Heart failure (HF) is a complex syndrome, with sinister implications once diagnosed, the mystery of which is still being unraveled despite decades of benchside and clinical research. Several definitions have been proposed for heart failure which again reflects our less than complete understanding of this enigma. A common definition used is: "HF is a pathophysiological state in which an abnormality of cardiac function is responsible for the failure of the heart to pump blood at a rate commensurate with the requirements of the metabolizing tissues, or does so only at elevated filling pressures". In case of children, this requirement includes growth and development.

The current American College of Cardiology (ACC)/American Heart Association (AHA) guidelines define HF as 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 blood. Our current understanding of HF is that of not just a case of cardiac dysfunction but that of a multi-organ syndrome which explains the myriad pathophysiological and clinical features that accompany it. While HF in adults has been the subject of voluminous research and generation of evidence-base, it has
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The pathophysiology and etiologies for heart failure in children are very different from those in adults. Common causes of adult heart failure including ischemia, hypertension and valvular inflammation are less common in children. Infants and children develop heart failure more commonly due to volume overload secondary to shunt lesions, and obstructive lesions of the heart. Less common causes include homeostatic abnormalities and cardiomyocyte dysfunction secondary to myocarditis / cardiomyopathies. Palliated congenital heart disease (CHD) leading to heart failure is increasingly being recognized.

With the aim of keeping this review focused on clinical aspects and management of heart failure, the pathophysiology of heart failure shall not be discussed in detail. Briefly, the manifestations of heart failure arise due to mismatch of the circulatory load and the ability of heart, or its components, to pump it in an adequate fashion. These can be accompanied or followed by compensatory changes in the regional perfusions and renal, muscular and endocrine physiology (notable among changes in virtually every organ). The outcome of this, manifesting as symptoms, is excess extracellular volume in lungs and periphery and decreased perfusion of vital organs like kidneys and brain as well as the muscles.

Causes of Heart Failure in Infants and Children

Children can have diverse causes of heart failure depending on the age, geographical location, and many other factors. Hence a descriptive epidemiology of heart failure in children is not possible. The causes of HF can be broadly classified into two groups; one due to volume overload of ventricle with preserved systolic function of the ventricle, the common example is heart failure secondary to a large left to right shunt. The second group consists of pressure overload, persistent arrhythmias, dilated cardiomyopathy and certain systemic disorders where the contractile function of ventricle is reduced (Table 1).

Table 2 enumerates the likely causes of heart failure by age at presentation. This is important, as the symptoms and signs of heart failure can be confusing or fairly non-specific in children. The lists are not all-exhaustive and the reader is referred to specialized books for complete enumeration of heart failure etiologies.

HF presenting on the first day of life are commonly due to metabolic abnormalities. Structural diseases that cause HF in neonates usually do not manifest on 1st day of life; rather it is the causes of fetal HF like Ebstein’s or abnormal heart rate/rhythm that predominate.

About 90% of all cases of HF in children occur before the end of first year of life and reflect the preponderance of CHD as a cause of HF. In the first week of life, obstructive and duct-dependent lesions can present with HF or acute circulatory shock. Development of HF due to left-to-right shunts usually waits the fall in pulmonary vascular resistance at 4-6 weeks, though large VSD, PDA, AVSD and aorto-pulmonary window can cause HF by 2nd week of life. Isolated ASD are mostly asymptomatic in children and if an infant is diagnosed to have ASD and is in failure, the likely diagnosis is TAPVC.

The myocardium perse is normal in most CHD and the heart failure, if not presenting in the first year, is unlikely to develop for the next 10 years unless complicated by infective endocarditis, anemia, infections or arrhythmias. Thus older children (usually beyond two years) are likely to have other causes for HF like acute rheumatic fever with carditis, decompensated chronic rheumatic heart disease, myocarditis, cardiomyopathies and palliated CHD (post Senning operation for transposition of great arteries or Fontan group of surgeries for univentricular hearts).

Epidemiology of Heart failure in Children

Epidemiology of heart failure in children is a difficult science given the fact that symptoms, etiology,
diagnostic criteria, and outcomes are quite heterogeneous. In Germany, a hospital based study at University Children’s Hospital at Essen studied the epidemiology of heart failure between 1989 and 1998. Heart failure occurred in 40% of all admissions for CHD and one-third of all admissions for all heart disease (congenital and acquired, n=1755); if post-operative congestive heart failure was excluded, HF accounted for a quarter of all CHD admissions. Incidence of HF was 289/1000 heart disease patients and 20.1/1000 of all pediatric inward admissions. In 70%, it occurred in the first year of life. Overall mortality in children with HF was 14%, more than double when compared to mortality in all heart disease patients. One large database from US found out that the heart failure in children (<18 years of age) was complicated by more frequent procedures, longer stay, but similar mortality as adults (7.5%). The cause was predominantly congenital heart disease in infants (<1 year of age) at 83% while it was present in only 34% in children older than 1 year of age. This study however was based on the findings of a large financial database that was exhaustive, but had limited clinical information available.

In developed countries, the annual incidence of CHD is about 8 per 1000 (0.8%) of live births, of which one-third to one-half are severe enough to warrant attention. Of these, