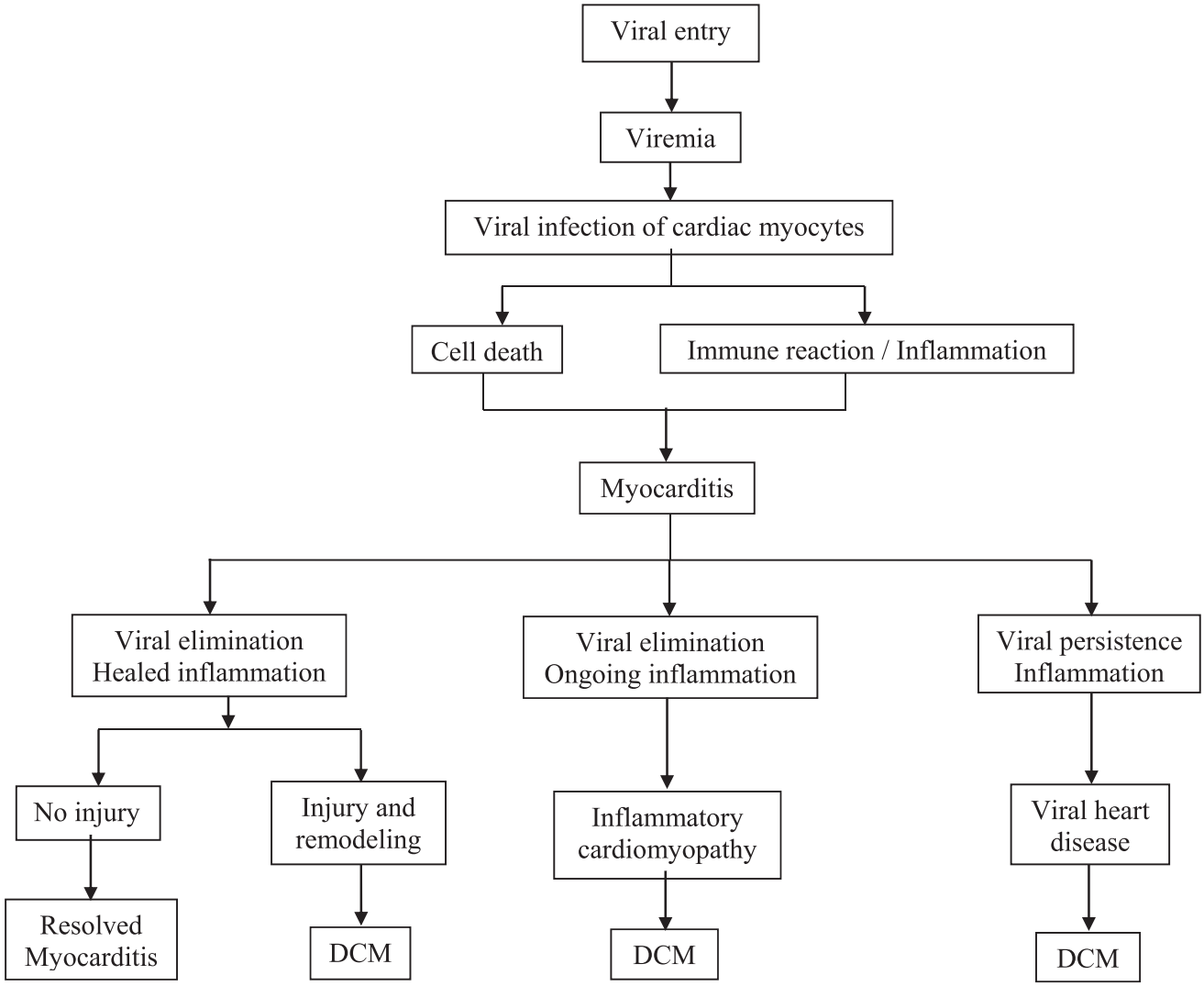


**Fig.1.Viral myocarditis – Pathogenesis**

The major clinical presentations are

i) Recent onset LV dysfunction: Children will have a viral prodrome and acute / sub acute onset of heart failure. This will be accompanied by variable LV dysfunction.

ii) Acute fulminant myocarditis (AFM): Flu like prodrome will be followed by a latency of 1-2 weeks. Child will present with severe congestive heart failure (CHF) / shock / multiorgan dysfunction within 2-3 days of onset of illness. Echocardiographic findings will be characteristic. It occurs in 10% of myocarditis.

iii) Acute coronary syndrome (ACS): This presentation is more common in adolescents and presents with chest pain and dyspnea. There will be features of myocardial infarction in ECG, accompanied by elevated troponins, 1 and T. Echo will demonstrate near normal LV function with regional wall motion abnormality. Coronary angiogram is normal.

iv) Arrhythmia: Myocarditis may present primarily as sustained tachycardia – SVT or VT. Rarely, recent onset complete heart block (CHB) could also be due to myocarditis.

v) Inappropriate tachycardia: Sinus tachycardia out of proportion to presence of fever is another mode of presentation.

vi) Sudden cardiac death (SCD): It can be a lethal manifestation of myocarditis in 8%-10% in children.

**Box 3. Clinical presentations in different age groups**

| | | |
|---|---|---|
| New born | : | Nonspecific symptoms |
| | | Sepsis like picture |
| | | Shock |
| | | CHF |
| Infant | : | Nonspecific symptoms |
| | | CHF |
| | | Shock |
| | | SIDS |
| Child | : | Nonspecific symptoms |
| | | Acute CHF |
| | | Arrhythmia |
| | | Acute coronary syndrome |
| | | Inappropriate tachycardia |
| | | Shock |

vii) 'Minimally' symptomatic child with cardiomegaly: Can be diagnosed to have myocarditis, usually by echocardiography.

The most common presentation will be a recent onset heart failure with the following physical signs. Baby may be pale with diaphoresis; facial puffiness is often present but edema is uncommon (Box 4).

**Box 4. Cardiac findings**

- Resting tachycardia, tachypnea
- Prolonged capillary refill time
- Reduced systolic BP / Hypotension
- Elevated JVP
- Cardiomegaly
- Soft S1, variable S2
- S3 gallop
- Low intensity systolic murmur at apex due to mitral regurgitation (MR)

**Table I. Acute fulminant and non-fulminant myocarditis - Differentiation**

| Features | | Acute fulminant myocarditis | Acute non-fulminant myocarditis |
|---|---|---|---|
| Prodrome | | Yes | Yes |
| Onset of illness | | < 3 days | 3 – 7 days |
| Shock | | Yes | No |
| CHF | | Severe | Yes |
| MODS | | Yes | Less likely |
| Tachycardia | | + + + | + + |
| Hypotension | | + + | + |
| CRP | | + + | + |
| Biomarkers | | + + | + |
| ECG-QRS | | Wider | Wide |
| ECHO | Ejection fraction | Marked decrease | Decrease |
| | LV | Minimal dilation | Dilated |
| | I V S | Thick | Thin |
| Short term mortality | | High | Low |
| Recovery | | High | Low |

## Acute fulminant myocarditis

It deserves special description because of its potential for early high mortality but excellent long term survival and function in survivors. The classical presentation is as severe heart failure and severe shock. Prodromal flu could be present. Child goes into shock / severe HF / MODS within 2-3 days of onset of illness. The classical echocardiographic findings are significantly impaired LV function, minimally dilated LV and thickened LV walls due to edema. The differentiation from non-fulminant myocarditis is given in Table I.

## Differential diagnosis

There is considerable overlap between viral myocarditis and dilated cardiomyopathy. Both share clinical picture of heart failure, cardiomegaly, apical mitral regurgitation (MR) murmur, nonspecific ECG changes, cardiomegaly with varying pulmonary venous hypertension (PVH), impaired LV function and MR. Rheumatic carditis is another major cause of recent onset CHF in a child. Endocardial fibroelastosis (EFE) can be an important differential diagnosis in early infancy. However, the incidence of EFE is fast declining. Restrictive cardiomyopathy (RCM) could be another differential diagnosis. Broncholitis can be also be a close differential diagnosis.

There are certain remediable causes of 'recent onset' LV dysfunction in infants. They are anomalous origin of the left coronary artery from the pulmonary artery (ALCAPA), coarctation of aorta (COA), severe aortic stenosis (AS), hypocalcemia, carnitine deficiency and cardiac complications of scorpion sting. Tachycardia induced cardiomyopathy (TIC) can be completely normalized by converting SVT into sinus rhythm. It is imperative to exclude all mechanical, electrical and metabolic causes of LV dysfunction before committing on the diagnosis of inflammatory cardiomyopathy. Recently Sagar, et al classified myocarditis into 3 subsets, based on symptoms, signs and investigations (Box 5).

**Box 5. Myocarditis – Sagar classification**

I. No symptoms - Possible subclinical acute myocarditis**

II. Symptomatic - Probable acute myocarditis**

III. Histology and immunohistochemical features in EMB - Definite acute myocarditis

***Should have one of the three: Positive biomarkers, ECG abnormalities, abnormal cardiac function*

## Investigations

Investigations are designed to reach a diagnosis, exclude certain illnesses, prognosticate and confirm the diagnosis. It can be divided into first and second line investigations.

**First line investigations** (always done)

i. Acute phase reactants: ESR (≥ 30 mm/hr) and CRP are elevated in 50%.

ii. Aspartate aminotransferase (AST): Elevation of AST is considered very useful and is a sensitive (85%) marker in viral myocarditis.

iii. Biomarkers: The usual biomarkers used are Trop T or Trop I, CK MB, BNP and Pro BNP. For troponins, with the usual cut off value of >0.10 ngm/mL, sensitivity and specificity are 55% and 94% and if it is ≥ 0.050 ngm/mL, sensitivity and specificity are 70% and 85% respectively. Trop T and Trop I are likely to be more positive in myocarditis presenting as ACS (75%). In a proper clinical setting, if LV dysfunction and positive Trop T/I are demonstrated, myocarditis is likely. If a child has chest pain and positive Trop T, 50% of them will have heart disease. Half of those children will have myocarditis. In subclinical myocarditis, Trop T is usually negative. CPK MB is less sensitive and less useful. Other blood tests done occasionally in myocarditis are complement, antimyosin antibodies, blood for viral antibodies (both acute and convalescent sera).

iv. Chest x-ray: Majority of children who present with sub-acute LV dysfunction (non fulminant) will show cardiomegaly (80%) (Fig.2). Those who present with arrhythmia and ACS will not have cardiac enlargement (Fig.3). Other findings are LA enlargement and mild pleural effusion.

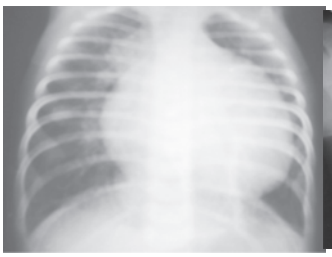

**Fig.2. CXR - Cardiomegaly with globular heart**

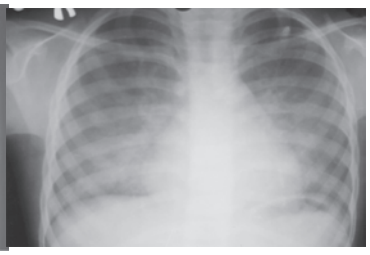

**Fig.3. CXR - No cardiomegaly but acute pulmonary edema**

v. ECG: It is a nonspecific but very useful test in suspected myocarditis. ECG abnormalities are present in 90%. Major abnormalities are sinus tachycardia

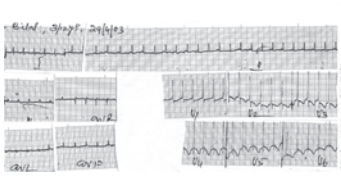

**Fig.4. Sinus tachycardia with T inversion V1 to V6**

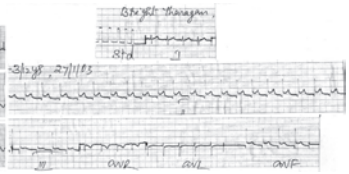

**Fig.5. STEMI (L II, III, aVF)**

(60%), ST-T changes (50%), LVH (40%), low voltages, LAE and acute myocardial infarction (AMI) pattern (Fig.4 and 5). The triad of ECG features in myocarditis are sinus tachycardia, low voltage complexes in precordial leads and ST-T changes. AV blocks, ectopics, SVT and VT can occur. CHB is rare. In acute coronary syndrome due to myocarditis, ST-elevation myocardial infarction (STEMI), T $^{-}$, ST $^{-}$ and deep Q are present.

ECG has both diagnostic as well as prognostic value. ECG features which mark poor prognosis are deep Q waves, LBBB, prolonged QTc, wide QRS (≥120 msec), VPCs, abnormal QRS axis. A normal ECG does not rule out viral myocarditis. Many young children may not show the expected low voltages.

vi. Echocardiography: Initial echocardiography (by transthoracic route) is done in all, using M-mode, 2D and colour flow mapping (CFM). It is one of the most useful investigations in suspected myocarditis. Apart from picking up abnormalities in myocarditis, it will exclude specific causes of LV dysfunction. Echo is abnormal in more than 70%. It is most useful when child presents with heart failure. LV is dilated. RV can also be affected. LV ejection fraction is uniformly reduced. There could be mild pericardial effusion. Regional wall motion abnormality (RWMA) is common. However it may also suggest presence of ALCAPA in infants. MR and less commonly TR can be picked up. High right ventricular systolic pressure (RVSP) is usually found in DCM rather than myocarditis. Hence echocardiography is used to pick up LV dysfunction, rule out structural heart disease, differentiate between acute non fulminant myocarditis and fulminant myocarditis, prognostication and evaluation of effectiveness of therapy (Box 5).

**Second line investigations** (not always done)

i. Radionuclide imaging: Nuclear imaging though useful is less commonly employed in the diagnosis of myocarditis. Gallium scan can pick up inflammation of myocardium. Indium labeled antimyosin antibodies pick up patchy necrotic areas. Technetium labeled single photon emission computed tomography (SPECT) can pick up myocardial necrosis in myocarditis. Sensitivity of such imaging is 83% and specificity is low (53%). They are not routinely used except in suspected sarcoidosis and concomitantly with other imaging modalities.

**Box 5. Myocarditis - Salient features in ECHO**

- Triad of echocardiographic features of AFM - Impaired LV function, minimally dilated LV and septal thickness
- EF can be preserved when child presents with ACS or arrhythmias
- Restrictive cardiomyopathy (RCM) - rare.
- EF - Significantly impaired with minimal LV dilatation in AFM
- Tissue Doppler characteristics may be more sensitive in myocarditis

ii. Cardiac magnetic resonance imaging (CMR): Cardiac MRI is the most promising new age imaging modality in myocarditis. It is being increasingly used in early diagnosis, characterization of pathology, prognostication and in performing guided endomyocardial biopsy. CMR is exquisitely sensitive, highly specific and makes early diagnosis possible, picking up subtle, patchy involvement. T2 weighted images are obtained and contrast CMR is done using gadolinium – both first pass and delayed. CMR looks at LV size, function, wall thickness and myocardial injury Gadolinium entrancement can be either early or late. The enhancement can be transmural and subepicardial. Lake Louis consensus criteria for myocarditis by MRI are global / regional myocardial signal intensity, increase in T 2 weighted images, increased global enhancement on gadolinium and focal lesions with non-ischemic enhancement.

iii. Endomyocardial biopsy (EMB): It is the gold standard for diagnosing myocarditis though not regularly done because of the following issues:

(a) Sampling error - Biopsy needle may not hit areas of myocarditis

(b) Inter observer variability in interpretation

(c) A hazardous procedure (of late the CMR guided EMB is being done to improve sensitivity).

Both histopathological examination and immunopathological tests can be carried out on specimens. The advanced tests include PCR, insitu hybridization (ISH), HLA antigens and various T cell markers. Dallas criteria is traditionally utilized for characterizing myocarditis. Lieberman also offers a clinico-pathological classification. Various new techniques of diagnosis have been applied to biopsy. PCR and ISH are the two most significant ones. These techniques have demonstrated a shift of etiology from coxsackie / adeno virus to HPV and herpes virus.

## Treatment

Treatment of myocarditis essentially remains supportive. There are new management modes which have thrown up variable results. Strategy is to categorize myocarditis into stable and unstable forms. All are admitted into PICU on account of its inherent mortality potential.

**I. Management of stable children:** Management of congestive heart failure using diuretics, ACE inhibitors or angiotensin receptor blocker (ARB) and aldosterone inhibitors.

a. Diuretics like frusemide are commonly used for symptom relief. Torsemide has been found to reduce bio transformation from myocarditis to DCM in rat model. However, translation into practice is yet to be shown.

b. ACE inhibitors: They are to be introduced early in the management. Either captopril or enalapril is used. Captopril is the preferred one as it has short half life and additional antioxidant property. ACE inhibitors in myocarditis have many advantages in addition to their hemodynamic role. They cause down regulation in immune response thereby reducing inflammatory activity, cell necrosis and fibrosis and biotransformation to DCM. The standard hemodynamic effects are afterload reduction, improving left ventricular ejection fraction (LVEF) and preventing cardiac remodeling.

c. Digoxin: It is either not indicated or to be withheld in myocarditis in spite of LV dysfunction as it increases proinflammatory cytokines, enhance myocardial injury and increase chance of arrhythmia.

d. Aldosterone antagonists: Spironolactone can be an additional drug as it may reduce fibrosis, inflammation, remodeling and can have a survival benefit.

e. β-Blockers: In a stable patient, β-Blockers could be used along with ACE inhibitors and diuretics. Carvedilol is the preferred drug, to be given carefully well titrated. Metoprolol may be harmful in the setting of acute myocarditis. β-Blockers are to be avoided in acute fulminant myocarditis, decompensated heart failure and acute unstable myocarditis.

f. Calcium channel blockers are not indicated in treatment. NSAIDs are absolutely avoided in myocarditis as they will enhance inflammation and may increase virus multiplication.

g. Rest / Activity: Rest is advised in acute stage for at least two weeks and physical activity is curbed for another 6 months. This is being advocated due to possible deleterious effect of exercise on virus multiplication and inflammation and possible risk of sudden cardiac death (SCD).

**II. Management of unstable children / hemodynamic compromise:** Child or infant should be offered support by an IV inotrope with or without use of IV vasodilators, initially.

a. IV inotropes: Either dobutamine or milrinone can be given. Dobutamine may be the preferred drug in a normotensive child. Dopamine is given in a hypotensive child. There is less experience in myocarditis with levosimendan. However, it could be useful in decompensated DCM.

b. Vasodilators: Either IV nitroprusside or IV nitroglycerin is given to off load the ventricle. They have to be carefully titrated to avoid hypotension.

c. Diuretics: IV diuretics are given to reduce pulmonary congestion. IV infusion of frusemide can be offered.

d. Other drugs: ACEI inhibitors are administered routinely in the absence of renal failure and hypotension. Digoxin is not to be used as well as β-blockers.

e. Mechanical ventilation: It is a useful supportive measure either noninvasive or invasive ventilation could be used.

f. Anti arrhythmic drugs: In documented arrhythmia they are used. Amiodarone is the preferred agent. β-blockers are also used.

g. Anticoagulants: In severe LV dysfunction (EF $\leq$ 20%) anticoagulants are used to prevent clot formation. Clots in the cardiac chamber is yet another indication.

h. ECMO: ECMO support is useful in severe myocarditis, especially in fulminant myocarditis. It has been proven to save lives in severe acute myocarditis.

i. Ventricular assist device (VAD): It is being increasingly used to bridge / support child with severe myocarditis in the west. Increasing miniaturization will increase its use in the future.

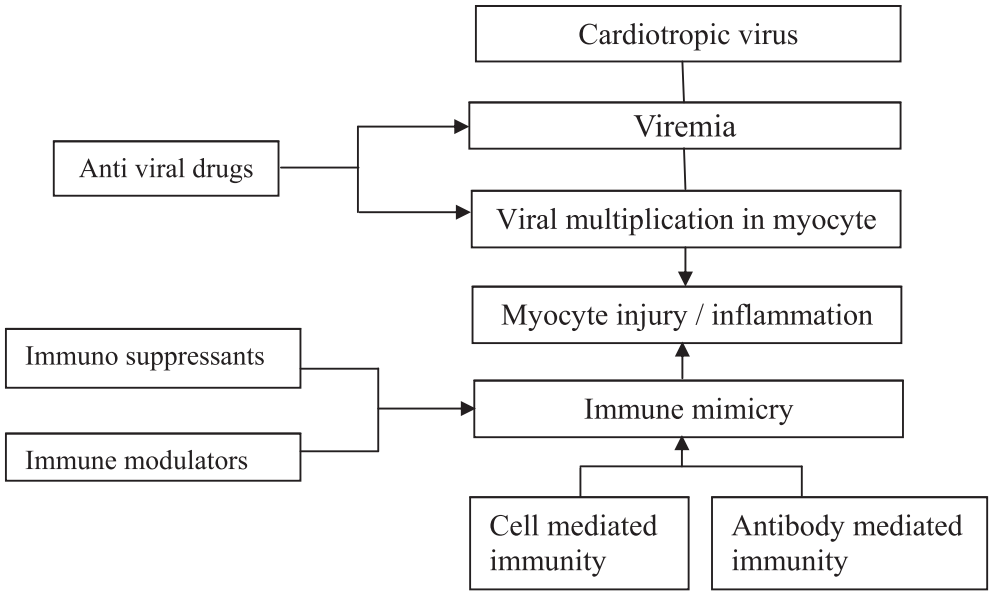


**Fig.6. Drugs based on etiopathogenesis**

**Specific / Targeted therapy**

These agents are used based on various etiopathogenetic mechanisms of viral myocarditis (Fig.6). They are antiviral agents, immuno suppressants and immunomodulators.

I. Anti viral therapy: Theoretically antiviral agents will be most useful in the early phase of the disease and by the time child presents with myocarditis, the initial phase would have been over. Hence, routine use of antiviral agents is not practiced. b interferon has been tried in entero and adeno viral myocarditis. IV ribavirin has been used in myocarditis due to RSV infection. interferon has also been tried. In Betaferon in chronic viral cardiomyopathy (BICC) trial, betaferon (IFN Beta 1b) was used in 143 patients with a better outcome, in terms of viral load and functional improvement. Still there are limited options currently for the use of antiviral agents.

II. Immunosuppression: Because of the immune mimicry involved in pathogenesis of myocarditis, the possible use of immune suppressants is an attractive option. The traditional drugs have been prednisolone, azathioprine and cyclosporine. They have been used both in adults and children. There have been more than 20 trials, both uncontrolled and controlled ones in myocarditis using immune suppressants. Many have shown improvement in histology but there has been no significant difference in survival and improvement of cardiac function. This is possibly because there is substantial spontaneous improvement in viral myocarditis. The only major study in children used prednisolone alone, prednisolone withazathioprine and with azathioprine and cyclosporine. A combination therapy showed improved outcome. However, a recent meta analysis in children demonstrated no significant benefit. Overall, the use of immuno-suppressants is limited.

There are specific circumstances where steroids are used. Sarcoidosis with myocarditis is treated with steroids. Giant cell myocarditis, which otherwise has a dismal prognosis is treated with steroids and cyclosporine for better outcome. It is interesting to note that in spite of weak evidence for steroids, steroids are used in 25% of myocarditis in USA.

Steroids are now used regularly in sarcoidosis with myocarditis, giant cell myocarditis and virus negative, lymphocytic, refractory myocarditis. Active virus multiplication is always ruled out before therapy.

III. Immunomodulation by IVIG: It is an attractive option as it modulates immune reaction rather than suppressing it and has been quite useful in various immunological conditions in children including Kawasaki Disease. At present, IVIG remains a class II indication, either a or b. IVIG has been documented to be more useful in HPV myocarditis. It has been difficult to preselect candidates who are likely to respond to IVIG. Those who

have viral persistence are less likely to respond, while those who have high antibody titers are more likely to respond. The dose is 1 g / kg / 12 hrs infusion for 2 consecutive days. The dose is split because of the high osmolality of IVIG which could be deleterious to children with myocarditis. Treatment strategy based on clinicopathological status is given in Box 6.

**Box 6. Myocarditis - Management aspects**

| | |
|---|---|
| A. Healed myocarditis | - No treatment |
| B. Inflammatory Cardiomyopathy | - Standard treatment Immuno suppression |
| C. Chronic viral heart disease | - Standard treatment and anti viral therapy |
| D. DCM | - HF treatment |

## Natural history / outcome

Myocarditis has variable and reasonably predictable outcome.

I. Myocarditis - Mildly symptomatic EF 40-50% improve within weeks and months.

II. Myocarditis - Symptomatic. EF : ≤ 35%

a. Complete recovery - 25%

b. Improvement - 25%

III. DCM - 50% will die / need transplant

In viral myocarditis the findings that indicate poor short term prognosis are AFM, low ejection fraction, high PA systolic pressure, neonatal presentation, age, need for ventilation / ECMO, VT and cardiac arrest. Mortality in hospital depends on syncope as a presentation, LBBB, EF < 35%, FC III-IV, - LVEDP, PAH and biopsy (e.g. Giant cell myocarditis). In AFM, early mortality is high (10-40%) but long term survival and recovery of LV function are very good. Transformation of viral myocarditis to DCM is the most vexing problem, once child survives the initial insult. Various studies have put this between 15-45%. Clinical studies have put spontaneous resolution as 70%, while histological studies have put it at 50%. A meta analysis involving 388 children showed a resolution of 57% at the end of 5 years, indicating more than half of myocarditis resolved.

## Future directions and new frontiers

Cardiac MR is being increasingly used to detect myocarditis much earlier and also to guide EMB and streamline treatment strategy. It could become the next generation gold standard in myocarditis. New specific targeted therapy is unlikely to evolve. However, advent of early diagnosis and possible tissue characterization by CMR may lead to judicious and more focused use of immunosuppressants and IVIG. Miniaturization of VAD may make it more attractive in a small child as a life saving measure as well as bridge to transplant. ECMO will be increasingly used in the future in the sickest of children. Future elucidation of pathogenesis of biotransformation to DCM may lead to discovery of treatment strategy to block this critical pathway and reduce incidence of DCM.

## Points to Remember

- ***Currently Coxsackie B, adenovirus and human parvo virus are the three leading causes of viral myocarditis.***
- ***Dallas criteria is the first and still the foremost histological classification of myocarditis.***
- ***The major presentations of myocarditis are recent onset CHF, acute fulminant myocarditis and chest pain syndrome in children.***
- ***Remediable causes of 'recent onset' LV dysfunction in infants, such as ALCAPA, undiagnosed CoA, hypocalcemia and scorpion sting should be recognized and treated.***
- ***Viral myocarditis can mimic bronchiolitis.***
- ***Cardiac biomarkers, AST and ESR are the three most useful blood investigations while echocardiography is the most useful one. Chest x-ray and ECG are abnormal in 90% of cases.***
- ***CMR is the most promising imaging modality in recognition and characterization of myocarditis.***
- ***Endomyocardial biopsy is utilized only in selected centers.***
- ***Mechanical ventilation, ECMO and LVAD are increasingly used to save a life in fulminant myocarditis.***
- ***Fulminant myocarditis, even if it has high acute mortality, recover completely once they survive.***
- ***Those who present with chest pain syndrome, arrhythmia and fulminant myocarditis have excellent long term prognosis.***
- ***Newer modalities of treatment like antiviral agents and immunosuppression have only limited role, though IVIG administration continuous to be popular.***

- ***Newer agents which could prevent biotransformation of myocarditis to DCM have to be developed in the future.***

## Bibliography


1. Myocarditis: Current trends in treatment. J Card Fail 2010; 16: 176-179.
2. Shultz JC, Hillard AA, Cooper LT, Rihal CS. Diagnosis and Treatment of Viral Myocarditis. Mayo Clin Proced 2009; 84 (11):1001-1009.
3. Canter CE, Simpson KE. Diagnosis and Treatment of Myocarditis in children in the current era. Circulation 2014; 129:115-128.
4. Dancea AB. Myocarditis in infants and children: A review for the pediatrician. Pediatr Child health 2001; 6(8): 543-545.
5. Levine MC, Klugman D, Teach SJ. Update on myocarditis in children. Curr opin Pediatr 2010; 22:278-283.
6. Magnani JW, Dec GW. Myocarditis: Current Trends in Diagnosis and Treatment. Circulation 2006; 113:876-890.
7. Caforio AL, Pankuweit S, Arbustini E, Basso C, Gimeno-Blanes J, Felix SB, et al. Current status of knowledge on etiology, diagnosis, management and therapy of myocarditis. A position statement of ESC working group on Myocardial and pericardial diseases. Eur Heart *J* 2013; 34:2636-2648.
8. Kindermann I, Barth C, Mahfoud F, Ukena C, Lenski M, Yilmaz A, et al. Update on Myocarditis. J Amer Coll Card 2012; 59:779-792.
9. Simpson KE, Anwar S, Canter CE. Myocarditis. In: Moss & Adams Heart Disease in infants, children, and adolescents. Ed. HD Allen, RE Shaddy, DJ Denny, TF Feltes, F. Gelta. 9th Edn, Wolters Kluwer. Philadelphia 2016pp
10. Schulneiss HP, Kuhl U, Cooper LT. The Management of Myocarditis. Eur Heart *J* 2011; 32:2616-2625.
11. Sagar S, Liu PP, Cooper LT. Myocarditis. Lancet 2012; 179:738-747.
12. Bowles NE, Ni J, Kearney DL, Pauschinger M, Schultheiss HP, McCarthy R, Hare J, et al. Detection of Viruses in Myocardial tissues by PCR J Amer Coll Card 2003; 42:466-452.
13. Lieberman EB, Hutchins GM, Herskowitz A, Rose NR, Baughman KL. Clinicopathologic description of myocarditis. J Am Coll Cardiol 1991; 18; 1617-1626.
14. Durani Y, Egan M, Baffa J, Selbst SM, Nager AL. Pediatric Myocarditis: Presenting clinical characteristics. Am J Emerg Med 2009; 27:942-947.
15. Drossner DM, Hirsh DA, Sturm JJ, Mahle WT, Goo DJ, Massey R, et al. Cardiac disease in Pediatric Patients presenting to a pediatric ED with chest pain. Am J Emerg Med 2011; 29:632-638.
16. Friedrich MG, Sechtem U, Schulz-Menger J, Holmvang G, Alakija P, Cooper LT, et al. Cardiovascular magnetic resonance in myocarditis: A JACC White Paper J Am Coll Cardiol 2009; 53(17):1475-1487.
17. Camargo PR, Snitcowsky R, da Luz PL. Mazzieri R, Higuchi ML, Rati M, et al. Favorable effects of immune suppressive therapy in children with dilated cardiomyopathy and active myocarditis. Pediatric Cardiology 1995; 16(2): pp61-68.
18. Hia CP, Yip WC, Tai BC, Quek SC. Cluck. Immune suppressive therapy in acute myocarditis; an 18 year systematic review. Arch Dis. Child 2004; 89(6): 580-584.
19. Mason JW, O'Connell JB, Herskowitz A, Rose NR, McManus BM, Billingham ME, et al. A clinical trial of immunosuppressive therapy for myocarditis. The Myocarditis Treatment Trial Investigators. N Engl J Med 1995; 333(5):269-275.
20. McNamara DM, Holubkov R, Starling RC, Dec GW, Loh E, Torre-Amione G, et al. Controlled trial of intravenous immune globulin in recent-onset dilated cardiomyopathy. Circulation 2001; 103(18):2254-2259.
21. Drucker NA, Colan SD, Lewis AB, Beiser AS, Wessel DL, Takahashi M, et al. Gamma globulin treatment of acute myocarditis in the pediatric population. Circulation 1994; 89(1):252-257.
22. Frustaci A, Chimenti C, Calabrese F, Pieroni M, Thiene G, Maseri A. Immuno suppressive therapy for active lymphocytic myocarditis: virological and immunological profile of responders versus non responders. Circulation 2003; 107(6):857-863.
23. Chan KY, Iwahara M, Benson LN, Wilson GJ, Freedom RM. Immunosuppressive therapy in the management of Acute Myocarditis in children: a clinical trial. J Am Coll Cardiol. 1991; 17(2):458-460.
24. Hufnagel G, Pankuweit S, Richter A, Schönian U, Maisch B. The European Study of Epidemiology and Treatment of Cardiac Inflammatory Diseases (ESETCID). First epidemiological results. Herz 2000; 25(3):279-285.
25. Lee KJ, McCrindle BW, Bohn DJ, Wilson GJ, Taylor GP, Freedom RM, et al. Clinical outcomes of acute myocarditis in childhood. Heart 1999; 82(2):226-233.
26. Kindermann I, Kindermann M, Kandolf R, Klingel K, Bültmann B, Müller T, et al. Predictors of outcome in patients with suspected myocarditis. Circulation 2008; 118(6):639-648.
27. Amabile N, Fraisse A, Bouvenot J, Chetaille P, Ovaert C. Outcome of acute fulminant myocarditis in children. Heart 2006; 92(9):1269-1273.
28. McCarthy RE 3rd, Boehmer JP, Hruban RH, Hutchins GM, Kasper EK, Hare JM, et al. Long term outcome of fulminant myocarditis as compared with acute non fulminant myocarditis. N Engl J Med 2000; 342(10):690-696.
29. Daubeny PEF, Nugent AW, Chondros P, Carlin JB, Colan SD, Cheung M, et al. Clinical features and outcome of childhood dilated cardiomyopathy (DCM). Results from a national population based study 2006; 114: 2671-26787.

**CARDIOLOGY**

# APPROACH TO MANAGEMENT OF ARRHYTHMIAS IN CHILDREN

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****Elamaran C**

**Abstract:** *Arrhythmias are not uncommon in pediatric population and vary in spectrum from benign normal variants to life threatening arrhythmias. Acute management is based on presence or absence of pulse, perfusion and QRS width in ECG. Chronic management aimed at prevention of recurrences is dictated by the specific arrhythmia.*

**Keywords:** *Narrow complex tachycardia, Wide complex tachycardia, Bradycardia, Supraventricular tachycardia, Ventricular tachycardia, Implantable defibrillator, Pacemaker*

Arrhythmias commonly seen in children can vary from normal benign variants to life threatening malignant arrhythmias. The approach is based on symptoms, rate, presence of hemodynamic compromise (pulse and perfusion) and ECG findings. The criteria for tachyarrhythmia and bradyarrhythmia are based on normal heart rate for age (Table I).[1]

**Table I. Normal heart rate by age**

| Age | Awake heart rate (bpm) | Mean (bpm) | Sleeping pulse rate |
|---|---|---|---|
| Newborn to 3 months | 85–205 | 140 | 80-160 |
| 3 months to 2 years | 100–190 | 130 | 75-160 |
| 2 years to 10 years | 60–140 | 80 | 60-90 |
| >10 years | 60–100 | 75 | 50-90 |

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Arrhythmia can be tachyarrhythmias or bradyarrythmias. Tachyarrhythmias can be further classified based on QRS duration as wide complex or narrow complex tachycardia. Wide complex tachycardia is one wherein QRS duration is more than 100 ms in children 4 to 16 years of age and more than 90 ms in children less than 4 years of age.

Narrow complex tachycardia one wherein QRS duration is less than 90 millisecond (ms) in children between 4 and 16 years of age and less than 86 ms in children less than 4 years of age.[2] Based on the P wave and QRS the various causes for narrow complex tachycardia can be made as follows

i. Regular with normal P wave and QRS: Sinus tachycardia, inappropriate sinus tachycardia and sinoatrial nodal re-entrant tachycardia.

ii. Grossly irregular narrow QRS complex: Tachycardia with irregular pattern or apparently absent atrial activity (Atrial fibrillation).

iii. Regular variations in QRS: Atrial tachycardia, atrial flutter or rarely atrioventricular nodal reentrant tachycardia (AVNRT), Saw tooth' pattern of atrial activity is seen in atrial flutter while isoelectric interval between atrial activity is seen in atrial tachycardia.

iv. P waves with no consistent relationship with QRS (AV disassociation): Junctional ectopic tachycardia.

v. No P waves: AVNRT

vi. P waves visible after QRS (ST segment) :AVRT.

## History and physical examination[3]

There is sudden or gradual onset and termination of palpitation. The frequency and regularity of palpitation has to be documented correctly. History of syncope should be asked for, as it can indicate an underlying significant cardiac disease and also increases the risk for sudden cardiac death. A family history of sudden cardiac death (SCD) may be associated with Wolff-Parkinson-White (WPW) syndrome, catecholaminergic polymorphic ventricular tachycardia, hypertrophic cardiomyopathy and arrhythmogenic right

ventricular dysplasia. Chest pain is rare in children. Bilateral sensory neural deafness may be associated with long QT syndrome.

Pulse rate and rhythm has to be carefully looked for as an **i**rregular pulse followed by a pause occurs in ventricular premature beats (VPBs) or atrial premature beats (APBs). Respiration can cause a variation in heart rate wherein inspiration increase and expiration decreases heart rate in sinus arrhythmia and is physiological. Complete and thorough clinical exam of the cardiovascular system has to be done to detect an underlying heart disease or failure.

## Basic investigations

Cardio thoracic ratio and pulmonary congestion has to be looked for in chest xray. A twelve lead ECG with rhythm strip helps to differentiate into tachy and bradyarrhythmias. In specific instances Holter monitoring is done which provides a continuous ECG recording for 24 hours and upto 1 week duration.In patients with intermittent or infrequent symptoms, transtelephonic monitors can detect arrhythmias for a period of upto 30 to 60 days which is known as event monitor. Effect of exercise on dysarrhythmias is checked by Treadmill testing. Echocardiogram can detect associated structural heart disease and LV dysfunction in children with dysarrhythmia.

## Special tests

**Electrophysiology study (EPS)** for diagnostic evaluation of foci of origin, risk of malignant arrhythmia and sudden cardiac death and ablation of aberrant pathway or ectopic foci can be done while Magnetic resonance imaging (MRI) can be done to evaluate an arrhythmogenic RV dysplasia and cardiomyopathy. Genetic testing can be done for arrthythmogenic RV dysplasia, catecholaminergic polymorphic ventricular tachycardia (VT).

## Acute management of tachycardia[1,4]

It depends on the charecteristics of pulse and perfusion. If pulse or signs of circulation are absent pediatric cardiac arrest algorithm has to be followed. If pulse is present and perfusion is adequate pediatric tachycardia with pulse and adequate perfusion algorithm needs to be followed. If perfusion is poor pediatric tachycardia with pulse and poor perfusion algorithm needs to be followed as per pediatric advanced life support algorithm (PALS).Acute management of arrhythmias is done in emergency room and pediatric intensive care unit.

## Chronic management

### A) No treatment

Asymptomatic ventricular premature depolarizations (VPD) and atrial premature depolarizations (APD) do not usually require drug therapy.

### B) Nonpharmacological treatment

In structurally normal heart without preexcitation, reassurance and educating the parents and the child about the methods to terminate SVT is only needed when the arrhythmia is infrequent with no hemodynamic compromise.

Vagal maneuver: A plastic bag filled with ice and water or a cloth soaked in ice water over the upper half of face is applied for 15-20 seconds without occluding nose or mouth. In an older child valsalva maneuver like blowing into a narrow straw, inducing gag reflex, head down position or carotid sinus massage can be tried to terminate the arrhythmia. Ocular massage is avoided since it may cause retinal injury.

### C) Antiarrhythmic drug therapy

Pulsed therapy (single dose oral therapy): Children with sporadic long lasting tachyarrhythmia are treated with a single dose of antiarrhthmic drug at the onset to terminate arrhythmia if vagal manoeuvres are not effective. Chronic pharmacological therapy is needed in long QT syndrome (LQTS), arrhythmogenic RV dysplasia, catecholaminergic polymorphic VT, arrhythmias persisting despite ablation, postoperative arrhythmia and arrhythmias in cardiomyopathy to prevent recurrences. Antiarrhythmic drug classification and their dosages are given in Table II and III respectively.

### D) Radiofrequency catheter ablation

Ablation of accessory pathway or the foci of origin of tachyarrhythmia terminates further episodes.

## Specific arrhythmias

**Sinus tachycardia** (Fig.1): Sinus node discharges faster than normal for patient's age (Table I) in response to hypoxia, hypovolemia, fever, sepsis, injury, pain, anxiety, anemia and cardiac failure. Management is targeted by treating the primary cause. ECG shows normal P-wave preceding QRS complex with constant PR interval.

**Table II. Vaughn Williams antiarrhythmic drug classification**

| Class | Action | | Drugs |
|---|---|---|---|
| I | Sodium channel blockers | | |
| | I A | Prolong action potential duration | Quinidine, procainamide, disopyramide |
| | I B | No change or shortening of action potential duration | Lidocaine, mexiletine, phenytoin |
| | I C | Mild prolongation of action potential duration | Flecainide, encainide, propafenone, |
| II | Beta-adrenergic blockers | | Propranolol, atenolol, metoprolol, nadolol |
| III | Potassium channel blockersProlong action potential duration | | Amiodarone, sotalol, ibutilide |
| IV | Calcium channel blocker | | Verapamil, diltiazem |
| Others | Adenosine, digoxin | | |

**Table III. Common antiarrhythmic drugs**

| Drug | Dose |
|---|---|
| **Class IA** Procainamide | IV: 0.4mg/kg/min for max 25min; then 20-80mcg/kg/min (max 2g/day). Oral: 5-8mg/kg/dose 4H. Level 3-10mcg/ml. |
| **Class IB** Lidocaine | IV: 1mg/kg (0.1ml/kg of 1%) over 2min; then 15-50mcg/kg/min: VF: 1mg/kg (0.1ml/kg of 1%) |
| Mexiletine | IV: 2-5mg/kg (max 250mg) over 15 min; then 5-20 mcg/kg/min (max 250mg/hr); Oral: 8mg/kg (max 400mg) stat; then 4-8mg/kg/dose (max 400mg) 8H starting 2hr after loading dose. |
| **Class IC** Propafenone | Oral: 70mg/m2/dose 8H; increased if required to 165mg/m2/dose 8H; IV: 2mg/kg over 2hr; then 4mcg/kg/min increased if required to max 8 mcg/kg/min. |
| **Class II** Propranolol if required. | IV: 0.02mg/kg test dose then 0.1mg/kg over 10 min (repeat x1-3 prn); then 0.1-0.3mg/kg/dose 3H. Oral: 0.2-0.5 mg/kg/dose 6-12H; slow increase to maximum of 1.5 mg/kg/dose (max 80mg) 6-12H |
| Atenolol | Oral: 1-2mg/kg/dose 12-24H; IV: 0.05mg/kg (adult 2.5mg) every 5 min until response (max 4 doses); then 0.1-0.2mg/kg/dose over 10min 12-24H. |
| Esmolol | 0.5mg/kg (500mcg/kg) IV over 1min; then 50 mcg/kg/min for 4min; if poor response repeat 0.5mg/kg and give 50-200mcg/kg/min; rarely given for >48hr. |
| **Class III** d, l-Sotalol | IV: 0.5-2mg/kg/dose over 10min 6H; Oral: 1-4mg/kg/dose 8-12H. |
| Amiodarone | IV: 25mcg/kg/min for 4hr; then 5-15mcg/kg /min (max 1.2g/24hr). Oral: 4mg/kg/dose 8H 1 wk; 12H 1 wk; then 12-24H. After starting tablets; taper IV infusion over 5 days. Reduce dose of digoxin and warfarin. Pulseless VF or VT: 5mg/kg IV over 3-5 min. |
| Ibutilide | 0.017mg/kg (max 1mg) IV over 10min; then wait 10min and repeat once if reqd. |
| **Class IV** Verapamil | IV: 0.1-0.2mg/kg over 10min; then 5mcg/kg/min. Oral: 1-3mg/kg/dose 8-12H. |
| Miscellaneous Adenosine | 0.1mg/kg stat by rapid IV push; increase by 0.05 mg/kg every 2min to max 0.35mg/kg. Pulmonary hypertension: 50mcg/kg/min (1ml/kg/hr of 3mg/ml) into central vein. |

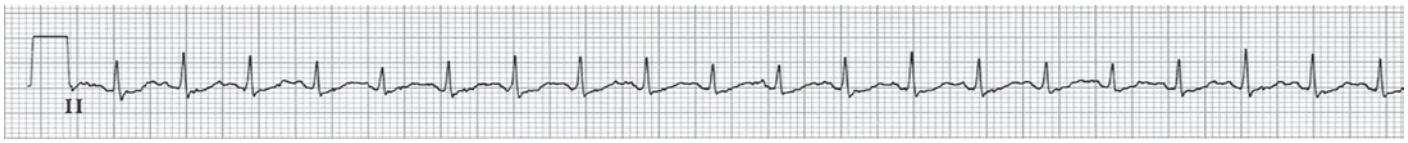



**Fig.1.Sinus tachycardia (Lead II)**

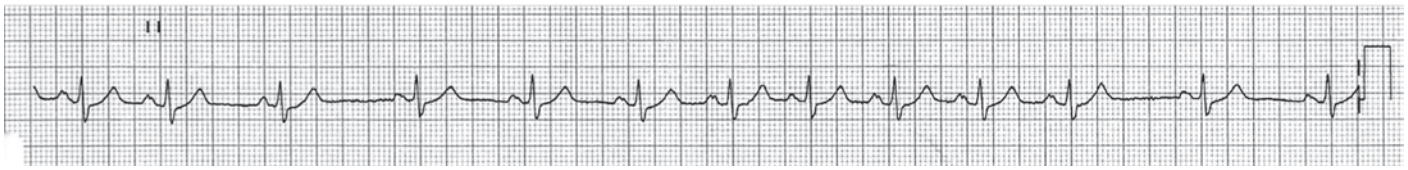



**Fig.2.Sinus arrhythmia (Lead II)**

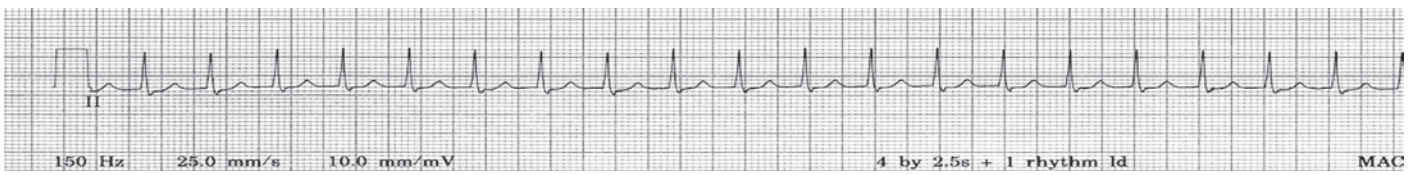



**Fig.3.AVNRT (Lead II) – Absent P waves**

**Sinus arrhythmia** (Fig.2): A normal variant with heart rate changes with respiratory cycle due to variation in parasympathetic impulse during respiratory cycle. ECG shows increased heart rate during inspiration and a decreased heart rate during expiration.

**Inappropriate sinus tachycardia:** Tachycardia disproportionate to the precipitating causes for sinus tachycardia. Treatment is by betablocker or calcium channel blockers. Radiofrequency catheter ablation can be done in refractory cases.

**Sinus node re entry tachycardia:** ECG is similar to sinus tachycardia and is triggered and terminated by atrial premature depolarization. It responds to vagal maneuvers, adenosine, beta blockers, amiodarone, calcium channel blockers and digoxin, Radiofrequency catheter ablation can be done in refractory cases.

**Supraventricular tachycardia (SVT):** Here rhythm originate above the ventricles, usually with a narrow QRS complex. It includes atrioventricular nodal reciprocating tachycardia (AVNRT), atrioventricular reciprocating tachycardia (AVRT), atrial tachycardia (AT) and junctional ectopic tachycardia (JET). Conventionally atrial flutter and atrial fibrillation are excluded.[5]

**Atrio ventricular nodal reciprocating tachycardia (AVNRT):** In addition to the normal pathway, there is an additional accessory pathway involved with re-entrant circuit in the AV node or perinodal atrial tissue. ECG shows narrow complex tachycardia with absent P waves (Fig.3).

For acute management of AVNRT, adenosine is the drug of choice, if vagal maneuvers fail. Verapamil is also very effective (80%–95%) but may cause severe hemodynamic deterioration in infants and in patients with heart failure and is therefore contraindicated in this group.

For chronic management of AVNRT, prophylactic pharmacological therapy is by administration of calcium channel blockers, beta blockers or digoxin. Class III drugs like amiodarone, sotalol are effective but are not for routine use due to proarrhythmic effects. Flecanide and propafenone is useful in structurally normal hearts. Pulse therapy as a single dose oral therapy (pill in the pocket) is given in the absence of LV dysfunction, sinus bradycardia or pre-excitation. In adolescents, single dose of flecanide (3mg/Kg) or a combination of diltiazem and propranalol is used. Decision for radiofrequency catheter ablation is made based on age, weight of the child (>15 Kg / >2 years), frequency, duration, symptoms, effectiveness of pharmacological therapy and associated structural heart disease

**Atrioventricular reciprocating tachycardia (AVRT):** There is an extra nodal accessory pathway between atrium and ventricle in addition to normal AV conduction system. ECG shows narrow complex tachycardia with QRS alternans (Fig.4).

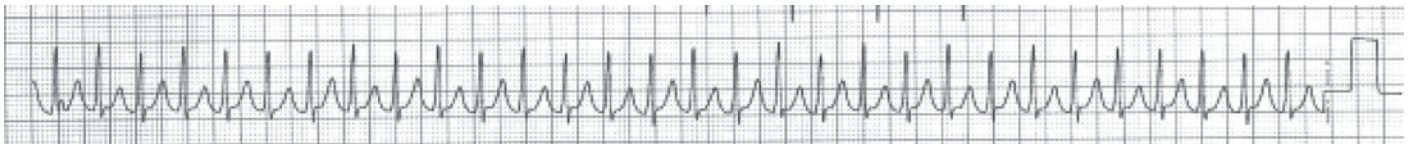


**Fig.4. AVRT (L II) - Narrow complex tachycardia with QRS alternans**

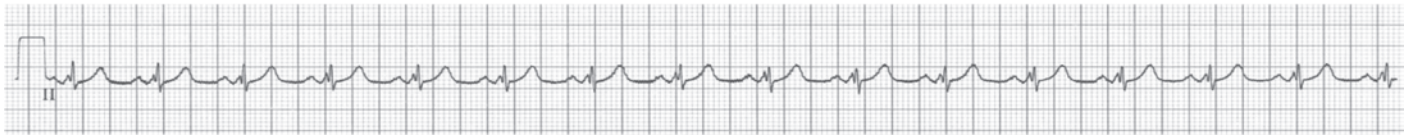



**Fig.5. Pre-excitation (L II) - short PR interval (<120msec), wide QRS, slur in initial portion complex (delta wave)**

Betablockers, sotalol, amiodarone, flecainide are used as prophylactic pharmacological therapy to prevent recurrences. Digoxin, diltiazem and verapamil are contraindicated since it increases the conduction in accessory pathway and may induce ventricular fibrillation. Radiofrequency catheter ablation is the preferred therapy in patients with WPW syndrome [pre excitation and tachyarrhythmia (Fig.5)] with hemodynamic instability.

**Focal atrial tachycardia** (Fig.6): It originates from single focus in the atrium at 100-250 bpm with P waves seen in second half of tachycardia cycle (RP duration longer than PR duration) with isoelectric baseline. In addition P wave morphology is usually different from that of the sinus P wave. It is usually benign but may lead to tachycardia induced cardiomyopathy.

Management with calcium channel blockers, beta blockers, flecanide, propafenone, sotalol and amiodarone are effective. Radiofrequency catheter ablation especially in drug refractory or incessant atrial tachycardia and in tachycardia induced cardiomyopathy.

**Multifocal atrial tachycardia** (Fig.7): It is secondary to causes like pulmonary disease and dyselectrolytemia. ECG shows multiple ectopic foci, charecterized by 3 or more P wave morphologies. The management is directed to correction of precipitating factors and may require calcium channel blockers.

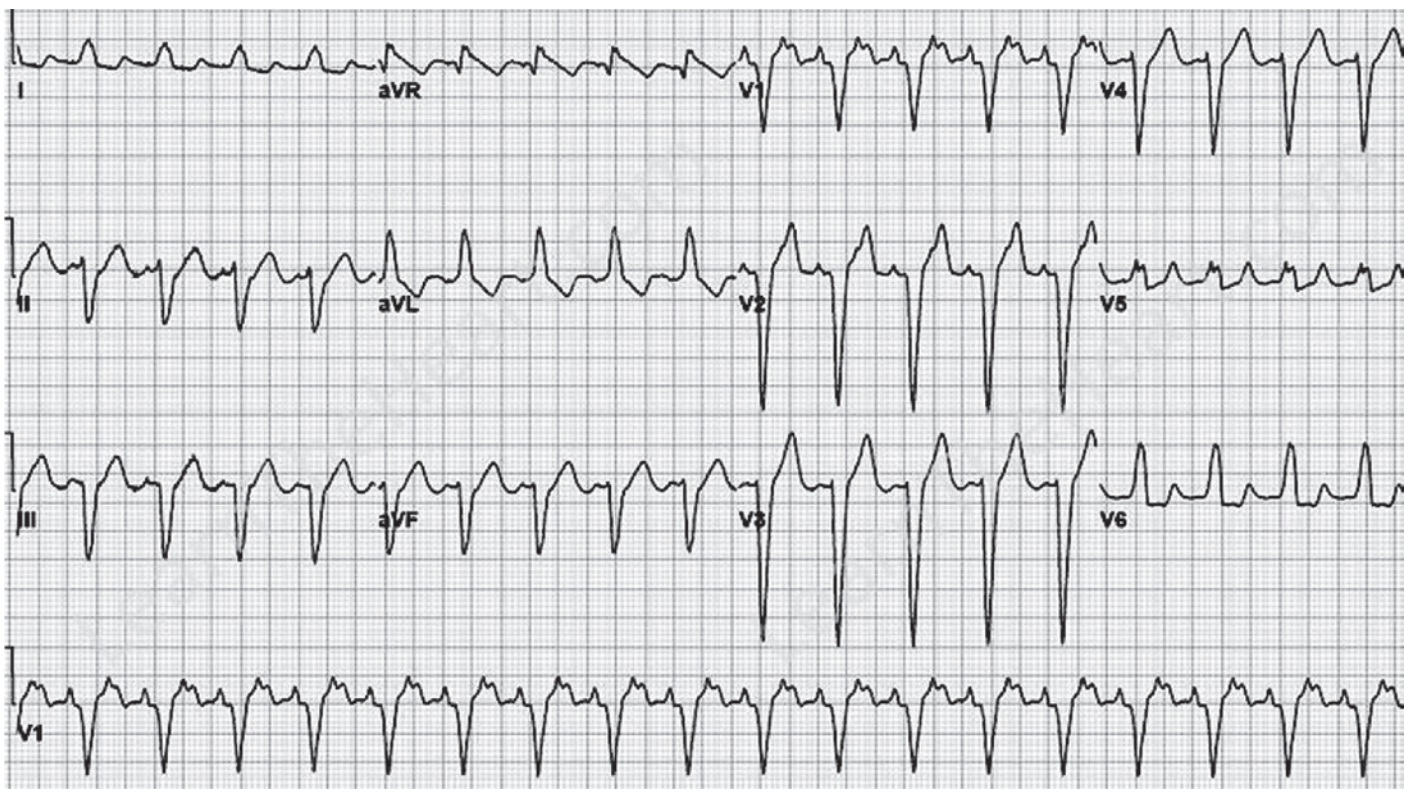



**Fig.6. Focal atrial tachycardia**

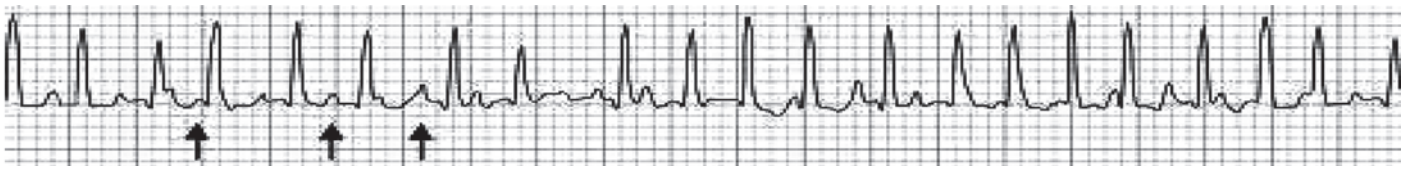


**Fig.7.Multifocal atrial tachycardia**

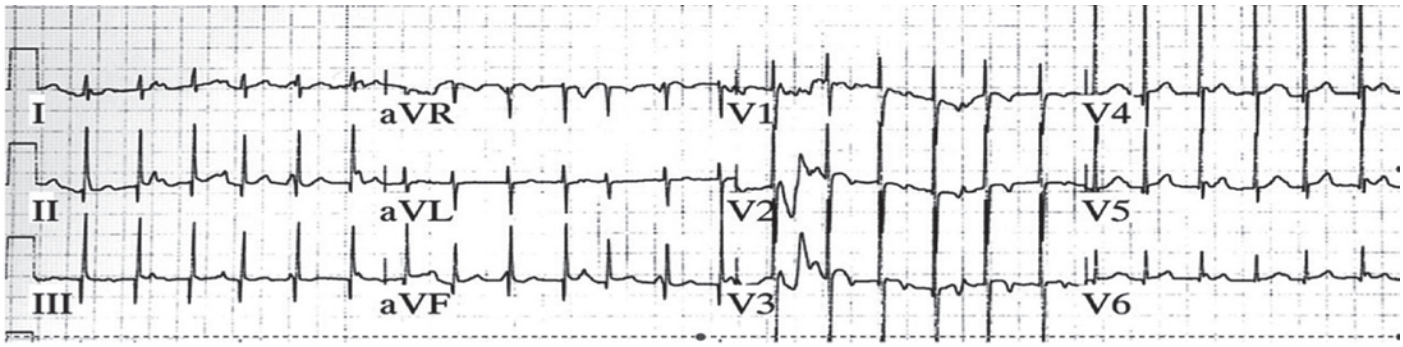



**Fig.8. JET Rate: 180-240 bpm**

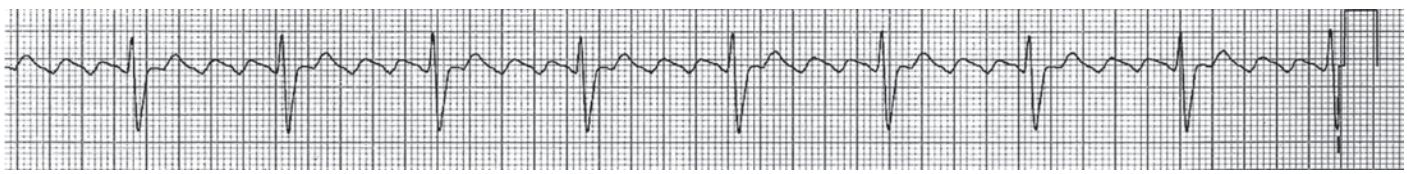


**Fig.9. Atrial rhythm (rate of 240-320 bpm and ventricular rate around 300 or 150 or 75bpm)**

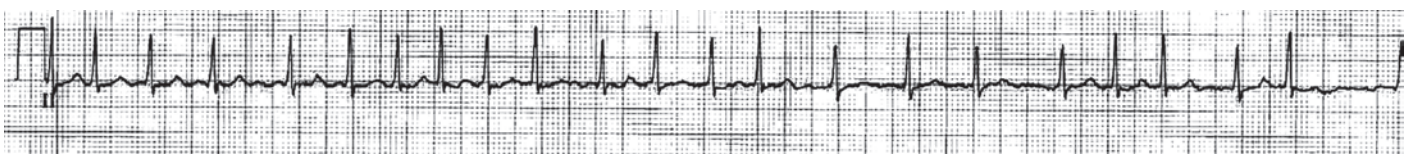


**Fig.10. Atrial fibrillation [fibrillatory waves and irregularly irregular ventricular rate, atrial rates > 350 bpm with rapid ventricular response (>100bpm)]**

**Junctional ectopic tachycardia (JET)** (Fig.8): Congenital JET is detected prenatally or during neonatal period and has a high family incidence with recessive inheritance while acquired JET is usually detected in early postoperative patients with significant hemodynamic deterioration. ECG shows narrow QRS complexes with AV dissociation.

Congenital JET is resistant to standard anti arrhythmic therapy except amiodarone and propafenone. Acquired JET has usually a limited course and is managed by discontinuation of inotropes and cooling, along with drugs including IV flecanide, amiodarone, procainamide and propafenone.[6,7,8] In resistant cases R wave synchronised atrial pacing, emergency AV ablation and ECMO can be done.

**Atrial flutter** (Fig.9): ECG shows flutter waves-with saw tooth pattern. Management is by rhythm control. In hemodynamically unstable children termination of atrial flutter is mostly achieved by electrical means either by DC cardioversion or by transesophageal pacing. If hemodynamically stable, ibutilide or procainamide may be given intravenously to convert atrial flutter to sinus rhythm. Conversion may also be achieved orally with d, l-sotalol, propafenone or a class IA drug such as quinidine.[9]

Chronic therapy is indicated if recurrences are frequent. In neonates recurrence of atrial flutter is infrequent and chronic therapy is seldom necessary. Digoxin, beta-blockers, and calcium channel antagonists decreases the atrioventricular conduction but are ineffective in conversion to sinus rhythm. d,l-sotalol, propafenone.and amiodarone are effective for rhythm control.

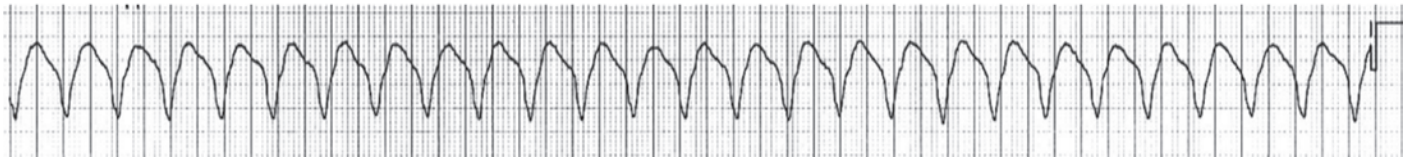


**Fig.11. Ventricular tachycardia**

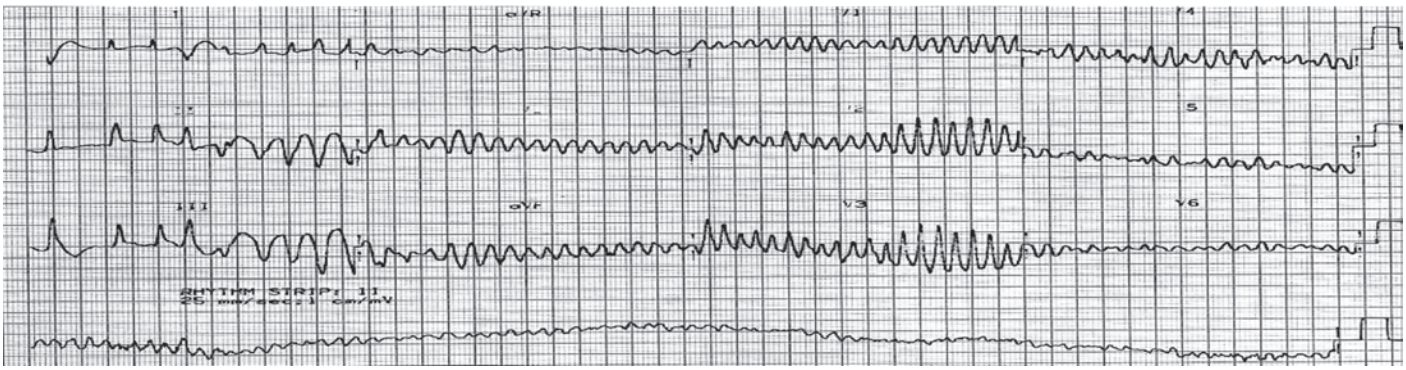


**Fig.12.Ventricular fibrillation- irregular rapid electrical activity with no P, QRS or T wave**

Radiofrequency ablation of the atrial reentry circuits can be given in selective cases.[10,11,12] Anticoagulant therapy targeting an INR between 2 to 3 is given in chronic atrial flutter to prevent thromboembolism. Cardioversion by DC version or pharmacological or by ablation, should be done only if anticoagulated or if arrhythmia is less than 48 hours or no atrial clots is detected in echo. Duration of anticoagulation therapy is for 3 weeks prior to cardioversion and continued for 4 weeks following cardioversion.

**Atrial fibrillation (AF)** (Fig.10): In ECG P waves are replaced by fibrillatory waves with rapid irregular ventricular response. Fixed R-R interval in AF indicates associated complete heart block or associated junctional/ ventricular tachycardia. Irregular wide QRS tachycardia suggests associated bundle branch block or conduction over accessory pathway. Rheumatic heart disease, WPW syndrome, hyperthyroidism, myocarditis, digitoxicity and familial AF are the common causes for AF in children.

Recurrent AF is when 2 or more episodes of AF occur. Paroxysmal AF is recurrent AF terminated within 7 days. Recurrent AF not terminated for more than 7 days is persistent AF while permanent AF is AF lasting for more than 1 year. AF in less than 60 years without any evident cardiac or non cardiac cause is lone AF and has a favourable prognosis compared to other groups.

Management is by treatment of precipitating factors and anticoagulation for at least 3-4 weeks before and after pharmacological or electrical cardioversion with target INR of 2 to 3.Ablation therapy is done for focal AF with origin from pulmonary veins.

Drugs used for rate control in pharmacological cardioversion are calcium channel blockers. Digoxin and verapamil are contraindicated in AF associated with WPW syndrome since it increases the conduction in accessory pathway leading to hemodynamic deterioration. For rhythm control in selected patients Class I drugs like quinidine, propafenone, flecanide and class III like amiodarone and sotalol are used which converts AF to sinus rhythm but with risk of proarrhyhmic effect.

**Ventricular tachycardia and fibrillation** (Fig.11): In ventricular tachycardia ECG shows wide QRS complex with AV disassociation while in ventricular fibrillation there is irregular rapid electrical activity with no P, QRS or T wave (Fig.12). Differentiation between ventricular tachycardia (VT) from supraventricular tachycardia (SVT) with aberrancy or bundle branch block can be made out by the characteristics given in Box 1.

In ventricular fibrillation, ECG shows irregular rapid electrical activity with no P, QRS or T wave. Acute management is by DC version and with drugs like IV lignocaine, IV amiodarone, IV procainamide. Chronic management of VT depends upon the presence of symptoms, presence or absence of structural heart disease and LV dysfunction and prognosis of that particular type of VT.[13]

**Box 1. Ventricular and supraventricular tachycardia - Differentiation**

VT

Capture or fusion beats

P wave rate less than QRS rate

QRS axis of -30 to -120

Similar QRS complexes in all chest leads (concordant) rS, Rs or QR in V1 and R, RS, QS or QR in V6

**Atrial fibrillation with pre excitation or bundle branch block**

Grossly irregular QRS

**Supraventricular rhythm with preexisting intraventricular conduction abnormality or bundle branch block**

Morphology and duration of QRS during tachycardia is similar to ventricular ectopics during sinus rhythm

**VT in structurally and functionally normal heart**: In accelerated idioventricular rhythm no treatment is given. In idiopathic LV tachycardia or verapamil sensitive VT with ECG showing VT with RBBB pattern, verapamil, beta blockers, radiofrequency ablation is the treatment. For right ventricular outflow tract tachycardia with ECG showing VT with LBBB pattern, beta blockers and radiofrequency ablation is the treatment. RVOT VT has to be differentiated from more malignant arrhythmogenic RV dysplasia (ECG-LBBB pattern VT with left axis deviation) which has a high risk for sudden cardiac death (SCD). For catecholaminergic polymorphic VT and exercise-induced VT, betablocker is the treatment.

Long QT syndrome can be acquired or congenital. In acquired LQTS drugs causing LQTS is withdrawn, dyselectrolytemia like hypokalemia, hypomagnesemia is managed. IV magnesium is the drug of choice for Torsades de pointes. In congenital LQTS, beta blockers, potassium supplement, mexilitine, left stellectomy and implantable defibrillator are the available drugs and treatment modalities respectively. The indications for implantable defibrillator is given in Box 2.

**VT in structurally or functionally abnormal heart:** In postoperative VTs correction of hemodynamics abnormalities with drugs like beta-blockers, sotalol or amiodarone are the treatment. In VT occurring in mitral valve prolapse beta blockers are given while in myocarditis, dilated or hypertrophic cardiomyopathy and arrhythmogenic right ventricular dysplasia,[14] amiodarone is therapy of choice.

**Box 2. Indications for implantable defibrillator**

**Class I: General agreement of indication**

Spontaneous sustained VT in association with structural heart disease

Nonsustained VT in patients with

a) LV dysfunction and inducible VT and VF

b) Spontaneous sustained VT in patients without structural heart disease that is not amenable to other forms of therapy

**Class II: No consensus**

Cardiac arrest presumed to be due to VF

Severe symptoms attributable to ventricular arrhythmias in patient awaiting cardiac transplantation

Inherited conditions with high risk of life-threatening ventricular arrhythmias

Recurrent syncope of undermined origin with ventricular dysfunction and inducible ventricular arrhythmias at EPS

Syncope in advanced structural heart disease with no other identifiable cause

## Bradyarrhythmia

Bradycardia is defined by a heart rate less than the lower limit of normal for age (Table I). Sinus bradycardia is asymptomatic and follow a benign course with normal increase in rate with exercise. ECG shows normal P wave morphology and axis preceeds each QRS complex (Fig.13).

## Sinus node dysfunction (SND)

a) **Sinus node pause/arrest** (Fig.14): There is lack of discharge from the SA node with no activation of the atria. ECG shows periods of absent P wave.

**b) Sinus node exit block** (Fig.15): There is delay or blocked activation of atria from SA node. ECG shows dropped P wave with (P-P interval in multiples of basic P-P interval).

c) **Tachycardia-bradycardia syndrome** (Fig.16): Severe sinus bradycardia or sinus pause is followed by tachycardia in the form of atrial fibrillation/flutter or junctional rhythm.

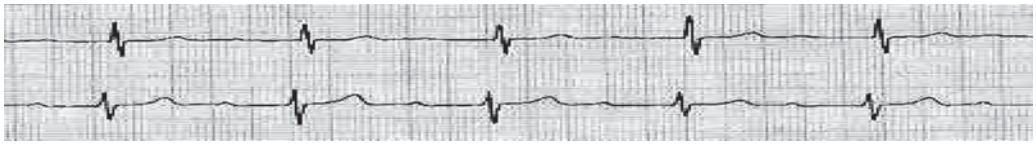


**Fig.13. Sinus bradycardia (Normal P wave morphology and at 40bpm)**

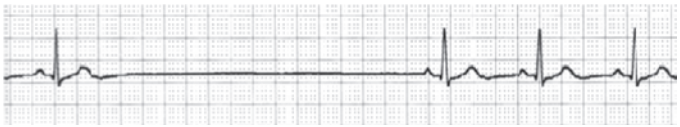


**Fig.14. Sinus pause**

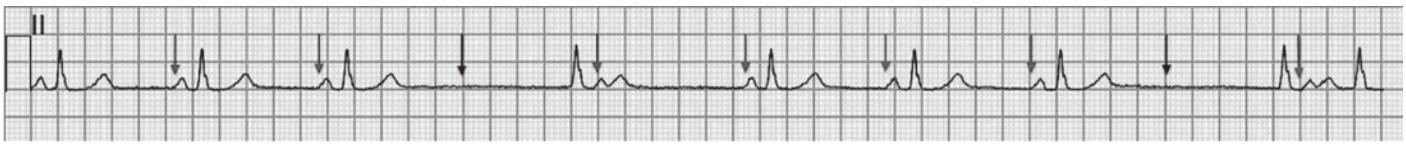



**Fig.15. Sinus node exit block - Dropped P wave**

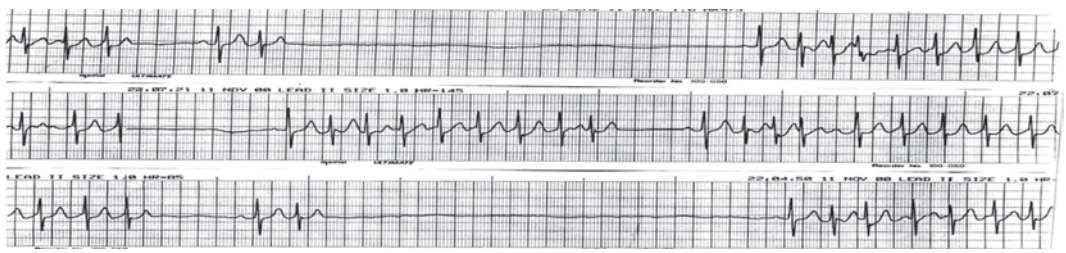


**Fig.16.Tachycardia-bradycardia syndrome (Atrial flutter alternating with periods of asystole)**

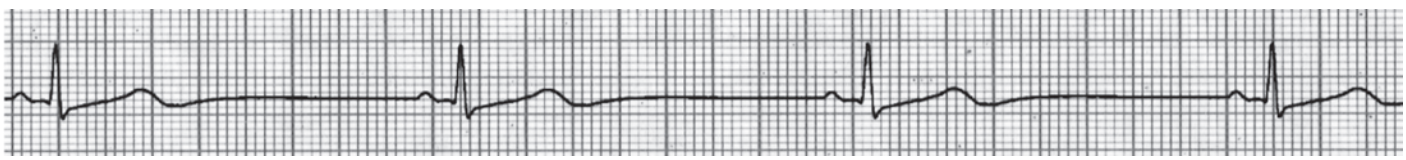


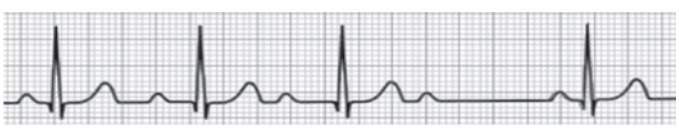
**Fig.17. First degree AV block (PR interval >200msec)**

## Atrio ventricular block

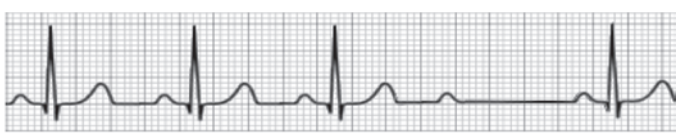
**First-degree atrioventricular heart block** (Fig.17): There is delay in atrio-ventricular conduction at the level of AV node with prolongation of PR interval beyond the normal ranges for age.

**Second-degree atrioventricular heart block** (Fig.18): Some atrial impulses are not conducted to the ventricles. It is classified as Mobitz type 1 (Wenckebach phenomena) and Mobitz type II. In Mobitz type 1 (Wenckebach) block: PR interval is progressively prolonged with each beat until a P wave is not followed by QRS complex, the cycle is constantly repeated and usually benign and the site of block is above the bundle of His. In Mobitz type 2, following a number of normal beats with no progressive prolongation

**Mobitz I or Wenckebach**



**Mobitz II**



**2:1 Block**

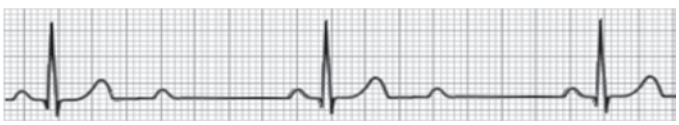


**Fig.18. Mobitz I, Mobitz II and 2:1 block**

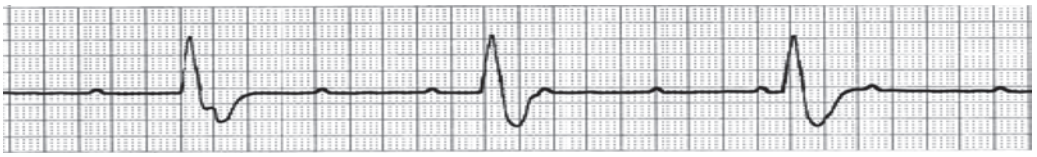


**Fig.19. Complete heart block (atrial rate at 88 bpm, Ventricular rate at 37 bpm**

**Box 3. Indications for pacing in the pediatric population**

**Class I (Recommended)**

1. Advanced second- or third-degree AV block associated with symptomatic bradycardia or ventricular dysfunction.
2. Sinus node dysfunction with correlation of symptom.
3. Postoperative advanced second- or third-degree AV block that is not expected to resolve or that persists at least 7 days after cardiac surgery
4. Congenital third-degree AV block with a wide QRS escape rhythm, complex ventricular ectopy, or ventricular dysfunction
5. Congenital third-degree AV block in the infant with a heart rate < 50-55 bpm or with congenital heart disease and a heart rate<70 bpm

**Class IIa (Is reasonable)**

1. Bradycardia-tachycardia syndrome with need for long term antiarrhythmic.
2. Congenital third-degree AV block beyond the 1st year of life with an average heart rate <50 bpm, abrupt pauses in ventricular rate that are two or three times the basic cycle length, or symptoms associated with chronotropic incompetence.
3. Long QT syndrome with 2:1 or third degree heart block
4. Asymptomatic sinus bradycardia in child with CHD and a) resting HR < 40 bpm b) pauses in ventricular rate >3 seconds c) impaired hemodynamics due to sinus bradycardia or loss of AV.

**Class IIb (May be considered)**

1. Congenital third-degree AV block with an acceptable rate, a narrow QRS complex, and normal ventricular function
2. Asymptomatic sinus bradycardia with a resting heart rate <40 bpm or pauses longer than 3 seconds
3. Neuromuscular disease with any degree of AV block including first degree heart block.

of PR interval, a P wave is not followed by QRS and the site of block is below Bundle of His. Mobitz type 2 may progress to complete heart block.

**Third-degree (complete) atrioventricular heart block** (Fig.19): No P waves are conducted to ventricles. ECG shows triad of fixed P-P iterval, fixed R-R interval with varying PR interval. In patients with block above the bundle of His (supra hisian) the escape rhythm is junctional with normal QRS complexes, with block below the bundle of His (infra hisian) the escape rhythm is ventricular with wide QRS complex.

## Management

Acute bradycardia with a pulse and poor perfusion is managed according to the PALS algorithm. The indications for pacing by Class I – II recommendation in pediatrics is given in Box 3.

## Conclusion

With newer antiarrhythmic drugs, better understanding of physiological mechanism in arrhythmia, technical advancement in radiofrequency ablation and implantable defibrillators in recent years, arrhythmias are more effectively treated.

## Points to Remember

- ***Arrhythmias in children are not uncommon.***
- ***Diagnosis is based on the ECG charecteristics.***
- ***Differentiation of supraventricular from ventricular tachyarrhythmias is essential.***
- ***Acute arrhythmias should be treated in pediatric intensive care unit.***
- ***Indications for antiarrhythmic drugs are clear cut while some may need implantable defibrillator or pacemaker.***

## References

1. American Heart Association. Pediatric assessment. In: Pediatric Advanced Life Support (PALS) provider manual 2005). MossvHeart disease in Infant, Children and Adults, 4th edn. M D Williams & Wilkins, Baltimore 1989; pp925-939.

2. American College of Cardiology Foundation and the Heart Rhythm Society: endorsed by the International Society for Computerized Electrocardiology. Circulation 2009; 119(10):e241-250.
3. Geggel RL, Flyer DC. History, growth, nutrition, physical examination, and routine laboratory studies. In: Nadas' Pediatric Cardiology, 2nd ed, Keane JF, Lock JE, Flyer DC (Eds), Saunders Elsevier, Philadelphia 2006; p129.
4. Chameides L, Hazinski M. Textbook of pediatric advanced life support. Dallas, American Heart Association, 1994; pp117-155.
5. Josephson ME, Wellens HJ. Differential diagnosis of supraventricular tachycardia. Cardiol Clin 1990; 8:411.
6. Garson A, Moak JP, Smith RT, Norton JB. Usefulness of intravenous propafenone for control of postoperative junctional ectopic tachycardia. Am J Cardiol 1987; 59:1422–1424.
7. Raja P, Hawker RE, Chaikitpinyo A, Cooper SG, Lau KC, Nunn GR, et al. Amiodarone management of junctional ectopic tachycardia after cardiac surgery in children. Br Heart J 1994; 72:261–265.
8. Walsh EP, Saul JP, Sholler GF, Triedman JK, Jonas RA, Mayer JE, et al .Evaluation of a staged treatment protocol for rapid automatic junctional tachycardia after operation for congenital heart disease. J Am Coll Cardiol 1997; 29:1046-1053.
9. LeudtkeSA, KuhnRJ, McGaffreyFM. Pharmacologicmanagement of supraventricular tachycardias in children. Part 2: Atrial flutter, atrial fibrillation and junctional and atrial ectopic tachycardia. Ann Pharmacother 1997; 31:1347–1359.
10. Beaufort-Krol GCM, Bink-Boelkens MThE. Sotalol for atrial tachycardia after surgery. PACE 1997; 20:2125–2130.
11. Benditt DG, Williams JH, Jin J, Deering TF, Zucker R, Browne K, et al. (Maintenance of sinus rhythm with oral d, l-sotalol therapy in patients with symptomatic atrial fibrillation and/or atrial flutter. Am J Cardiol 1999; 84:270–277.
12. Leudtke SA, Kuhn RJ, McGaffrey F. Pharmacologicman - agement of supraventricular tachycardias in children. Part 2: Atrial flutter, atrial fibrillation and junctional and atrial ectopic tachycardia. Ann Pharmacother 1997; 31:1347–1359.
13. Pfammatter JP, Paul T.Idiopathic ventricular tachycardia in infancy and childhood. J Am Coll Cardiol 1999; 33:2067–2072.
14. Marcus FI, Fontaine G. Arrhythmogenic right ventricular dysplasia/cardiomyopathy: a review. Pacing Clin Electrophysiol 1995; 18:1298–1314.

## CLIPPINGS

***Tight Glycemic Control in Critically Ill Children. HALF-PINT Study Investigators and the PALISI Network.***

Critically ill children with hyperglycemia did not benefit from tight glycemic control targeted to a blood glucose level of 80 to 110 mg per deciliter, as compared with a level of 150 to 180 mg per deciliter. Optimal target blood glucose levels in critically ill children are unknown. In the HALF-Pint randomized trial of intensive insulin therapy (IIT), a lower target blood glucose level (80 to 110 mg/dL did not reduce the number of intensive care unit-free days in critically ill children when compared with a higher target level (150 to 180 mg/dL Mortality was nondiferent between the groups. However the rates of hypoglycemia and health care associated infections wer much hgher in the lower target group. These results are consistent with trials in adults and it is recommended against treatment with IIT regimens that target blood glucose levels between 80 to 110 mg/dL [4.4 to 6.1 mmol/L] in critically ill children.

***Agus MS, Wypij D, Hirshberg EL, Srinivasan V, Faustino EV, Luckett PM, et al. Tight Glycemic Control in Critically Ill Children. HALF-PINT Study Investigators and the PALISI Network. N Engl J Med 2017; 376(8):729.***

## ERRATUM

**Article titled "Renal imaging in pediatric nephro-urology. When and what?" Indian J Pract Pediatr 2016; 19(2): 110 – 118.**

It is regretted that the name of author was incorrectly printed in the content. The authorship of the article should read as "Arpana Iyengar". The error is deeply regretted.

Editorial Board
Indian Journal of Practical Pediatrics

**CARDIOLOGY**

# CARDIOVASCULAR ISSUES IN SYSTEMIC CONDITIONS

***Shakuntala Prabhu**
****Sumitra Venkatesh**

**Abstract:** *Systemic conditions are generally an interdisciplinary challenge in clinical practice. Heart gets directly or indirectly involved by different mechanisms. A cardiovascular history and thorough examination helps to evaluate underlying cardiac dynamics. Diagnostic methods, especially two-dimensional echocardiography is often required, which can be used for screening as well as for the detection of early stages of the disease. In view of a high degree of morbidity and mortality, clinicians in care of these patients should be equipped with knowledge and awareness of cardiac involvement to support the heart and tailor the management of the systemic illness.*

**Keywords**: *Cardiovascular issues, Systemic conditions*

Heart is not just an innocent bystander and is affected in a wide range of systemic conditions. Often, cardiac involvement in systemic diseases is not well recognized, as the dominant manifestations frequently reside in other organ systems. However, cardiac involvement accounts for a serious degree of morbidity or mortality. The heart and the circulation are important targets in systemic diseases that may cause cardiac failure in the end stage of the illness or life-threatening problems due to acute cardiac events.

Cardiovascular history and examination is essential to assess cardiac dynamics. Diagnostic methods especially imaging techniques are required, which can be used for screening and for the detection of early stages of the disease. Chest X-ray may show an enlarged heart due to cardiac failure or dilatation. Blood tests for myocardial damage (cardiac enzymes - particularly troponins) and/or heart failure (including brain natriuretic peptide (BNP) are helpful. A 12-lead ECG helps to detect arrhythmias and chamber dilatation. Two-dimensional echocardiography is the most important diagnostic technique in cardiology for the detection of structural and functional disturbance and cardiac tissue injuries. The quality of echocardiography and success rate of detecting cardiac pathology in patients with primary non-cardiac problems depends on the competence and expertise of the investigator. Especially in this scenario, clinical knowledge about the influence of the systemic disease on cardiac anatomy and physiology is essential for an accurate diagnosis. Other investigations like cardiac catheterisation, MRI scan, Doppler flow studies, nuclear cardiology and cardiac scans can be carried out, if relevant information is not obtained on echocardiogram.

Cardiac involvement in systemic condition can present in many ways (Box 1). Also cardiomyopathy is common in several conditions and may be caused by diffuse myocardial ischemia due to vasculitis. Infiltration usually causes myocarditis and pericarditis.[1,2] There are many systemic conditions affecting the heart. This article deals with the cardiovascular issues frequently encountered in systemic conditions like hypothyroidism, nutrition deficiencies, diphtheria, scorpion sting and chemotherapy induced cardiomyopathy.

**Box 1.Systemic conditions-Cardiac manifestation**

Pericarditis

Myocarditis or myocardial fibrosis due to myositis

Vasculitis with rhythm and conduction disturbances

Diastolic or systolic heart failure

Endocardial involvement with valvular disease

Pulmonary hypertension (secondary to concomitant lung disease or recurrent lung embolism)

Arterial hypertension.

Syncope

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### Hypothyroidism

Hypothyroidism is one of the most common endocrine abnormalities in children. Thyroid hormone exerts direct cellular effect on almost all tissues of the body including heart which has been recognized for several decades. The cardiac effects of hypothyroidism depends on the severity and duration of the disease and can range from subtle abnormalities to overt and easily recognizable manifestations. Lack of thyroxine is known to be associated with both structural and functional alterations in the myocardium and causes dyslipidemia with increased risk of atherosclerosis.[3-5] Septal and ventricular free wall hypertrophy are the commonest echocardiographic findings followed by pericardial effusion systolic/diastolic dysfunction, along with the presence of prolonged PR-interval, QTc prolongation and bradycardia.[6] Bradycardia and systemic hypertension is seen in severe cases, while the mild and moderate ones may have low to normal blood pressures.[7] Narrow pulse pressure and slightly increased mean arterial pressure with some degree of exercise impairment are the most common findings in patients with overt hypothyroidism. Many studies have found significant correlation between raised TSH levels and serum total cholesterol and LDL cholesterol. Hypothyroidism accounts for about 2% of all cases of hyperlipidemia and is second only to diabetes mellitus as a cause of secondary hyperlipidemia.[8]

## Nutritional deficiencies and heart

Macronutrients and micronutrient deficiencies are very common in the Indian subcontinent due to multiple causes like poverty, malnutrition and religious practices. These deficiencies cause significant cardiac morbidity ranging from dilation of the cardiac chambers to cardiomyopathy and cardiac failure. Urban food fads of fat-laden junk foods also increase the risk of heart disease as young adults. A diet high in fat increases the risk of hypertension which in turn causes increase in left ventricular mass, cardiomyocyte hypertrophy and left ventricular dysfunction. Excessive dietary sugars (carbohydrates) expose the heart to insulin and insulin-like growth factor which can also lead to left ventricular hypertrophy and dysfunction as seen in adults with hypertension.[1] A sodium rich diet can also precipitate or worsen congestive cardiac failure in borderline cases.

Specific nutrient deficiencies cause specific cardiac issues, a few of which will be covered in this discussion. These nutrients are either antioxidants or nutrients which are known to affect myocardial energy production. Endogenous antioxidants include those like zinc in superoxide dismutase or selenium in glutathione peroxidase, free radical scavengers (e.g. vitamins A, C or E) and metal chelators. Early recognition and optimization of many vitamin deficiencies helps in prevention of heart failure and cardiomyopathies.[2]

Selective deficiency of thiamine, selenium and calcium can lead to cardiac failure. Vitamins A, C and E help in protection of the vasculature while Vitamin B6, B12 and folate help in reduction of homocysteine. Carnitine and co-enzyme Q help, in improving the exercise capacity in children with cardiac failure.

Hypocalcemia induced cardiomyopathy is a well-known cause of treatable cardiomyopathy that responds dramatically to calcium supplementation. Also, low levels of serum calcium is pro-arrhythmogenic with higher incidence of prolongation of QTc, torsades de pointes and ventricular fibrillations. In cases associated with hypocalcemia, Vitamin D, another important nutrient, helps in improving myocardial contractility.[9,10]

Magnesium is an important mineral that helps in maintaining the sodium-potassium homeostasis mechanism in the body. Hypomagnesemia is associated with an increased incidence of ventricular ectopics and tachycardia. Magnesium deficiency also causes cardiac failure in children.[2] Ventricular arrhythmia in idiopathic cardiomyopathy may at times respond to magnesium supplementation.

Zinc is another antioxidant and its deficiency causes apoptosis of the cardiomyocytes. Many cardiac medications like ACE-inhibitors and thiazide group of diuretics also increase urinary loss of zinc.

Selenium is a trace element found in small quantities in the soil. Food grown in certain parts of the world may have poor concentrations of selenium due to low content in soil. Meat and seafood have the greatest concentrations of selenium. Selenium supplementation stops the progression of the cardiac disease but does not reverse the damage. Selenium deficiency in developed nations is seen more often in the chronically ill, malnourished patients with malabsorption and those on un-supplemented total parenteral nutrition. Selenium (Se) deficiency also is encountered when nutrient-limited diets are used for patients with phenylketonuria and refractory epilepsy (ketogenic diet).

Vitamin B1 (Thiamine) is a co-enzyme for decarboxylation in the carbohydrate metabolism. Deficiency of thiamine causes high-output cardiac failure due to accumulation of lactate and pyruvate that causes

severe vasodilation. The response to thiamine therapy is rapid and complete with no residual damage to the heart.

Vitamin B6, B12 and folate are necessary for the conversion of homocysteine to methionine and hence a deficiency of both would predispose to an early coronary artery disease (CAD). A hyperhomocysteinemia state promotes early atherosclerosis and causes ischemic attacks by various mechanisms and is best avoided by vitamin B supplementation.

Association of vitamin C deficiency with heart disease in children is unknown, but it helps significantly in those with hypertension due to its action on the cardiac vasculature as shown by multiple studies in adults. Vitamin C also enhances the benefit of vitamin E especially in those children undergoing cardiac transplant.[1]

Co-enzyme Q10 is an endogenous fat-soluble quinolone and an antioxidant with membrane stabilizing properties which is found in the mitochondria of myocardium, liver and kidney.

Carnitine helps in improving muscle metabolism due to its action on Kreb's cycle and is a very useful supplementation in patients with cardiomyopathy, cardiac surgery and even myocardial infarction.

Congestive heart failure (CHF) is a systemic illness as there is chronic neurohormonal activation. Environmental factors (e.g. reduced sunlight exposure and dietary $Ca^{2+}$/ intake) and the treatment with diuretics and ACE-inhibitors also play an important role in this condition as previously mentioned.[1,3] Disturbances in minerals and micronutrients are an integral feature of any paediatric illness and are likely to contribute to its progressive nature.

In recognizing the importance of a dyshomeostasis in $Ca^{2+}$, $Mg^{2+}$, vitamins D and $B_1$, Zn and Se in CHF, its prevention and management will need to be addressed in everyday practice.[2] Thus, patients with CHF need daily nutrient supplement in addition to their habitual diet.[11]

## Diphtheria

Diphtheria is a toxin-mediated disease caused by Corynebacterium diphtheriae. The incidence of diphtheria has greatly reduced following introduction of vaccine in the early twentieth century, though outbreaks have been reported.

The manifestations of C. diphtheriae infection are influenced by the anatomic site of infection, the immune status of the host and the production and systemic distribution of toxin. Initial infection usually is localized and is categorized by the site of involvement.

Toxic cardiomyopathy occurs in 10%–25% of patients with respiratory diphtheria and is responsible for 50%–60% of deaths. The cardiac toxicity occurs usually during the 2nd and 3rd weeks of illness as the pharyngeal disease improves (it is a poor prognostic sign if it occurs early) or insidiously as late as in the 6th week. Tachycardia disproportionate to fever, conduction disturbances, dilated and hypertrophic cardiomyopathy, cardiac arrhythmias and heart failure are the complications noted. Temporary transvenous pacing may improve the outcome.[12]

Treatment goals focus on critical care needs and complications of the disease. Mechanical ventilation may be inevitable because of the combination of airway obstruction by the diphtheritic membrane and associated peripharyngeal oedema.

Specific antitoxin is the mainstay of therapy and should be administered early based on clinical diagnosis. Antitoxin is administered as a single empirical dose of 20,000–100,000 units based on the degree of toxicity, site and size of the membrane and duration of illness.

The role of antimicrobial therapy is to halt toxin production, treat localized infection and prevent transmission of the organism to contacts. Erythromycin and penicillin are the drugs of choice.

## Scorpion sting envenomation

Scorpion sting is an acute, life-threatening, rural emergency. The case fatality rates range from 3%- 22% in children hospitalized for scorpion sting in India, Saudi Arabia and South Africa. There are over 80 species of scorpions in India, of which only two are of medical importance. Cardiovascular effects are particularly prominent following the stings by the species called Mesobuthustamulus (Indian red scorpion). Scorpion stings are most often accidental and may be total, partial or non-existent, depending on the envenomation by the scorpion. The venom contains various amino acids, serotonin, hyaluronidase and other enzymes. The toxin acts by opening sodium channels and inhibiting calcium dependent potassium channels, thus causing an autonomic storm that presents as vomiting, excessive salivation, sweating, hypertension, tachycardia, cold extremities, myocardial dysfunction and pulmonary edema.[13]

Severe vasoconstriction occurs due to the catecholamine surge and accumulation of endothelins. Hypertensive stress leading to myocyte toxicity and LV

failure and arrhythmias is common in children. Hypotension and bradycardia may be seen in the first 1-2 hours of sting due to cholinergic stimulation, but bradycardia with hypertension beyond 4 hours of the sting suggests severe LV dysfunction. The level of toxicity depends on the species and the dosage of venom to weight ratio. Symptoms are most severe within 4-5 hours after the sting and subside within 1-2 days. Pulmonary edema may occur within half hour after the sting and can present as tachypnea and refractory cough in pale – looking children with respiratory distress.[14] At times, this can occur even when the child seems to be recovering and hence a periodic, thorough clinical examination is important in such cases. X-ray chest shows pulmonary vascular congestion with a normal cardiac silhouette and inter-lobar effusions. Echocardiography mostly shows LV systolic dysfunction but LV dilation or regional wall motion abnormalities are rare.

Prazosin forms the main stay of therapy and acts by activating the venom-inhibited potassium channels causing a decrease in the preload, after load and blood pressure. It is also a phospho-diesterase inhibitor and prevents myocardial injury. Pediatric dosage is 30 microgram/kg/dose in all with an autonomic storm, given as an emergency drug through naso-gastric tube in cases of severe vomiting. Blood pressure, pulse rate and respiration must be monitored every 30 minutes for 3 hours, every hour for next 6 hours and later every 4 hours till improvement. A repeat dose of prazosin can be given at the end of 3 hours according to clinical response and later every 6 hours till extremities are warm, dry and peripheral veins are seen easily. Diazepam is often used to keep the child calm and some may require NSAIDS for pain management. In case of pulmonary edema, diuretics forms the main stay of therapy to decrease the fluid load along with dobutamine and sodium nitroprusside or nitroglycerine.[13] Scorpion anti-venom if available should be given within 30 minutes of the sting for optimal effect.

## Drugs causing cardiotoxicity

There are multiple drugs that are used for therapy in children and there has always been a pursuit of initiatives to improve their safety profile. Chemotherapy for pediatric malignancies have greatly enhanced survival rates in childhood cancers since over 4 decades now, but this has an associated increase in the long-term side-effects of these very drugs. Anthracyclines form the mainstay therapy in most childhood cancers (hematological and solid tumors). The common ones are doxorubicin, daunorubicin and epirubicin, but the mechanism by which they cause cardiac damage is still unclear. The risk factors that have been identified most certainly are higher cumulative dose and younger age.[15] The acute manifestations are hypotension and arrhythmias, which are usually benign and resolve spontaneously. The chronic effects are postulated to cause decrease in cardiac tissue (especially left ventricular wall thickness) that causes cardiac dysfunction and cardiac failure. There are multiple studies that show subclinical cardiotoxicity in children treated with anthracyclines ranging from 0%-57%. Though congestive cardiac failure can occur at any dose, the risk increases substantially if the cumulative dose is more than 300mg/m2 and if the duration of therapy has been longer.[16] Several studies have also shown a four times female preponderance in developing cardiotoxicity following anthracycline therapy and Lip Shultz et al have attributed this to "differences in oxidative stress, differential expression of multi-drug resistance gene and body composition".[17]

The other drugs with known cardiac side-effects in paediatric population are cisplatin, cytarabine, cyclophosphomide, ifosfamide and rare ones such as fluorouracil, amsacrine and tyrosine kinase inhibitors. Most case reports mention arrhythmias as the commonest side-effect of cisplatin as it decreases the levels of calcium and magnesium in blood and other rarer ones such as myocardial infarction and cerebral vascular accidents. Cytarabine affects the pericardium mainly, especially in higher doses. Cyclophosphomide therapy may be severely toxic in high doses in older patients and cause congestive cardiac failure or myocarditis usually by 2 weeks of therapy.

Radiation (especially to the mediastinum) causes pericarditis, cardiomyopathy, valvulitis, arrhythmias and coronary artery disease. Clinical presentation of pericarditis in such cases may be silent or occur with pleuritic chest pain, friction rub and dyspnea. Cardiomyopathy following thoracic radiation may be dilated, restrictive or hypertrophic with effect on diastolic function more often than systolic. Mitral and aortic valvulitis is generally seen with fibrosis but with or without calcifications. Radiation induced cardiovascular damage depends on multiple factors like duration after completion of therapy (longer the duration, more is the likelihood), volume of the heart exposed, younger age, techniques and dosage. A baseline echocardiography prior to radiation therapy is mandatory to rule out effusion due to the malignancy itself. Most studies have shown that limiting the radiation dosage to less than 25 gray does significantly decrease the risk of cardiotoxicity in children.

Most protocols now recommend two-dimensional echocardiography (2D echo) prior to and after 3 weeks of chemotherapy or radiation therapy in all cases of pediatric cancers specially with a hemoglobin of over 9g/dl and normothermia.[15] Children on anthracycline and mediastinal radiation should have an ECG, echocardiogram and radionuclide angiocardiography (at some centers) prior to start of therapy and also monitor lipid profile, family history for early coronary disease, blood pressure, fasting glucose levels and physical activity levels on a long-term basis.

## Conclusion

A wide variety of systemic conditions may affect the heart by various mechanisms like increasing metabolic demand on the heart, causing arrhythmias, affecting chambers (size and function) and layers of the heart. The true prevalence and clinical importance of cardiac abnormalities in most systemic conditions, both at the time of presentation and during evolution of the disease is difficult to comprehend from the existing literature data.

Echocardiography is the best non-invasive modality giving reliable details of cardiac involvement and is easily available and reproducible. In children, because of a narrow window of opportunity, most clinicians complement clinical assessment with point-of-care echocardiogram to detect subclinical heart involvement in these conditions to tailor the management and support the heart through the illness.

## Points to Remember

- ***Heart is affected in most systemic conditions of childhood.***
- ***Hypothyroidism in addition to direct effect on heart, affects it indirectly by causing hyperlipidemia and atherosclerosis.***
- ***Selective deficiency of thiamine, selenium and calcium can lead to cardiac failure***
- ***Cardiac involvement in diphtheria during the second and third week of illness is responsible for 50%-60% of deaths.***
- ***Scorpion sting causes cardiac toxicity due to catecholamine surge.***
- ***Commonest drugs causing cardiac toxicity are anthracyclines and other anti metabolites.***
- ***A high index of clinical suspicion and timely evaluation to diagnose the underlying cardiovascular involvement is advised to reduce the morbidity and mortality.***
- ***Echocardiogram is a non-invasive modality that can aid in detection of subclinical cardiac involvement in appropriate situations.***

## References


1. Alsafwah S, LaGuardia SP, Arroyo M, Dockery BK, Bhattacharya SK, Ahokas RA, et al. Congestive Heart Failure is a Systemic Illness: A Role for Minerals and Micronutrients. Clin Med Res 2007; 5:238-243.
2. Witte/ KK, Clark AL. Chronic heart failure and multiple micronutrient supplementation: realistic hope or idealistic conjecture?/ Heart Fail Monit 2005; 4:123–129.
3. Klein I, Danzi S. Thyroid disease and the heart. Circulation 2007; 116:1725-1735 .
4. Crowley WF Jr, Ridgway EC, Bough EW, Francis GS, Daniels GH, Kourides IA, et al. Noninvasive evaluation of cardiac function in hypothyroidism. Response to gradual thyroxine replacement. N Engl J Med 1977; 296:1-6.
5. Kabadi UM, Kumar SP. Pericardial effusion in primary hypothyroidism. Am Heart J 1990; 120:1393-1395.
6. Fredlund BO, Olsson SB. Long QT interval and ventricular tachycardia of "torsade de pointe" type in hypothyroidism. Acta Med Scand 1983; 213:231-235.
7. Klein I, Danzi S. Thyroid disease and the heart. Circulation. 2007; 116:1725–1735.
8. Patil VC, Patil HV, Agrawal V, Patil S. Cardiac tamponade in a patient with primary hypothyroidism. Indian J Endocrinol Metab 2011; 15(Suppl2):S144–S146.
9. Martins D, Wolf M, Pan D, Zadshir A, Tareen N, Thadhani R, et al. Prevalence of cardiovascular risk factors and the serum levels of 25-hydroxyvitamin D in the United States: data from the Third National Health and Nutrition Examination Survey. Arch Intern Med 2007; 167:1159–1165.
10. Mheid Al, Patel RS, Tangpricha V, Quyyumi AA. Vitamin D and cardiovascular disease: is the evidence solid? Eur Heart J 2013; 34(48):3691–3698.
11. Norman PE, Powell JT. Vitamin D and cardiovascular disease. Circ Res 2014; 114(2):pp379–393.
12. Lakkireddy DR, Kondur AK, Chediak EJ, Nair CK, Khan IA. Cardiac troponin I release in non-ischemic reversible myocardial injury from acute diphtheric myocarditis./ Int J Cardiol/ 2005; 98/ (2): 351–354./
13. Maheshwari M, Tanwar CP. Scorpion Bite Induced Myocardial Damage and Pulmonary Edema. Heart Views 2012; 13(1):16–18.
14. Bahloul M, Kallel H, Rekik N, Ben Hamida C, Chelly H, Bouaziz M. Cardiovascular dysfunction following severe scorpion envenomation. Mechanisms and physiopathology. Presse Med 2005; 34(2):115-120.

15. De Caro E, Smeraldi A, Trocchio G, Calevo M, Hanau G, Pongiglione G. Subclinical cardiac dysfunction and exercise performance in childhood cancer survivors. Pediatr Blood Cancer 2011; 56(1):pp122–126.
16. Fulbright JM, Huh W, Anderson P, Chandra J. Can anthracycline therapy for pediatric malignancies be less cardiotoxic? Curr Oncol Rep 2010; 12(6): pp411–419.
17. Lipshultz SE, Lipsitz SR, Mone SM, Goorin AM, Sallan SE, Sanders SP, et al. Female sex and higher drug dose as risk factors for late cardiotoxic effects of doxorubicin therapy for childhood cancer. New Eng J Med 1995; 332(26):1738-1744.

## CLIPPINGS

**Frequency of Evidence-Based Screening for Retinopathy in Type 1 Diabetes.**

In patients who have had type 1 diabetes for 5 years, current recommendations regarding screening for diabetic retinopathy include annual dilated retinal examinations to detect proliferative retinopathy or clinically significant macular edema, both of which require timely intervention to preserve vision. During 30 years of the Diabetes Control and Complications Trial (DCCT) and its longitudinal follow-up Epidemiology of Diabetes Interventions and Complications (EDIC) study, retinal photography was performed at intervals of 6 months to 4 years.

The researchers used retinal photographs from the DCCT/EDIC study to develop a rational screening frequency for retinopathy. Markov modeling was used to determine the likelihood of progression to proliferative diabetic retinopathy or clinically significant macular edema in patients with various initial retinopathy levels (no retinopathy or mild, moderate, or severe nonproliferative diabetic retinopathy). The models included recognized risk factors for progression of retinopathy.

Overall, the probability of progression to proliferative diabetic retinopathy or clinically significant macular edema was limited to approximately 5% between retinal screening examinations at 4 years among patients who had no retinopathy, 3 years among those with mild retinopathy, 6 months among those with moderate retinopathy, and 3 months among those with severe nonproliferative diabetic retinopathy. The risk of progression was also closely related to mean glycated hemoglobin levels. The risk of progression from no retinopathy to proliferative diabetic retinopathy or clinically significant macular edema was 1.0% over 5 years among patients with a glycated hemoglobin level of 6%, as compared with 4.3% over 3 years among patients with a glycated hemoglobin level of 10%. Over a 20-year period, the frequency of eye examinations was 58% lower with our practical, evidence-based schedule than with routine annual examinations, which resulted in substantial cost savings.

***The DCCT/EDIC Research Group. Frequency of Evidence-Based Screening for Retinopathy in Type 1 Diabetes. N Engl J Med 2017; 376:1507-1516.***

## NEWS AND NOTES

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**CARDIOLOGY**

# PEDIATRIC PULMONARY HYPERTENSION - RECENT MANAGEMENT GUIDELINES

***Rani Gera**
****Smita Ramachandran**

**Abstract:** *Pediatric pulmonary hypertension(PH) is being diagnosed increasingly due to improved recognition and increased survival of sick children. Pulmonary hypertension is defined as a mean pulmonary arterial pressure greater than 25 mmHg at rest. Though there is improved understanding of pediatric PH management remains challenging. Echocardiography is the noninvasive investigation of choice for initial screening while cardiac catheterisation should be performed at diagnosis before initiation of PH directed therapy, except in critically ill children. The response to treatment in PH is variable in children and hence requires constant monitoring to titrate the treatment to the response.*

**Keywords:** *Pediatric pulmonary hypertension, Guidelines, Newer therapies*

Pulmonary hypertension (PH) is defined as mean pulmonary artery pressure (mPAP) > 25 mm Hg in children above 3 months of age at sea level. The other defining criteria of PH are given in Box 1.[1] PH in children have been associated with considerable morbidity and mortality, however with early interventional strategies, better and timely treatment the outcomes are gradually improving.[1] There are many differences in the associations and outcome in pediatric PH compared to adult PH. In children it is associated with lung growth and development, including many prenatal and early postnatal influences.[2]

**Box 1. PH definition[1]**

PH: mPAP >25 mmHg in children >3 mo of age at sea level

PAH: mPAP >25 mmHg PAWP 2 WU/m2

IPAH or isolated PAH: PAH with no underlying disease known to be associated with PAH Referred to as HPAH with positive family or genetic evaluation

PHVD: Broad category that includes forms of PAH but includes subjects with elevated TPG (mPAP–left atrial pressure or PAWP >6 mmHg) or high PVRI as observed in patients with cavopulmonary anastomoses without high mPAP

*IPAH, idiopathic pulmonary artery hypertension; mPAP, mean pulmonary artery pressure; PAH, pulmonary artery hypertension; PAWP, pulmonary artery wedge pressure; PH, pulmonary hypertension; PHVD pulmonary hypertensive vascular disease; PVRI, pulmonary vascular resistance index; and TPG, transpulmonary pressure gradient.*

**Causes[3]**

a) Neonatal: Persistent pulmonary hypertension (PPHN), bronchopulmonary dysplasia, infections, congenital diaphragmatic hernia

b) Cardiac: Left to right shunts, transposition of great vessels, obstructive lesions

c) Acquired: Chronic hypoxia (cystic fibrosis), scoliosis, vasculitis, airway obstruction

d) Idiopathic: Familial, sporadic

## Clinical presentation

Children with PH most commonly present with cyanosis but may manifest with subtle features even in the advanced stage. If IPAH is untreated, the most common presenting symptom is breathlessness and children frequently present with poor appetite, faltering growth, lethargy, tachypnea, tachycardia and irritability.[3,4] Usual clinical signs are clubbing, cardiomegaly, engorged neck veins and accentuated pulmonary second sound. The severity of symptoms determines the prognosis. WHO classification of PH is given in Box 2.

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**Box 2. WHO Classification of pulmonary hypertension (PH)[1]**

**1) PAH**

a) Idiopathic

b) Heritable: BMPR2, ALK1, ENG, SMAD9, CAV1, KCNK3

c) Drug and toxin induced

d) Pulmonary arterial hypertension associated with other disease (APAH): Connective tissue disorder, HIV infection, portal hypertension, CHD, Schistosomiasis

e) Pulmonary veno-occlusive disease (PVOD) and or pulmonary capillary hemangiomatosis (PCH)

**2. PH due to left-sided heart disease**: LV systolic dysfunction, LV diastolic dysfunction, valvular disease, congenital/acquired left heart inflow/outflow tract obstruction and congenital cardiomyopathy

3**. PH caused by lung disease or hypoxemia:** Chronic obstructive pulmonary disease, interstitial lung disease, other pulmonary diseases with mixed restrictive and obstructive pattern, sleep-disordered breathing, alveolar hypoventilation syndromes, long-term exposure to high altitudes, developmental lung diseases

**4. Chronic thromboembolic disease**

**5. PH with unclear or multifactorial mechanisms**

- Hematological disorders: Chronic hemolytic anemia, myeloproliferative disorders, splenectomy
- Systemic disorders: Sarcoidosis, pulmonary histiocytosis, lymphangioleiomyomatosis
- Metabolic disorders: Glycogen storage disease, Gaucher disease, thyroid disorders
- Others: Tumor obstruction, fibrosing mediastinitis, chronic renal failure, segmental PH

## Investigations and diagnosis

A complete and early diagnosis is imperative for the management of PH as severity is inversely proportional to recovery. The investigations recommended by the consensus statement on the management of pulmonary hypertension are as follows:

1. General laboratory work: Complete blood count, platelet count, urinalysis, electrolytes, BUN, creatinine, Brain natriuretic peptide or N-terminal pro b-type natriuretic peptide *(NT-proBNP)*, uric acid
2. Respiratory studies: Arterial blood gas, chest x-ray, chest CT, pulmonary function tests, ventilation/ perfusion scan, polysomnography
3. Coagulation studies: Factor VIII; factors II, V and VII; factor V Leiden, lupus anticoagulant protein C, protein S, b-2 glycoprotein antibodies, cardiolipin IgG, IgM antibody, antithrombin III mutation, platelet function assay
4. Portal hypertension: Liver function panel, hepatitis screen, abdominal/liver ultrasound
5. Thyroid panel (TSH, free T4, total T4), CTD
6. ESR/CRP, ANA, anti-DNA, anti-cardiolipin antibodies, CH50 complement (C3, C4), ANCA, rheumatoid factor
7. HIV testing, toxins, drugs

## Specific tests

The noninvasive test of choice for initial screening for PH is echocardiography. Echo is useful not only for identifying potential causes of PH but also for evaluating RV function and assessing related comorbidities. Serial echocardiograms should be performed especially in the setting of changes in therapy or clinical condition.

Cardiac catheterization is recommended before initiation of PAH-targeted therapy cexcept in ritically ill patients requiring immediate initiation of empirical therapy. Cardiac catheterization should include acute vasoreactivity testing (AVT) unless there is a specific contraindication. AVT in children is undertaken to assess the response of the pulmonary vascular bed to pulmonary-specific vasodilators.

The minimal hemodynamic change that defines a positive response to AVT for children should be considered as a ≥20% decrease in PAP and PVR/SVR without a decrease in cardiac output. In children with IPAH or familial PAH (isolated PVHD), the result is used to define the likelihood of response to long-term treatment with CCB therapy and for prognosis.

## Treatment[6]

Management of PH in infants with BPD begins with aggressively treating the underlying lung disease.

1. Screening for PH by echocardiogram is recommended in infants with established BPD.
2. Evaluation and treatment of lung disease, including assessments for hypoxemia, aspiration, structural airway disease and the need for changes in respiratory support, are recommended in infants with BPD and PH before initiation of PAH-targeted therapy.
3. Evaluation for long-term therapy for PH in infants with BPD should follow recommendations for all children with PH and include cardiac catheterization to diagnose disease severity and potential contributing factors such as LV diastolic dysfunction, anatomic shunts, pulmonary vein stenosis and systemic collaterals.
4. Supplemental oxygen therapy is reasonable to avoid episodic or sustained hypoxemia and with the goal of maintaining $O_2$ saturations between 92% and 95% in patients with established BPD and PH.
5. PAH-targeted therapy can be useful for infants with BPD and PH on optimal treatment of underlying respiratory and cardiac disease.
6. Treatment with inhaled nitrous oxide (iNO) can be effective for infants with established BPD and symptomatic PH.
7. Serial echocardiograms are recommended to monitor the response to PAH-targeted therapy in infants with BPD and PH.

Inhalational nitric oxide (NO) is the first line of treatment for children with PH in intensive care units, PPHN (persistent pulmonary hypertension) of newborns and also for post operative cases.[7] It causes rapid fall in the pressures in pulmonary artery via the stimulation of guanylyl cyclase and hence increased production of cyclic guanylate monophosphate (cGMP) in pulmonary smooth muscle cells. It has also been seen to reduce the requirement of ECMO on early institution in neonates.[8]

The response to treatment in PH is variable in children and hence require constant monitoring to titrate the treatment to the response[5] and early institution of pharmacotherapy reduces the need for transplantation.[9]

## Calcium channel blockers (CCB)

CCBs should be given only to those patients who are reactive as assessed by acute vasoreactivity test (AVT) and are >1 year of age and are contraindicated in children who have not undergone or are nonresponsive to AVT and in patients with right-sided heart dysfunction because of the potential for negative inotropic effects of CCB therapy.[1] Nifedipine and amlodipine are the commonly used CCBs.

## Phospodiesterase inhibitors

Sildenafil is the most potent agent and acts by selectively inhibiting phosphodiesterase V.[10] American heart association (AHA) recommends its use in children with low risk for PH[1] along with endothelial receptor anatagonists.[1] Recent research has suggested that another PDE type 5 inhibitor,vardenafil, may be more effective than sildenafil, however these are in vitro studies.[11]

## Prostacyclin inhibitors

Intravenous and subcutaneous PGI2 or its analogs should be initiated without delay for patients with higher-risk PAH.[1] It acts by reducing PVR, inhibiting platelet aggregation, and reducing smooth muscle cell proliferation. The intravenously used agents are epoprostenol, treprostinil; inhalation agent is iloprost and oral is beraprost.

## Anticoagulation (AHA recommendations)[1]

1. Anticoagulation with warfarin may be considered in patients with IPAH/HPAH, patients with low cardiac output, those with long-term indwelling catheters and those with hypercoagulable state.
2. Targeting the therapeutic range for international normalized ratio between 1.5 and 2.0 is recommended for young children with PAH.
3. Anticoagulation should not be used in young children with PAH because of concerns for harm from hemorrhagic complications.

## Combination therapies

Combination therapies are used primarily in adults. They can be added as combination or as add on therapy but are still in research stages in children.[1]

## Newer therapies

Some novel agents which can improve useful in future are[12,13,14]

1. Rho-kinase inhibitors: Current evidence states that activation of the small GTPase RhoA and its downstream effector Rho – associated kinase (ROCK) are important in the pathogenesis of PH.
2. Vasoactive intestinal peptides
3. Estradiol derivatives
4. Apoptosis and gene therapy

## Follow up

After initiation of treatment child should be followed up properly and a cardiac catheterization is recommended within 3 to 12 months after the initiation of therapy to evaluate response or with clinical worsening. The six minute walk distance (6MWD) should be used to follow exercise tolerance in pediatric PH patients of appropriate age during follow up. MRI can be useful not only as part of the diagnostic evaluation but also during follow-up to assess changes in ventricular function and chamber dimensions.

## Conclusion

Advances in the pharmacological therapies have improved the outcome in pediatric PH but early diagnosis and institution of therapy is the key to modify the disease process. It also requires drug titration in the pediatric population as compared to the adults. Novel therapies under investigation may prove to be fruitful in future.

## Points to Remember

- ***Pulmonary hypertension in infants and children though rare is associated with significant morbidity and mortality.***
- ***Targeted pulmonary vasodilator therapies have demonstrated hemodynamic and functional improvement in children.***
- ***Management of pediatric PAH remains challenging as treatment decision are based mainly on results from evidence-based adult studies.***

## Reference


1. Abman SH, Hansmann G, Archer SL, Ivy DD, Adatia I, Chung WK, et al. Pediatric Pulmonary Hypertension: Guidelines From the American Heart Association and American Thoracic Society. Circulation 2015; 132:2037-2099.
2. Abman SH, Raj U. Towards improving the care of children with pulmonary hypertension: the rationale for developing a Pediatric Pulmonary Hypertension Network. Prog Pediatr Cardiol 2009; 27:3–6. doi: 10.1016/j.ppedcard.2009.09.002.
3. Hawkins A, Tulloh R. Treatment of pediatric pulmonary hypertension. Vasc Health Risk Manag 2009; 5:509-524.
4. Tulloh R. Congenital heart disease in relation to pulmonary hypertension in paediatric practice. Paediatr Respir Rev 2005; 6:174-180.
5. Andrews R. Pulmonary hypertension in pediatrics. Curr Opin Ped 2002; 14:603-605.
6. National Pulmonary Hypertension Centres of the UK and Ireland Consensus statement on the management of pulmonary hypertension in clinical practice in the UK and Ireland. Thorax 2008; 63:ii1–ii41.
7. Davidson D, Barefield ES, Kattwinkel J, Dudell G, Damask M, Straube R, et al. Inhaled nitric oxide for the early treatment of persistent pulmonary hypertension of the term newborn: a randomized, double-masked, placebo-controlled, dose-response, multicenter study. The I-NO/PPHN Study Group Pediatrics 1998; 101 (3 Pt 1): 325–334.
8. Ortitz RM. Extracorporeal membrane oxygenation in pediatric respiratory failure. Pediatr Clin North Am 1987; 34(1):39–46.
9. Adriaenssens T. Advanced therapy may delay the need for transplantation in patients with the Eisenmenger syndrome. Eur Heart J 2006; 27(12):1472–1477.
10. Reffelmann T. Therapeutic potential of phosphodiesterase inhibition for cardiovascular disease. Circulation 2003; 108(2):239–244.
11. Toque HA. Vardenafil, but not sildenafil or tadalafil, has calcium-channel blocking activity in rabbit isolated pulmonary artery and human washed platelets. Br J Pharmacol 2008; 154(4):787–796.
12. Fukumoto Y, Matoba T, Ito A, Tanaka H, Kishi T, Hayashidani S, et al. Acute vasodilator effects of a Rho-kinase inhibitor, fasudil, in patients with severe pulmonary hypertension. Heart 2005; 91(3):391–392.
13. Tofovic SP. 2-Ethoxyestradiol is antimitogenic and attenuates monocrotaline-induced pulmonary hypertension and vascular remodeling. Vascul Pharmacol 2008; 48: 4–6.
14. Altieri DC. Survivin and apoptosis control. Adv Cancer Res. 2003; 88:31–52.


## NEWS AND NOTES

**KUDANTHAI NEOCON 2017**

**XIV ANNUAL CONVENTION OF NATIONAL NEONATILOGY FORUM, TAMIL NADU CHAPTER**

**Venue:** Hotel Paradise Resort, Thanjavur Main Road, Kumbakonam, **Dates: 6th, 7th and 8th October, 2017**

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GENERAL ARTICLE

# DISASTER RELATED INJURIES - PEDIATRIC PERSPECTIVE

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**Shilpa C

**Abstract:** *India has long been susceptible to natural disasters because of its distinctive geographic and climatic conditions. Added to this, the changing demography, increasing urbanization, depletion and destruction of environmental resources, pollution, epidemics and pandemic have all intensified disaster risks. Disaster exposure involves not just personal injury but also loss and adversity leading to impact on whole communities with the pediatric population being the most vulnerable. However data available on the management and helping the kids cope with disaster are meager. This article deals with the short and long term consequences of disaster related illnesses, injury and perceived needs of care especially among pediatric population and management of crush injuries.*

**Keywords:** *Disaster, Injuries, Post traumatic stress, Crush injuries.*

Disaster is derived from Latin which means “ill started”. A disaster is defined as any catastrophic event that has an unexpected abrupt onset affecting the lives of many. Mcfarlane and Norris (2006) categorized disasters as events that are powerful to impact and upset the daily life of an individual.[1] These happenings left people to be faced with damage to life or harm physical and mental wellbeing. Earthquakes, floods, cyclones, hurricanes, bombings are a few examples of major natural and manmade disasters causing great havoc on human lives.[1]

## Epidemiology

India is susceptible to natural disasters because of its distinctive geographic and climatic conditions. To add to this and make worse the changing demography, increasing urbanization, depletion and destruction of environmental resources, pollution, epidemics and pandemics have intensified disaster risks. Nearly 68% of the total landmass is liable to drought, 60% to earthquakes of various intensities, 12% to flood and river erosions and 8% to cyclones.[2] These events threaten the country’s economic growth and manpower. However, it has been difficult to quantify the burden of disaster related injuries amongst children due to the absence of clear age cut offs and injury classification for pediatric patients.[3]

Pediatric population are more vulnerable in disaster as they have special needs. They require help from adults to be supervised, fed and protected from harmful exposures. They are prone to rapid spread of infections and toxins. The ongoing process of growth and development also pose challenges in providing healthcare. There is a need for pediatric care providers and specialists along with the availability of pediatric equipments and medicines.

## Consequences of disaster

Disasters may result in a wide array of consequences. They range from physical events like physical injury, risk to life, mental health sequelae like sadness, grief, major depression, anxiety and post traumatic stress disorder, social issues like being rendered homeless, difficulties in seeking medical aid and transportation. Norris and Wind categorized the consequences of disasters into 4 major groups[1] (Box 1).

**Box 1. Disaster consequences**

1. Traumatic stressors - Comprise of dangers to life, witnessing aversive, ugly and shocking scenes
2. Loss - Bereavement (experiencing extreme despair and agony due to the death of a loved one during the event). Loss due to animate or inanimate objects
3. Ongoing adversities - Lack of shelter, food and safe drinking water.
4. Community effects - Disaster exposure involves not just personal injury but create the potential for community-wide economic, environmental, governmental, social and cultural disruptions that can influence mental health

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## Classification of injuries

Maintenance of accurate records of types of injuries following disasters is crucial for epidemiological purposes as well as planning of intervention programs.[4] Despite the fact of injury registries exist there are many lacunae for e.g. no uniform injury classification system, no clear age cut offs for pediatric population leading to challenges in categorizing the types of disasters as well as evaluation of pediatric injury patterns.

First challenge is absence of an upper age limit ~~of~~ for pediatric patients. While some studies consider less than 14 years as a child others consider it as less than 18 years. Second challenge is the substantial dissimilarity in classifying pediatric injuries. The other challenges include marked scarcity in reporting data related to pediatric traumatic injuries and no availability of comprehensive data registries following large scale mishaps.[3-5]

Jacquet GA, et al[3] in their systemic review on earthquake related injuries in children classified and summarized the injuries as follows: 1) based on injury type-fractures (18.1% to 55.2%), soft tissue injuries (7.6% to 70.2%) and crush injuries **(**6.3% to 18.7%) with special mention made to the secondary consequences of renal failure and the need for dialysis and 2) based on location - fracture of extremities (17.1% to 60.8%), head trauma (3.2% to 61%) and spinal trauma - 4.9% to 31.1%. Sever MS et al in their review on incidence of crush syndrome in the Gujarat earthquake that happened in 2001, of the 20,023 deaths that occurred, 33 of the 35 who had crush injuries required dialysis.[6]

The other disaster related illness include a) psychological impact: Fear is a normal reaction to danger. A child may be afraid of recurrence, injury, or death after an earthquake/disaster. They may fear being separated from their family or being left alone. Children may even interpret disasters as punishment for real or imagined misdeeds, b) Indirect injuries and c) complications of injury such as wound infections.

## Types of disaster

The list of major natural disasters and the common co-occurring injuries are as follows

**Earthquakes:** Sudden release of energy in the earth's crusts creates seismic waves that result in earthquakes. Injuries occurring during earthquakes are many, with crush injuries being the most common. The extent of injuries is severe amongst individuals staying in and around the epicenter during an earthquake or indoors and also in those who are inside buildings (residential or commercial). If the incident occurs at night, injuries will be concentrated on pelvis, chest and legs since victims will be lying down. On the other hand if earthquakes occur during daytime, the hospital is likely to see victims with head trauma and lacerations. Earthquakes not only causes fatal and non-fatal injuries but also deleterious effects on infrastructure, communication and transportation.[2,5,6,7,8]

**Tsunamis:** It is defined as a "large harbour wave" in Japanese. It is due to sudden vertical displacement of water .Aquatic earthquakes, volcanoes, landslides may also result in tsunamis. Extensive destruction and large number of deaths as a consequence follows high impact tsunamis with children being most susceptible to injuries. A large majority of deaths are attributed to drowning.[9, 10]

**Flood:** Floods are the leading cause of deaths due to natural disasters. Worldwide Asia is the most affected and India is no exception. Studies report more deaths from floods than all other disasters recorded. To mention a few, victims may suffer from hypothermia, polytrauma from falling debris. Immediate causes of death include drowning, trauma or fatal injuries and over extended time period it is from infectious disease.[11]

**Cyclones:** Cyclones are characterized by inward spiraling winds that rotate about a zone of low pressure. Such storms created over the tropical oceans are known as tropical cyclones. A tropical cyclone usually originates over tropical or sub-tropical waters and rotates clockwise in the southern hemisphere and counter-clockwise in the northern hemisphere. Depending on their location and strength, tropical cyclones are referred to as hurricanes (western Atlantic/eastern Pacific), typhoons (western Pacific), and cyclones (southern Pacific/Indian Ocean).[12,13]

There are many human health impact of cyclones. Death rates are high especially in developing nations and severe injuries among survivors are commonly seen. Type of morbidities include falls, blunt trauma, lacerations, drowning, asphyxiation, isolated bone and soft tissue injury and psychological consequences like continued suffering and anguish, depression, post traumatic stress disorder and psychiatric sequel. After the cyclone there may be outbreaks of infectious diseases. There will be loss of routine hygiene, sanitation, shelter and belongings with detrimental effects on heath care system and infrastructure noted.

**Hurricanes:** Not only the rising storm during hurricane but also the winds accompanying them can prove deadly. They cause large objects to fly making structures to collapse resulting in crush injuries and lacerations. Additional

preparedness in the form of improvements in forecasting, early warning signs, public education on safety measures, early evacuation and shelter measures could reduce cyclone and hurricane related morbidity and mortality.[13,14]

**Tornadoes:** A tornado is a narrow, violently rotating column of air that extends from the base of a thunderstorm to the ground. Because wind is invisible, it is hard to see a tornado unless it forms a condensation funnel made up of water droplets, dust and debris. Tornadoes are the most violent of all atmospheric storms. If the victim is outdoors during a tornado he can sustain abrasions, lacerations due to flying objects set into motion by winds. Bone and soft tissue injuries occur frequently. Chances of occurrence of compound fractures are more. Often the victims end up with crush injuries as they remain indoors within buildings when hit by a tornado as they occur with little or no previous warning.

### Management

Triage: Patients should be categorized by severity of injuries and treatment prioritized in terms of available resources and chances of survival.[15] Airway, breathing and circulation should be assessed. The level of disability should be gauged and a secondary survey done. Patient should be transferred while stable anticipating future needs.[16]

## Prevention of injuries and disabilities

In the repercussions of a disaster, all efforts should be focussed in helping children in a holistic manner with special emphasis on psychosocial support - a humane supportive approach. Following a natural disaster, both the relief workers and the affected population are at risk for external injuries, by the falling debris from the buildings which might have become structurally weaker. Additionally they also are at risk for suicide. In the acute aftermath of a disaster, public authorities need to take proactive lead like ensuring access to healthcare and essential needs like water and food. Following a disaster, attempts must be made to provide psychological first aid by identifying all those children who will be benefitted. To reduce their stress both short term and long term counseling should be enabled. Whenever a child is faced with disaster his/her reaction varies considerably depending upon age, exposure and assistance given by caretakers. On any occasion subjecting them to situations beyond the usual purview of human experience may lead to difficulty in perceiving and coping with the events. This may result in confusion, insecurity and emotional chaos. Children may develop symptoms of stress, grief, depression, anxiety and bereavement. Planning out how to help these children is very crucial. Enabling the children to understand and manage their feeling, teaching them coping techniques and restricting exposure to anxiety producing information are some of the ways to reduce their psychological stress. Long term needs include community based rehabilitation and rebuilding environment safely for future.[17,18]

## Crush syndrome

It is the syndrome of traumatic rhabdomyolysis causing myoglobinuric renal failure, muscle re-perfusion involvement of muscle mass, prolonged compression (usually 4-6 hours) compromised local circulation, release of toxins triggering hypovolemic shock and hyperkalemia.[19] Crush syndrome is very common in earthquake situations and can result in compartment syndrome with loss of limb as well as multi-organ failure and hyperkalemic states. First described in 1941 by Bywaters and Stead in the battle of Britain where in 4 patients with crush injury developed renal failure and died. Myoglobin was first identified as cause of renal failure in 1943. By waters and Stead used a rabbit model to identify myoglobin as a cause of renal failure.[19]

Rhabdomyolysis can occur due to various causes. The cellular injury in rhabdomyolysis occurs due to stretch of sarcolemmal due to compression. This causes influx of sodium, water and calcium across electrochemical gradients resulting in cell swelling and lysis which in turn causes release of toxins (myoglobin, potassium, lactate). In a child with crush syndrome renal function test (electrolytes, BUN and creatinine) and creatine kinase are done to check for renal status, hydration status and status of muscle.

Treatment is by early hydration in rhabdomyolysis. Vigorous hydration with atleast 20ml/kg/hr in children is essential. If urine output <2ml/kg/hr, consider giving mannitol 1g/kg to increase the elimination of myoglobin by the kidney. Early and aggressive hydration may not prevent loss of limbs, but may save kidneys and prevent multi-organ failure. Early fasciotomy to preserve limbs due to elevated compartment pressures and antimicrobial therapy to prevent or treat sepsis is mandatory.[6, 20]

## Complications

Crush injuries can affect the kidneys more than limbs. The common complications are, sepsis, DIC, ARDS, acute renal failure, cardiac arrhythmias, multi organ failure and tetanus.[6,21]

## Points to Remember

- ***Disaster is any catastrophic event either natural or manmade with the potential to affect lives of many.***
- ***Pediatric population being more vulnerable they are required to be supervised by adults.***
- ***The burden of disaster related injuries amongst children is difficult to quantify.***
- ***Disasters may result in a wide array of consequences.***
- ***For any disaster always make a disaster preparedness plan.***
- ***Triage and aggressive initial management could save the lives of many.***
- ***During rehabilitation special emphasis needs to be on psychosocial support.***

## References


1. Norris FH, Sherrieb K, Galea S. Prevalence and Consequences of Disaster-Related Illness and Injury from Hurricane Ike. Rehabil Psychol 2010; 55(3): 221–230.
2. Disaster-preparedness-and-resiliency-India. www.give2asia.org. Accessed on 2nd April 2017.
3. Jacquet GA, Hansoti B, Vu A, Bayram JD. Earthquake-related injuries in the pediatric population: a systematic review. PLoS Curr 2013; 5.
4. Cassidy LD. Pediatric disaster preparedness: the potential role of the trauma registry. J Trauma 2009; 67(2 Suppl):S172-178.
5. Cantor MR, Leaming JM. Evaluation and management of pediatric major trauma. Emergency Medicine Clinics of North America 1998; 16(1):229-256.
6. Sever MS, Vanholder R., Lameire N. Management of crush-related injuries after disasters. N Engl J Med 2006; 354:1052-1063.
7. Dong ZH, Yang ZG, Chen TW, Chu ZG, Deng W, Shao H. Thoracic injuries in earthquake-related versus non-earthquake-related trauma patients: differentiation via Multi-detector Computed Tomography. Clinics 2011; 66(5):817-822.
8. Farfel A , Assa A, Amir I , Bader T, Bartal C , Kreiss Y, et al. Haiti earthquake 2010: a field hospital pediatric perspective. Eur J Pediatr 2011; 170:519–525.
9. McCarty DL. Tsunamis. In: Hogan DE, Burstein JL, editors. Disaster Medicine. Lippincott Williams & Wilkins; Philadelphia 2002; pp229–234.
10. Tsunamis. EM-DAT the International Disaster Database. Available at: http://www.emdat.be/disaster-profiles Accessed on 2nd April, 2017.
11. Doocy S, Daniels A, Murray S, Kirsch TD. The Human Impact of Floods: a Historical Review of Events 1980-2009 and Systematic Literature Review. PLOS Currents Disasters. 2013 Apr 16. Edition 1. doi: 10.1371/currents.dis.f4deb457904936b07c09daa98ee8171a
12. Doocy S, Dick A, Daniels A, Kirsch TD. The Human Impact of Tropical Cyclones: a Historical Review of Events 1980-2009 and Systematic Literature Review. PLOS Currents Disasters. 2013Apr16. Edition1. doi:10.1371/currents.dis. 2664354a5571512063ed29d25 ffbce74.
13. Keim ME. Cyclones, Tsunamis, and Human Health. The Key Role of Preparedness Oceanography 2006; 19(2):40-49.
14. Kim YW, Kim SY, Kim H, Ahn ME. Disaster-Related Injury Management: High Prevalence of Wound Infection After Super Typhoon Haiyan. Disaster Med Public Health Prep 2016; 10:28–33.
15. Xiang B, Cheng W, Liu J, Huang L, Li Y, Liu L. Triage of pediatric injuries after the 2008 Wen-Chuan earthquake in China. J Pediatr Surg. 2009; 44(12):2273-2277.
16. Zhao J, Shi Y, Hu Z, Li H. Sichuan earthquake and emergency relief care for children: report from the firstly arrived pediatricians in the epicenter zone. Pediatr Emerg Care. 2011; 27(1):17-20.
17. Neria Y, Nandi A and. Galea S. Post-traumatic stress disaster following disasters: A systematic review. Psycho Med 2008; 38(4): 467-480.
18. Garfin DR., Silver RC, Gil-Rivas V, Guzmán J , Murphy JM., Cova F, et al .Children's Reactions to the 2010 Chilean Earthquake: The Role of Trauma Exposure, Family Context, and School-Based Mental Health Programming. Psychological Trauma: Theory, Research, Practice, and Policy. 2014, June 2. Advance online publication. http://dx.doi.org/10.1037/a0036584
19. Bywaters EGL. Ischemic muscle necrosis, crushing injury, traumatic edema, crush syndrome, traumatic anuria, compression syndrome; type of injury seen in air raid casualties following burial beneath debris. JAMA 1944; 124:1103–1109.
20. Yokota J. Crush Syndrome in Disaster. Japan Med Assoc J 2005; 48(7):341-352.
21. Afshar M, Raju M, Ansell D, Bleck TP. Narrative review: tetanus-a health threat after natural disasters in developing countries. Ann Intern Med 2011; 154(5):329-335. http://dx.doi.org/10.7326/0003-4819-154-5-201103010-00007

**DRUG PROFILE**

# PHARMACOTHERAPY OF HEART FAILURE

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**Abstract:** *Heart failure in children can have a wide range of etiologies that range from congenital to acquired causes and the presentation also varies in different clinical settings. Most of the guidelines in children are based on adult literature. Safety profile and drug dosages also vary according to the age and underlying pathophysiology. A systematic review of the commonly used drugs in heart failure is given in this article.*

**Keywords**: *Heart failure, Diuretics, Inotropes*

Heart failure (HF) has been defined as an abnormality of cardiac structure or function leading to failure of the heart to deliver oxygen at a rate commensurate with the requirements of the metabolizing tissues, despite normal filling pressures (or only at the expense of increased filling pressures).[1] When the demand is high, as in severe anemia and thyrotoxicosis, high output failure could occur and when the contractility of heart is decreased, low output failure manifests. The treatment of acute heart failure is aimed at decreasing the congestive symptoms with diuretics and increasing the contractility with positive inotropic agents. Pharmacotherapy is required for both the volume overload and pressure overload groups of heart failure but treatment of underlying defect by surgery or device closure is the primary treatment for some of these.

## Drugs used in heart failure

### Cardiac glycosides

Cardiac glycosides are used in the treatment of congestive cardiac failure since early 1785.[2] Digoxin, the only oral inotropic drug, is a digitalis glycoside which inhibits the sodium potassium adenosine triphosphatase (Na-K-ATPase), resulting in increased intracellular calcium levels and thereby inceased cardiac contractility. Inhibition of Na-K-ATPase reduces sympathetic flow from the central nervous system and reduces the renal sodium reabsorption which leads to suppression of renal renin secretion. The vagal tone is increased thereby prolonging the refractory period and slowing conduction through the sinus node and the atrioventricular node.

Role of digoxin in the present day management of heart failure in children is being questioned by many clinicians due to the factors like its narrow therapeutic index, limited published data on efficacy in children and the widespread availability of newer drugs like angiotensin-converting enzyme inhibitors (ACEi) and beta blockers.[3]

Indications: Digoxin is indicated in heart failure associated with reduced systolic function of heart. In most cases of heart failure, digoxin is combined with a diuretic and an angiotensin converting enzyme inhibitor. Its role in heart failure secondary to left to right shunt lesions, where systolic function of the myocardium is preserved, is not well defined. Digoxin is used for slowing ventricular rate in tachyarrhythmias such as supraventricular tachycardia (SVT), atrial flutter and atrial fibrillation (AF).[4,5]

Digoxin is shown to decrease symptoms in patients with heart failure. However, it has not been shown to provide survival benefit in adults or in children. Lower dose may reduce the incidence of side effects and toxicity.[6] In a post hoc analysis of DIG trial, higher serum digoxin levels were associated with increased mortality in men with heart failure.[7] Scant data exist for digoxin therapy in children with heart failure. Utility of digoxin in heart failure secondary to volume overload of the ventricle, as seen in left to right shunt lesions, is less clear, since the myocardial contractility is normal in such cases.[8]

There are not many randomized control trials using digoxin in the management of heart failure in children. Small uncontrolled studies examining the acute hemodynamic effects of digoxin in children with heart failure due to large left-to-right shunts showed conflicting results.[9,10,11] There are no data on the efficacy of digoxin in heart failure in children with LV systolic dysfunction or

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**Table I. Digoxin dose - Infants and children[5]**

| Age | Total digitalizing dose mcg/kg/24 hr | | Daily maintenance dose mcg/kg/24 hr | |
|---|---|---|---|---|
| | **PO** | **IV** | **PO** | **IV** |
| Premature newborn | 20 | 15 | 5 | 3-4 |
| Full term newborn | 30 | 20 | 8-10 | 6-8 |
| <2 year | 40-50 | 30-40 | 10-12 | 7.5-9 |
| 2-10 years | 30-40 | 20-30 | 8-10 | 6-8 |
| **>10 years/ adults** | **0.75-1.5mg** | **0.5-1mg** | **0.125-0.5mg** | **0.1-0.4mg** |

*PO: per oral, IV: intravenous.*

valvar regurgitations and no data on long-term survival in any of these trials.

Dosage (Table I): Rapid digitalization is usually not indicated when using digoxin for heart failure except for treatment of acute tachyarrhythmias. The maintenance dose is given in twice daily doses for children under 10 years and once daily for children above 10 years. Digoxin "holiday" is generally not needed in children.[4]

Monitoring: Heart rate and rhythm should be monitored. Periodic ECGs are recommended when up titrating the dose or using diuretics. Serum $Ca^{2+}$, $K^{+}$, renal parameters need to be monitored. If suspecting toxicity, serum digoxin levels should be measured (sample taken at least 6 hours after the dose). Toxicity is usually seen at >2 ng/ml level. Dose of digoxin should be halved when using amiodarone. Parents must be demonstrated as to how to give the exact dose. They should be alerted not to change dose on their own and to keep the digoxin bottle away from the reach of children. Parents must be explained about the symptoms of possible digitoxicity.

Side effects: As digoxin has a very narrow therapeutic index, side effects are expected. The common side effects are cardiac arrhythmias like sinus bradycardia, sinoatrial and atrioventricular blocks, atrial and nodal ectopic beats, atrial tachycardia with block and ventricular arrhythmias including ventricular tachycardia (VT). Apart from these, there can be gastrointestinal side effects like nausea, vomiting, abdominal pain and diarrhea, CNS manifestations like lethargy, confusion, disorientation, vertigo, headache, fatigue, anxiety, depression, delirium and hallucinations, endocrine or metabolic effects like hyperkalemia and ocular effects like blurred vision, haloes, yellow/green vision, diplopia, photophobia and flashing lights.[4]

Contraindications: These include hypertrophic obstructive cardiomyopathy, Wolff-Parkinson-White syndrome and high-grade AV block. It needs to be used with caution in patients with renal failure, hypokalemia, myxedema, acute myocarditis, premature infants with impaired renal clearance, and co-administration with drugs inhibiting AV conduction (beta-blockers, amiodarone, verapamil, diltiazem). In these settings, dose reduction of the drug is appropriate.[2]

## Diuretics

**Loop diuretics**: They are widely used in heart failure because of the symptomatic relief from fluid overload within minutes of administration. Diuretic therapy remains the cornerstone in management of acute heart failure because of the decongestive effects as congestion is main component of heart failure. Despite being widely used, there is very limited evidence from prospective randomized studies to guide the prescription and titration of diuretics and higher doses may be actually harmful.[12] Few recent randomized trials have shown that continuous infusion of loop diuretics did not offer benefit but were associated with adverse events like hyponatremia, prolonged hospital stay and increased rate of readmissions which is probably due to the limitations of congestion evaluation as well as to the deleterious effects linked to drug administration, particularly at higher dosage.[13] Several diuretic agents are available but the most commonly used is furosemide.

Furosemide is a loop diuretic and is the preferred agent in heart failure due to its rapid onset of action and high efficacy with greater fluid clearance. The increasing doses have increasing efficacy and it remains effective even at low glomerular filtration rate (GFR). Furosemide is three times more potent than thiazide diuretics. Furosemide also has a venodilatory effect and increases systemic venous

capacitance, reducing preload. Furosemide is indicated in heart failure, pulmonary edema, hypertension, renal failure and for fluid overload due to other causes. When using diuretic, one must make sure that there is no hypovolemia (as may be seen in postoperative setting and in newborn). Serum Na, $K^+$, $Ca^{2+}$ and blood sugar are the parameters to be monitored.

Torsemide is also a loop diuretic similar to furosemide, but is more potent (10mg of torsemide is equivalent to 40mg of furosemide), has a higher bioavailability and a longer duration of action. In an open label study on children, torsemide was considered better than furosemide for control of heart failure. It is more expensive than furosemide.

**Thiazides**: These drugs inhibit the sodium–chloride transporter at the distal portion of the ascending limb of loop of Henle and the first part of the distal tubule thereby preventing maximal dilution of urine and thus increasing free water clearance and excretion of sodium and chloride through the renal tubular epithelium. They are less effective in patients with reduced glomerular filtration, as they exert their diuretic effects from the luminal side of the nephron. Although they are less potent than loop diuretics, they may work in synergy with them when a sequential segmental nephron blockade is achieved. They also decrease peripheral vascular resistance by a mechanism which at present, is not well understood, resulting in a decrease of blood pressure.[14] Except for metolazone, thiazides are relatively milder diuretics and are rarely used in the treatment of heart failure.

Hydrochlorothiazide is the most often used drug in this category. Primary indications for thiazide diuretics are mild hypertension and edema. The dose of hydrochlorthiazide is 2mg/kg/day in two divided doses. Like furosemide, it also causes excretion of Na, $K^+$ and chloride along with water. Hydrochlorothiazide is available as 12.5gm, 25mg, 50mg tab. The drug is quite inexpensive. Metolazone is ten times more potent than hydrochlorthiazide and is useful in resistant cases of hypertension and heart failure. Intermittent doses of metolazone may help to overcome diuretic resistance which may occur due to fluid overload, mesenteric congestion (inadequate absorption) and low renal blood flow. The dose is 0.2-0.4mg/kg/day in children. Electrolytes must be monitored closely.

**Potassium sparing diuretics**: Spironolactone is an aldosterone blocking agent, the other such drug is eplerenone. They act on the distal convoluted tubule, producing moderate diuresis with Na and chloride excretion and sparing of $K^+$. Spironolactone is often used in combination with furosemide for heart failure. It promotes magnesium and potassium retention, increases uptake of myocardial norepinephrine, attenuates formation of myocardial fibrosis and decreases mortality associated with both progressive ventricular dysfunction and malignant ventricular arrhythmias.[15] Spironolactone has been shown to improve survival in adult patients with heart failure. No such specific benefit has been shown in children, but the drug is effective. Two small observational studies in children, using spironolactone have shown benefit in controlling heart failure.

Monitor serum $K^+$ and renal functions especially if renal impairment is present. There are conflicting results from studies to state that adding spironolactone to existing therapy in patients with heart failure and a preserved ejection fraction did not significantly reduce the incidence of the primary outcome.[16] Guidelines have recommended adding spironolactone to treatment with ACE inhibitors and â blockers. A prospective observational study in Copenhagen has highlighted the danger of renal impairment and of hyperkalemia. It may be associated with more frequent adverse effects than is generally realised. Doses of other diuretics may need to be reduced and frequent laboratory monitoring is essential.[17]

## Vasodilators

Angiotensin converting enzyme inhibitors (ACEi): They decrease the adrenergic drive and block the heart failure induced activation of renin angiotensin aldosterone axis. Increased levels of aldosterone and angiotension II have been associated with poor outcome in heart failure. ACEi also increase bradykinin which has natriuretic properties. Currently ACEi therapy is recommended as the first line treatment for heart failure, when it is not secondary to an obstructive lesion and include a) heart failure due to ventricular dysfunction, b) hypertension, c) significant valvular regurgitation (even without heart failure) and d) heart failure secondary to large left to right shunts where the role of ACEi is less convincing, but is often used. ACEi are classified into 3 classes;

Class I - Captopril is the active form of the drug and is metabolized in liver,

Class II – Enalapril and ramipril: Pro-drugs which are metabolized to the active form and Class III - Lisinopril which is excreted without being metabolized by the kidney

Improvement in symptoms and survival has been shown in adults with symptomatic heart failure on ACEi. Later, ATLAS trial showed that high dose of lisinopril was

more beneficial than a low dose. Therefore, one must up titrate the dose to the maximum tolerable permissible doses for maximum benefit. There are no randomized trials in children, the trials may be considered unethical at this stage. Several small observational studies have proven the efficacy and safety of these drugs in children. There is one study showing survival benefit with ACEi in children with idiopathic dilated cardiomyopathy. ACEi have been found to be useful in valvular regurgitation and large left to right shunts, if the systemic vascular resistance is elevated at the baseline.

Captopril: It is the most often used ACE inhibitor in pediatric practice, especially in neonates and infants where enalapril may induce renal dysfunction. The starting dose is 0.1mg/kg/dose and is gradually increased to 0.5-1mg/kg/dose three times a day (increased after every 4 to 5 doses). Maximum dose is 2mg/kg/dose. BP and renal parameters should be monitored when up titrating the dose.

Enalapril: It is useful for older children. It is longer acting and given twice daily. The dose is 0.1-0.5 mg/kg/dose twice a day. The initial dose may be smaller. Monitoring is as for captopril. Ramipril and lisinopril are other ACEi and both are commonly used for hypertension. The doses for heart failure in children are not defined. Blood pressure (BP), renal parameters, serum $K^+$ should be monitored, initially and whenever the dose is increased. In a relatively stable patient, ACE inhibitor therapy can be initiated in the outpatient department.

## Angiotension receptor blockers (ARBs)

Angiotensin-converting enzyme (ACE) inhibitors and β-blockers can lower total mortality and heart failure hospitalizations by 25% to 40% across all ages, functional capacities, degrees of left ventricular dysfunction and causes.[18,19] The extended 12-year study of the Studies of Left Ventricular Dysfunction Prevention and Treatment trials (X-SOLVD) demonstrated a significant benefit with a reduction of cumulative all-cause death compared with placebo (50.9% vs 56.4%).[20]

ARBs are competitive antagonists for the angiotension II receptors. They block the cell surface receptor for angiotensin unlike ACEi, which are converting enzyme inhibitors. ARBs do not inhibit bradykinin breakdown and hence cough is much rarer. Also ARBs are not nephrotoxic. However, a meta-analysis of randomized trials in adults did not show any advantage of ARBs over ACEi. Side effects are same as for ACEi except that cough does not occur. Other drugs in this group are candesartan and valsartan. Studies in children are in progress, primarily for treatment of hypertension. A combination of ACEi and ARBs is currently not recommended in pediatric patients.

Hydralazine: It is a non ACEi peripheral vasodilator, resulting in relaxation of arterial smooth muscles. Hydralazine does not produce hyperkalemia and is safe in patients with renal impairment. It should be used in patients in whom ACEi or ARBs are not tolerated or are contraindicated.

## Beta blockers

Heart failure results in activation of sympathetic nervous system and increased levels of circulating catecholamines. Chronic activation of sympathetic nervous system leads to worsening of heart failure by inducing myocardial apoptosis and fibrosis. Circulating catecholamines also induce peripheral vasoconstriction along with renal retention of salt and water. Beta blockers antagonize these deleterious effects. In addition, beta blockers also have anti arrhythmic effect.

Indications for beta blockers include mild, moderate or compensated heart failure, secondary to ventricular dysfunction (Beta blockers should not be initiated in acute decompensated heart failure), SVT and other tachyarrhythmias and hypertension.

The benefits of beta blocker therapy in adult patients with heart failure have been shown in several studies. In addition to metoprolol, carvedilol has been shown to decrease mortality and risk of clinical progression of heart failure. Carvedilol is a non-selective beta blocker which also has an anti-oxidant property. Due to its alpha blocking effect, carvedilol exerts a vasodilatory effect. It improves functional class and fractional shortening in children with ventricular dysfunction. Side effects include dizziness, hypotension and headache. The first multicentre, randomized, double blind, placebo controlled trial for carvedilol in children was recently published by Shaddy and colleagues. There was no statistically significant difference between carvedilol and placebo and the authors postulated that this may be due to unexpectedly low rate of events for patients in worsened category and that the trial may have been underpowered. Clinical analyses show that withdrawal of chronic beta blockade should be avoided when possible during hospitalization and that beta blocker therapy be initiated as soon as hemodynamic stability and a euvolemic state are achieved. This strategy may increase adherence to beta blockers after discharge and lower re hospitalization and mortality rates.[21]

## Newer drugs for heart failure

Nesiritide: It is a recombinant form of beta type natriuretic peptide (BNP). It produces vasodilatation and diuresis and is given intravenously. In adult patients with acute decompensated heart failure, Nesiritide has shown benefit, the primary side effect being hypotension. Later, two reviews which analyzed data from clinical trials, concluded that adult patients with acute heart failure who received Nesiritide, had increased mortality. There are no randomized, controlled trials for pediatric patients, but as the BNP levels are increased in children with heart failure, Nesiritide should be useful. An open trial in 30 children with heart failure demonstrated improved diuresis when Nesiritide was used. In a more recent study, 32 children received 55 Nesiritide infusions starting at 0.01mcg/kg/min and up titrated to a max of 0.03mcg/kg/min. Authors concluded that urine output improved significantly with Nesiritide. It could be given safely. The thirst decreased and NYHA class improved. Hypotension is a well-known side effect of Nesiritide and blood pressure should be carefully monitored. Its advantage over other diuretics is that electrolytes are not affected adversely.

Levosimendan: It is a calcium sensitizer and improves heart failure by prolonging the effects of calcium in the myocardium. The level of calcium in myocardium is not changed and hence incidence of arrhythmia due to calcium overload is not increased. Levosimendan has been shown to possess positive chronotropy, positive inotropy and vasodilatory effects without increasing myocardial oxygen consumption. It has also been shown to reduce circulating pro-inflammatory markers and markers of apoptosis. Several studies have shown the beneficial effect of levosimendan in adult patients with low output heart failure. It produces improvement in symptoms, increase in cardiac output and decrease in pulmonary venous pressure. The dose is 0.1-0.4mcg/kg/min as continuous intravenous infusion. Pediatric experience was reported by Namachivayam, et al in 15 children with severe heart failure refractory to conventional therapy.[22] The drug was well tolerated and two third of patients could be weaned from catecholamine support. The ventricle function improved in those with acute heart failure, but not in those with long standing dysfunction. It is a useful addition to the armamentarium of drugs for heart failure and should be considered in cases which are refractory to conventional therapy.

Vasopeptidase inhibitors: These are a newer group of drugs which is yet to be licensed to be used in children. They act by inhibiting the two enzymes neprilysin and angiotensin converting enzyme. Omapatrilat and sampatrilat can be used as oral agents in cases of chronic congestive heart failure. Neprilysin is an enzyme which metabolizes BNP and inhibition of this causes natriuresis as a result of increased BNP levels. In a study among comparing enalapril and omapatrilat in adult patients, omapatrilat was found to reduce the risk of death and hospitalization in chronic heart failure but was not more effective than ACE inhibition alone in reducing the risk of a primary clinical event.[23] In a randomised, double-blind, parallel trial of 573 patients with New York Heart Association (NYHA) class II-IV congestive heart failure, where omapatrilat and lisinopril on exercise tolerance and morbidity were compared, omapatrilat was found to have some advantages over lisinopril.[23]

## Conclusion

Drugs available today for treatment of cardiac failure only improve symptoms and that too, not to any degree of perfection. Despite advances in management of heart failure, the condition remains a major public-health problem, with high prevalence, poor clinical outcomes and large health-care costs. Emerging strategies for heart failure management include individualised therapy, novel approaches to diagnosis and tracking of therapeutic response, pharmacological agents aimed at new targets and cell-based and gene-based methods for cardiac regeneration. Hence, we need to recognise the type of heart failure in a given child and wisely use the available drugs.

## References

1. Dickstein K, Cohen-Solal A, Filippatos G, McMurray JJ, Ponikowski P, Poole-Wilson PA, et al. ESC guidelines for the diagnosis and treatment of acute and chronic heart failure 2008: The task force for the diagnosis and treatment of acute and chronic heart failure 2008 of the European Society of Cardiology. Developed in collaboration with the Heart Failure Association of the ESC (HFA) and endorsed by the European Society of Intensive Care Medicine (ESICM) Eur J Heart Fail 2008; 10:933-989.
2. Withering W. An account of the foxglove and some of its medical uses, with practical remarks on dropsy, and other diseases. In: Willins FA, Keys TE, editors. Classics of Cardiology. 1Volume I. New York, NY: Henry Schuman, Dover Publications 1941; pp231–252.
3. Jain S, Vaidyanathan B. Digoxin in management of heart failure in children: Should it be continued or relegated to the history books? Ann Pediatr Cardiol 2009; 2(2): 149-152.
4. Drug Therapy of Cardiac Diseases in Children. Working Group on Management of Congenital Heart Diseases in India. Indian Pediatr 2009; 46:310-338.

5. IAP Drug Formulary 2015. 4th edn. (eds) Jeeson C Unni, Menon PSN, Nair MKC, Bansal CP. Publication of IAP. Pixel Studio, Cochin: 2015; pp110-112.
6. The effect of digoxin on mortality and morbidity in patients with heart failure. Digitalis Investigation Group. N Engl J Med 1997; 336:525-533.
7. Adams KF, Gheorghiade M, Uretsky BF, Patterson JH, Schwartz TA, Young JB. Clinical benefits of low serum digoxin concentrations in heart failure. J Am Coll Cardiol 2002; 39:946-953.
8. Rathore SS, Curtis JP, Wang Y, Bristow MR, Krumholz HM. Association of serum digoxin concentration and outcomes in patients with heart failure. J Am Med Assoc 2003; 289: 871-878.
9. Berman W, Yabek SM, Dillon T, Niland C, Corlew S, Christensen D. Effects of digoxin in infants with congested circulatory state due to a ventricular septal defect. N Engl J Med 1983; 308:363-366.
10. Kimball TR, Daniels SR, Meyer RA, Hannon DW, Tian J, Shukla R. Effect of digoxin on contractility and symptoms in infants with a large ventricular septal defect. Am J Cardiol 1991; 68:1377-1382.
11. Seguchi M, Nakazawa M, Momma K. Further evidence suggesting a limited role of digitalis in infants with circulatory congestion secondary to large ventricular septal defect. Am J Cardiol 1999; 831408-1411.
12. Felker GM. Loop diuretics in heart failure. Heart Fail Rev 2012; 17(2):305-311. doi: 10.1007/s10741-011-9245-3.
13. Palazzuoli A, Ruocco G, Ronco C, McCullough PA. Loop diuretics in acute heart failure: beyond the decongestive relief for the kidney. Critical Care 2015; 19:296. https://doi.org/10.1186/s13054-015-1017-3.
14. Roush GC, Kaur R, Ernst ME, Diuretics: a review and update. J Cardiovasc Pharmacol Ther 2014; 19:5-13.
15. Soberman JE, Weber KT. Spironolactone in congestive heart failure. Curr Hypertens Rep 2000; 2(5):451-456.
16. Pitt B, Pfeffer MA, Assmann SF, Boineau R, Anand IS, Claggett B, et al. Spironolactone for heart failure with preserved ejection fraction. N Engl J Med 2014; 370:1383-1392.
17. Svensson M, Gustafsson F, Galatius S, Hildebrandt PR, Atar D. Hyperkalaemia and impaired renal function in patients taking spironolactone for congestive heart failure: retrospective study. Br Med J 2003; 327:1141.
18. Foody JM, Farrell MH, Krumholz HM. Beta-blocker therapy in heart failure: scientific review. JAMA 2002; 287: 883-889.
19. Garg R, Yusuf S. Overview of randomized trials of angiotensin-converting enzyme inhibitors on mortality and morbidity in patients with heart failure. Collaborative Group on ACE Inhibitor Trials. JAMA 1995; 273:1450-1456.
20. Demers C, Mody A, Teo KK, McKelvie RS. ACE inhibitors in heart failure: what more do we need to know? Am J Cardiovasc Drugs 2005; 5(6):351-359.
21. Zafrir B, Amir O. Beta blocker therapy, decompensated heart failure, and inotropic interactions: current perspectives. Isr Med Assoc J 2012; 14(3):184-189.
22. Namachivayam P, Crossland DS, Butt WW, Shekerdemian LS. Early experience with Levosimendan in children with ventricular dysfunction. Pediatr Crit Care Med. 2006; 7(5):445-448.
23. Packer M, Califf RM, Konstam MA, Krum H. Comparison of Omapatrilat and Enalapril in Patients with chronic heart failure. Circulation 2002; 106:920-926.


## NEWS AND NOTES

**29th Annual Conference of Indian Society of Pediatric Nephrology**
**October 13-15, 2017**

**Pre-conference Workshop: 13 October, 2017 –**
**'Critical Care Pediatric Nephrology and RRT'**
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**SURGERY**

# LAPAROSCOPY IN PEDIATRICS

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*****Raghul M**

**Abstract:** *Minimally invasive surgery offers many advantages such as smaller incisions, greater surgical precision, decreased risk of infection, reduced length of stay and decreased cost of care. Considering these benefits, it ought to be the standard of care for infants and small children. In this review, recent progress in minimally invasive surgery and the challenges which can be tackled are described.*

**Keywords:** *Minimally invasive surgery, Laparoscopy, Appendicectomy, Thoracoscopy*

Pediatric surgeons were among the pioneers of laparoscopic surgery in the early 1970s, but the vast potential of this "minimally invasive" approach to treat children with surgical conditions has only recently gained momentum.[1] The earliest description of diagnostic laparoscopy was by Cortesi, et al.[2] However, diagnostic laparoscopy was originally introduced in 1910 by the Swedish physician - Hans Christian Jacobeus who published his results from diagnostic laparoscopy and thoracoscopic procedures.[3] Therapeutic laparoscopy was made popular following the description of laparoscopic appendicectomy by a German gynecologist - Kurt Semm in 1983[4] and of laparoscopic cholecysytectomy by the German surgeon – Erich Muhe in 1985.[5] Advancements in development of instrument components particularly illumination, optics, fiberoptic transmission, insufflation and video-apparatus have progressed alongside development of techniques for minimal access into the abdominal cavity. Development of pediatric laparoscopy was marked by Gans in his contribution to the development of pediatric miniature instruments in 1970.[6] Laparoscopy offers the surgeon the option of achieving high standard surgical treatment while keeping tissue trauma to a minimum.

An increasingly sophisticated and informed patient population often requests laparoscopy over open traditional procedures. Parents frequently select surgeons based on their laparoscopic skills. Advances in pediatric anesthetic monitoring and support equipment have also made a huge contribution. The result is an increasingly wider application to the use of laparoscopy in children. Jen and Shew observed an increase in the utilization of laparoscopy for the management of appendicitis in children from 18.6% in 1999 to 52.4%.[7] Several diagnostic and therapeutic procedures have been demonstrated to be safely and efficiently undertaken with laparoscopy with several advantages over traditional approach.[8]

The development of 3mm and 2mm instruments has advanced the frontiers of diagnostic as well as therapeutic laparoscopy in infant and neonatal population. In the evaluation of the neonate with abdominal distension, free gas on plain abdominal radiograph in the absence of corresponding clinical signs of peritonism (a pathological condition marked by the symptoms of peritonitis without actual inflammation), laparoscopy has been used to evaluate the condition and arrive at more focused management decisions with improved outcome.

Better access, panoramic visual field, quick recovery and reduced complication rates and physiological stress response in laparoscopic surgery are potential advantages when compared to open surgery. The delicate fluid balance in infants is further compromised due to evaporation of the body fluids from exposure of abdominal contents at laparotomy. This is minimized by the laparoscopic approach. Improvement of laparoscopic equipments is on-going to further limit any drying effect of the gas and light on abdominal viscera. The procedures commonly performed through laparoscopy are given in Box 1.

The anesthetists also face few challenges. In addition to routine preoperative optimization and intraoperative monitoring, diagnosis and treatment of effects of carboperitoneum (creation of a pneumoperitoneum by

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**Box 1. Common laparoscopy procedures**

**Upper gastrointestinal tract**

Ladd's procedure for intestinal malrotation, pyloromyotomy, reduction of intussusceptions, intestinal duplication cyst, adhesiolysis and resection of Meckel's diverticulum

**Lower gastrointestinal tract**

Appendicectomy, Laparoscopic-assisted ano-rectoplasty (LAARP), pull through for Hirschsprung's disease

**Solid intra-abdominal organs**

Splenectomy, deroofing of splenic cyst, abdominal cystic masses, adrenal gland excision and cholecystectomy

**Gynecology**

Ovarian cystectomy, ovarian detorsion, oophorectomy and diagnostic laparoscopy for chronic abdominal pain

**Urology**

Laparoscopy for impalpable testis, Fowler-Stephens stage 1 orchidopexy, ligation of varicocele, pyeloplasty, heminephrectomy and nephrectomy

carbon dioxide insufflation during laparoscopic surgery) and maintenance of intra abdominal pressure (IAP) between 6-12 mm Hg are needed. Vigilant observation of the effects of carboperitoneum and tailoring the management accordingly is the key to successful management.

In advanced appendicitis, laparoscopic approach offered significant advantages with better outcomes than open approach with less wound-related complications in the authors' experience. The ability to give a thorough

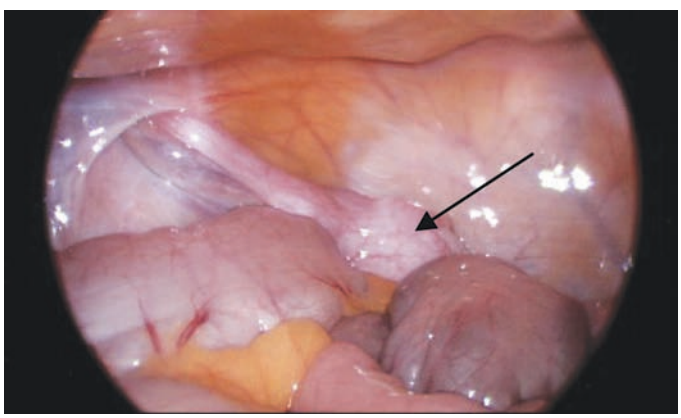

**Fig.1. Undescended intra abdominal testis**

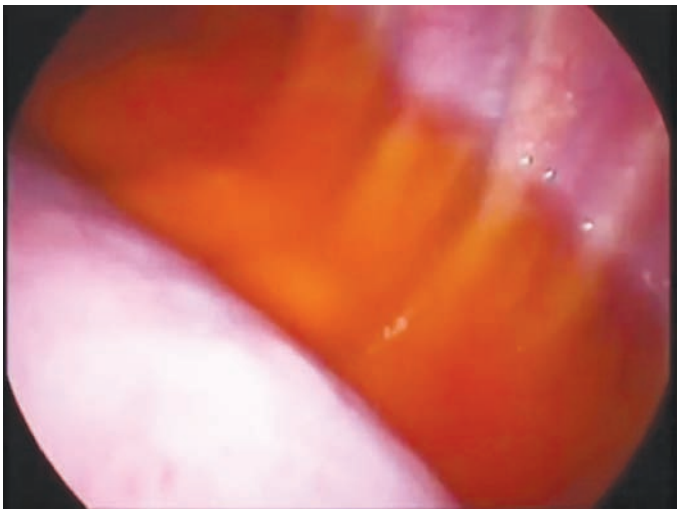

**Fig.2. Early empyema - Thoracoscopic view**

peritoneal lavage offers the advantage with lesser post operative adhesions.

Laparoscopic-assisted ano-rectoplasty (LAARP) procedure has offered the advantage of placing the bowel within the muscle complex thus avoiding post operative incontinence and neuronal injury with minimal post operative complication.[9]

Laparoscopic gubernaculum preserving orchiopexies have increased the testicular lifespan and have dramatically lessened the incidence of testicular atrophy. Further, the chances of removing a nubbin testis if at all present at the opposite side are also high (Fig.1).

Newer advancements in the field have evolved with retroperitoneoscopy for nephrectomies for non functioning kidneys, adrenal lesions and heminephrectomies for infected duplex systems. This has achieved greater advantage of absence of paralytic ileus and rapid post operative recovery due to very minimal carbon dioxide absorption.[10]

Early thoracoscopic surgeries in children with empyema have decreased the need for open thoracotomies. Further, the morbidity with respect to hospital stay, ambulation and chest symptoms has drastically come down (Fig.2).

The main advantages of laparoscopic surgery for patients are less postoperative pain, therefore less need for postoperative analgesics, reduced wound complications, minimal scarring, a shorter hospital stay and an earlier return to normal activities including feeding, bowel movements and school.

Laparoscopic surgery in children is here to stay. But

the challenge ahead is to define more objectively the relative benefits of various laparoscopic and open techniques. Meanwhile, the potentials of endoscopic surgery should continue to be explored in appropriate settings and fetal endosurgery is one exciting example.[11]

Laparoscopic approach allows better visualization of obscure structures and areas, such as the lower esophageal sphincter complex and the small vagus nerves running along the esophageal muscle. Modern high-definition digital cameras and monitors dramatically magnify these small details and angled telescopes allow views around corners simply unavailable in open cases. When this visualization is combined with the meticulous precision possible to the well-practiced minimally invasive surgery (MIS) surgeon who knows how to "move small," surgery may be completed with similar or superior mechanical results as open cases. Reductions in both duration of surgery and complications have been reported for pyloromyotomy, fundoplasty, tracheo-esophageal fistula repair, duodenal-atresia repair and other cases performed in infants.[12,13]

Closely related to cost and precision is speed. Not only does longer operating times cost more in terms of operating room resources, but longer time of surgery appears to increase the risk of complications. Early in any given surgeon's experience, operating times for laparoscopic cases can exceed the expected time for open procedures. The learning curve is well documented;[14-17] however, as surgeons become more facile, operating times can drop dramatically. Information gained from MIS offers surgeons new options for resolving clinical uncertainty because the cost to the patient is diminished, the power of exploration is greater than radiographic studies or other tests, or both.[18] For example, in malrotation, an upper gastrointestinal tract study may be nondiagnostic, but the stakes of missing malrotation are large, as volvulus, although rare, may be catastrophic. Laparoscopic exploration reliably diagnoses malrotation and can provide information that contrast studies cannot. Meanwhile, the laparoscopic Ladd procedure is at least as effective in preventing volvulus as the open Ladd surgery.

## Conclusion

Minimally invasive surgery is more than technique and technology; it is a choice. The hospital must choose to install the right equipment, bear higher instrument attrition costs, specially train the staff and tolerate new learning curves. The surgeon must choose to add unfamiliar and uncomfortable methods to his repertoire. He must also choose the patients for whom MIS can really reduce risks: there is a demonstrable gap between "can" and "should." Properly applied, MIS may offer better information, similar (or superior) mechanical results, more surgical options, shorter hospital stays, lower costs and risks to the patient.

## References


1. Gans SL, Berci G. Advances in endoscopy of infants and children. J Pediatr Surg 1971; 6:199-233.
2. Cortesi N, Ferrari P, Zambarda E, Manenti A, Baldini A, Morano FP. Diagnosis of bilateral abdominal cryptorchidism by laparoscopy. Endoscopy. 1976; 8: 33–34.
3. Badani, K.K.; Patel, H.R.H. & Hemal, A.K. (2006). Historical development of keyhole surgery, In: Minimally Invasive Surgery: Looking through the keyhole, H. Patel, J. Joseph, (Eds.), 2-3, MA Healthcare Ltd, ISBN 1-85642-296-8, London, United, Kingdom
4. Semm, K. (1983). Endoscopic appendectomy. Endoscopy,Vol.15, No.2, (March 1983), pp. 59-64, ISSN 0013726X
5. Mühe E. Long-term follow-up after laparoscopic cholecystectomy. Endoscopy 1992 ; 24(9):754-758.
6. Tantoco, J.G.; Glick, P.L. & Levitt, M.A. (2005). History of pediatric minimal access surgery, In: Pediatric Minimal Access Surgery, J.C. Langer, C. T. Albanese, (Eds.), 12, Taylor & Francis Group, ISBN 0-8247-5447-6, Florida, USA.
7. Jen HC, Shew SB. Laparoscopic versus open appendectomy in children: outcomes comparison based on a state wide analysis. J Surg Res 2010; 161(1): 17-19.
8. Mattei P. Minimally invasive surgery in the diagnosis and treatment of abdominal pain in children. Curr Opin Pediatr 2007;19:338-343. 10.1097/MOP. 0b013e328 10c8eaf
9. Gurusamy R, Raj SV, Maniam R, Regunandan SR. Laparoscopic-assisted Anorectoplasty: A Single-center Experience. J Indian Assoc Pediatr Surg 2017 Apr; 22(2):114-118. doi:10.4103/jiaps.JIAPS_266_16.
10. Esposito C, Giurin I, Iaquinto M, Escolino M, Salerno MC, De Filippo G, et al. Laparoscopy or retroperitoneoscopy for pediatric patients with adrenal masses? Minerva Pediatr 2015; 67(6):525-528.
11. Kimber C, Spitz L, Cuschieri A. Current state of antenatal in utero surgical interventions. Arch Dis Child Fetal Neonatal Ed 1997; 76:F134-F139.
12. Bax NMA, Ure BM, van der Zee DC, van Tuijl I. Laparoscopic duodenoduodenostomy for duodenal atresia. Surg Endosc 2001; 15(2):217-219.
13. Georgeson KE, Owings E. Advances in minimally invasive surgery in children. Am J Surg 2000; 180(5):362–364.
14. Ford WD, Crameri JA, Holland AJ. The learning curve for laparoscopic pyloromyotomy. J Pediatr Surg 1997; 32(4):552–554.

15. Fujimoto T, Lane GJ, Segawa O, Esaki S, Miyano T. Laparoscopic extramucosal pyloromyotomy versus open pyloromyotomy for infantile hypertrophic pyloric stenosis: which is better? J Pediatr Surg 1999; 34(2): 370–372.
16. Oak SN, Parelkar SV, Akhtar T, Joshi M, Pathak R, Viswanath N, et al. Minimal access surgery in children - 5 years institutional experience. J Minim Access Surg 2005; 1(3):121–128.
17. Oomen MW, Hoekstra LT, Bakx R, Heij HA. Learning curves for pediatric laparoscopy: how many operations are enough? The Amsterdam experience with laparoscopic pyloromyotomy. Surg Endosc 2010; 24(8):1829-1833.
18. Esposito C, Centonze A, Settimi A. The efficacy of laparoscopy in detecting and treating associated congenital malformations in children. Surg Endosc 2002; 16(8):1242.

## CLIPPINGS

**Growth throughout childhood of children born growth restricted**

Many studies that examine growth in growth-restricted children at birth do not discriminate between fetal growth restriction (FGR) and small for gestational age (SGA). These terms however are not synonymous. In SGA, stunting and increased weight gain have been reported. We do not know if this holds true for FGR. Our aim was to study postnatal growth until age 12.5 years in a cohort of children born with FGR due to early onset placental insufficiency and its relation to FGR severity.

This was a prospective cohort study, follow-up of an antenatal randomised controlled trial in two tertiary centres. Children aged 12.5 years born after FGR, with mothers who had severe early onset hypertensive pregnancy disorders (n=96). Main outcome measure considered was anthropometry at age 12.5 years in SD scores (SDS).

Mean height SDS (SD) corrected for target height was " 0.09 (0.94), mean body mass index (BMI) SDS was 0.00 (1.16) and mean head circumference SDS was –0.37 (1.11). Catch-up growth was at fastest rate between term age and 3 months and similar for height (0.55 SDS/months) and weight (0.49 SDS/months). Neither FGR severity nor gestational age was related to height and BMI at age 12.5 years.

Children born growth restricted due to early onset placental insufficiency have height and BMI scores comparable to their age-matched peers at age 12.5 years. FGR severity was not related to height and BMI at age 12.5 years. These reassuring results differ from most studies that examine SGA children.

***Beukers F, Rotteveel J, van Weissenbruch MM, Ganzevoort W, van Goudoever JB, van Wassenaer-Leemhuis AG. Growth throughout childhood of children born growth restricted. Arch Dis Child 2017 Aug; 102(8):735-741. doi: 10.1136/archdischild-2016-312003. Epub 2017 Mar 30.***

***Potential danger of isolated platelet transfusion in patients with dengue infection.***

Prophylactic platelet transfusions in stable patients with dengue fever may delay normalization of platelet counts and may actually increase the duration of hospitalization,. However, the potential for harm by isolated platelet transfusions will be markedly higher when the endothelium is more activated.The following suggestions may be useful for the use of platelet transfusions in patients with dengue. First, avoid isolated platelet transfusions if possible (however, the need for platelet transfusion needs to be decided by the treating clinician in each patient, on a case by case basis). Second, if platelet transfusions are required for a patient, first infuse fresh frozen plasma/cryosupernatant (providing ADAMTS13 supplementation), then infuse platelets. The need of the hour is systematic studies to assess if these suggestions for transfusion practices translate into a reduction in multi-organ system failure and mortality .

***Eapen CE, Nair SC. Potential danger of isolated platelet transfusion in patients with dengue infection. Indian J Med Res 2017; 145:158-160.***

**RADIOLOGY**

# ABDOMINAL TUBERCULOSIS

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The diagnosis of abdominal tuberculosis is often challenging given the non-specific presenting features. Very few have lung lesions in the chest x-ray. Mantoux test is usually not helpful. Radiology may provide insights into possible tuberculous etiology in abdomen, prior to invasive methods for obtaining specimens to view the bacillus or for culture.

The tubercle bacilli may enter the gastro-intestinal tract through the ingestion of infected milk or sputum. Hematogenous route or contiguous spread from neighbouring foci are also possible routes. When the mucosa is invaded, tubercles form in the lymphoid tissue of the submucosa. At this juncture ultrasound or CT abdomen are normal. In about two weeks, caseation sets in and inflammation spreads from the primary site. Spread through the deeper layers of the gut wall and onto the serosa involves the peritoneum giving rise to peritoneal tuberculosis. At this point of time, imaging can pick up ascites. Peritoneal fluid with synechiae in an otherwise

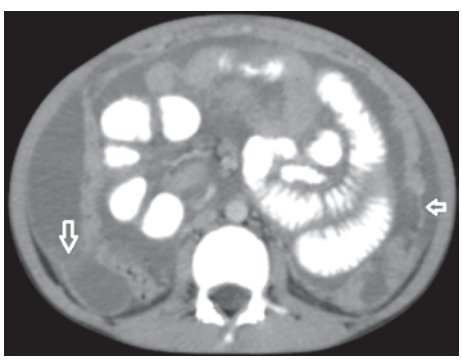

**Fig.1. Peritoneal tuberculosis [Synechiae (arrows) in the peritoneal fluid]**

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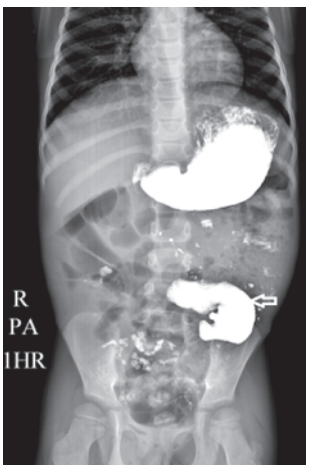


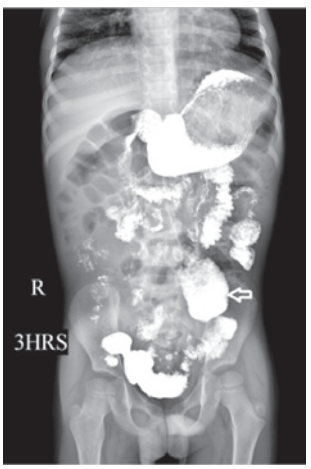


**Fig.2 and Fig.3.Distended loop of bowel**

normal abdomen is characteristic of tuberculosis. The synechiae enhance on contrast examination. Fig.1 is a CT picture showing grey fluid with strands running across. The bowel seems normal. There may also be smaller, thickly septated loculations and clumped up loops matted together due to fibrous peritoneal reaction. Sometimes a group of small bowel loops are seen constantly clumped up together and CT may demonstrate a confining thick fibrous rind around the loops. This is called sclerosing encapsulating peritonitis or abdominal cocoon.

Tuberculous ulcers are superficial but cicatricial healing and accompanying endarteritis cause strictures. The commonest site of involvement is the ileocecal region. Reasons put forward are physiological stasis, increased rate of fluid and electrolyte absorption, minimal digestive activity and abundance of lymphoid tissue at this site. The frequency of proximal or distal bowel involvement is much less. The terminal ileum, ileocecal junction and the cecum are simultaneously affected in a majority of children with abdominal tuberculosis. Barium meal examination of a child in Fig.2 and Fig.3 shows a persistently dilated loop in the one hour and three hour films which represents hold up of barium due to luminal narrowing. In the six hour film (Fig.4) in the same child barium has moved on into the terminal ileum which takes an upright course to join a pulled up cecum. Flocculation of the barium is also seen low in the right iliac fossa. A late film (Fig.5) in another patient shows a classical goose neck deformity consisting

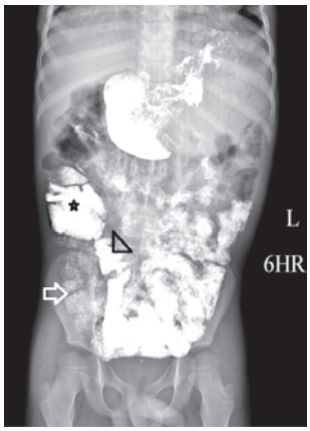


**Fig.4.Pulled-up cecum cecum (*), flocculation (arrow), ileum (arrow head)**

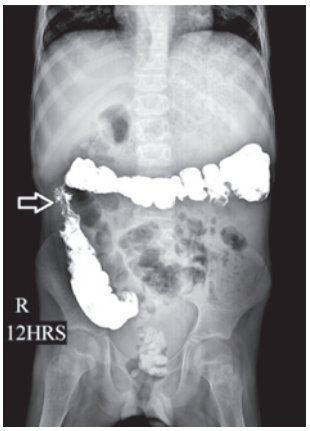


**Fig.5. Goose-neck deformity (arrow) fibrosed cecum**

of a mildly dilated terminal ileum going upwards to a retracted, fibrosed and narrowed cecum. While barium series only delineate the lumen of bowel, CT also reveals what is actually occurring in the wall and in the surroundings. Fig.6 shows a thickened wall of the cecum with surrounding inflammatory change in the retroperitoneal fat, seen as loss of normal hypodensity of fat. There is a mildly dilated ileal loop with enhancing wall. In Fig.7 there is a narrowed segment of bowel with thickened walls. Nodes, mesenteric and omental thickening can also be seen.

From the ulcers in the mucosa the bacilli may travel through the lymphatic channels to lymph nodes. Nodes may also be reached through the hematogenous route. Abdominal lymphadenopathy is the most common manifestation of abdominal tuberculosis. Ultrasound and CT can pick up nodes. The most commonly involved nodes are mesenteric nodes, omental nodes, nodes at the porta

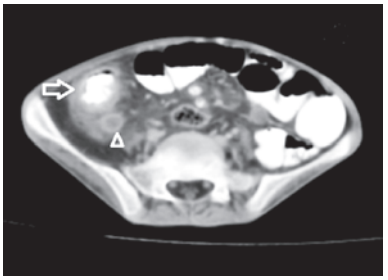

**Fig.6.Thickened cecal wall (arrow), ileal loop (arrowhead) with enhancing wall**

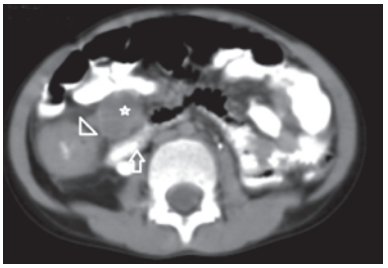

**Fig.7.Narrowed terminal ileal loop (arrow), thickened cecum(arrow head), nodes (*)**

hepatis, along the celiac axis and peripancreatic region. Enlarged nodes are seen as round or oval structures (Fig.7). Contrast enhanced CT may reveal peripheral enhancement with hypodense centres due to caseous necrosis.

Isolated abdominal solid organ involvement is uncommon. Mode of spread is by blood. The genitourinary system is the most commonly involved, followed by liver, spleen and pancreas and is more often seen in the young adult than in children because of the long latent period. Renal involvement is in the form of papillary cavitation, fibrosis causing infundibular stenosis, abscesses and even loss of renal function.

## NEWS AND NOTES

**55th National Conference of Indian Academy of Pediatrics**
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**CASE REPORT**

# LOWER GASTROINTESTINAL BLEED - A RARE CAUSE

***Sumathi Bavanandam**
****Nirmala Dheivamani**

**Abstract:** *Vascular malformations (VM) are rarely seen in children and clinical manifestations depend on site involved. Labia majora is the most common site of vascular malformations of pelvic region and less common sites include rectum, vagina, uterus and bladder. We report a girl with rectal bleed secondary to vascular malformation.*

**Keywords**: *Arteriovenous malformation, Hemangioma, Rectal bleed, Children*

Ten years old girl born of non- consanguineous parents presented with intermittent episodes of passing painless fresh bleeding per rectum of six months duration. There was no history of melena. She also complained of easy fatiguability and exertional dyspnea. She was anemic without any puffines of face, pedal edema or respiratory distress at rest. Her left thigh and gluteal region were bigger than the right with discrepancy of 5 centimeters width at mid thigh level and length discrepancy of 3 centimeters when compared to right. side. There was bluish skin discolouration and venous engorgement over left thigh area. External genitalia were normal. Haemic murmur was present on auscultation of the heart while other system examinations were normal. Investigations showed hemoglobin of 4.4gms/dL, total WBC count 5900 cells/ $mm^3$, P48% / L51% / E1% and platelet count 3.8 lakhs with a retic count of 5%. Peripheral smear study showed severe microcytic hypochromic anemia. Renal function tests, blood glucose, liver function tests, coagulation profile and urine routine were within normal limits. Doppler study of lower limbs showed absent great saphenous vein, dilated superficial veins with varicosities in left lower limb. She

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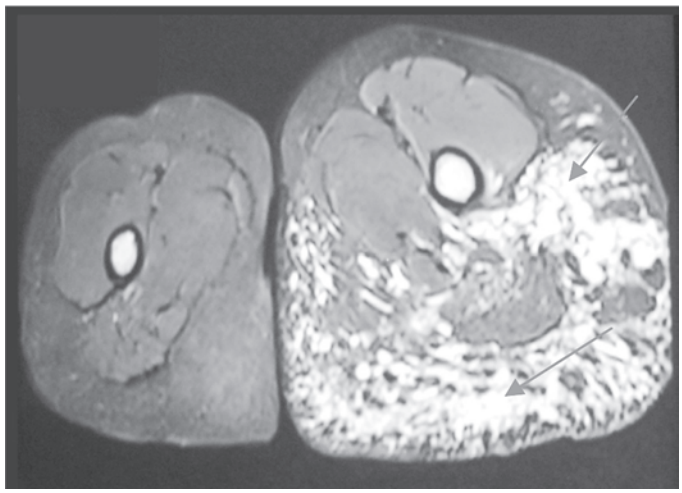

**Fig.1. MRI pelvis and thighs - Extensive vascular malformation (arrows)**

was hemodynamically stabilised with packed red cell transfusions. MRI abdomen with pelvis and thigh showed lobulated unencapsulated lesion in subcutaneous and intermediate plane of left sacrosciatic region along sacral plexus in the posterior aspect of pelvis involving left gluteal muscles, posterior compartment of left thigh up to the level of left knee joint consistent with venous vascular malformation without any identifiable feeders or draining veins (Fig.1). Upper GI endoscopy was normal. Colonoscopy showed bluish vascular lesions of varying sizes in proximal and distal colon. She was advised hematinics. As endovenous laser therapy is not available in our centre, she was referred for therapeutic intervention to a specialised gastro intestinal centre but the patient was lost for follow up.

## Discussion

Vascular malformations (VMs) as a cause of lower gastro intestinal bleed is less common in children. The outcome depends upon the site and severity of the bleed. VMs can occur as focal or diffuse lesions and are classified by flow characteristics and channel content. VMs are best categorized according to combined biological and radiological classification proposed by Mulliken, Glowacki in 1982 and later by Jackson.[1,2]

Slow-flow vascular malformations namely venous and lymphatic malformations are typically treated by

sclerotherapy whereas fast-flow arteriovenous malformations often require embolizations. Some VMs, such as VMs of the rectum or uterus, are best managed surgically. VM can be diagnosed by physical examination when the skin is involved as in this child or with increased pulsatility, bruit or thrill. Typically, these anomalies are caused by germ line or somatic mutations in the TIE2 gene, which is involved in signalling between the endothelial and the mesenchymal cells during vasculogenesis and angiogenesis.[3,4]

The most common site involved in the female pelvis is the perineum; especially the labia majora.[5] Less commonly, the rectal wall, vagina, uterus or bladder may be affected. Children with pelvic VM need follow up for puberty related and renal problems. Some of the syndromes like Klippel-Trenaunay syndrome and Parkes Weber syndrome typically affect a lower extremity and the adjacent pelvis. Classical features of Klippel-Trenaunay syndrome is a congenital disorder classically characterized by findings of a port-wine stain (nevus flammeus), abnormal venous structures (such as varicosities and slow-flow venous malformations) and osseous and soft-tissue hypertrophy and lymphatic abnormalities. Our child had venous malformation with limb hypertrophy with intermittent bleeding per rectum. Diffuse venous malformations of the lower extremities with extension into the perineum and buttock are typically associated with painful swelling and patients are at increased risk for venous thrombosis.[6] The clinical workup often requires tests like angiography, blood pool scan, magnetic resonance imaging, doppler studies and endo-sonography. MRI study shows increased signal intensity on T2 weighted images and venous malformations are generally septated lesions with intermediate to decreased signal intensity on T1-weighted images. Hemorrhage or thrombosis or high protein content phleboliths in venous channels can be appreciated.[7,8] Some of the treatment modalities include endovenous laser, percutaneous or endoscopic sclerosant injection or surgery.[9] Summarising, VMs can be focal or diffuse with varied clinical manifestations requiring characterization of the specific type of VM based on clinical and imaging findings which is essential for management.

## References


1. Mulliken JB, Glowacki J. Hemangiomas and vascular malformations in infants and children: a classification based on endothelial characteristics. Plast Reconstr Surg 1982; 69(3):412-422.
2. Jackson IT, Carreño R, Potparic Z, Hussain K. Hemangiomas, vascular malformations, and lymphovenous malformations: classification and methods of treatment. Plast Reconstr Surg 1993; 91(7):1216-1230.
3. Vikkula M, Boon LM, Mulliken JB. Molecular genetics of vascular malformations. Matrix Biol 2001; 20(5-6):327-335.
4. Boon LM, Mulliken JB, Enjolras O, Vikkula M. Glomuvenous malformation (glomangioma) and venous malformation: distinct clinicopathologic and genetic entities. Arch Dermatol 2004; 140(8):971-976.
5. Herman AR, Morello F, Strickland JL. Vulvar venous malformations in an 11-year-old girl: a case report. J Pediatr Adolesc Gynecol 2004; 17(3):179-181.
6. Krokidis M, Venetucci P, Hatzidakis A, Iaccarino V. Sodium tetradecyl sulphate direct intralesional sclerotherapy of venous malformations of the vulva and vagina: report of five cases. Cardiovasc Intervent Radiol 2011; 34:S228-S231.
7. Flors L, Leiva-Salinas C, Maged IM, Norton PT, Matsumoto AH, Angle JF, et al. MR imaging of soft-tissue vascular malformations: diagnosis, classification, and therapy follow-up. Radiographics 2011; 31(5):1321-40.
8. Ernemann U, Kramer U, Miller S, Bisdas S, Rebmann H, Breuninger H, et al. Current concepts in the classification, diagnosis and treatment of vascular anomalies. Eur J Radiol 2010; 75(1):2-11.
9. Christenson BM, Gipson MG, Smith MT. Pelvic Vascular Malformations. Semin Intervent Radiol 2013; 30(4):364-371.


## CLIPPINGS

***CHEO Researchers Identify Practices Leading to Safer Outcomes in Procedural Sedation for Children. www.sciencenewsline.com/news/2017082117580022.html***

When children and youth present at an emergency department and require an immediate painful procedure, it is standard to sedate the patient so they can tolerate the treatment. Procedural sedation is commonly used for painful or uncomfortable procedures like setting fractures, repairing lacerations and draining abscesses in emergency departments worldwide. The low rate of serious adverse events and significant interventions supports the safety of procedural sedation in the hands of emergency department physicians. While all sedation medications and combination of medications are effective and safe in the hands of experienced providers, ketamine-alone is associated with the fewest serious adverse events and significant interventions, making it a logical choice for providing procedural sedation for children in emergency departments.

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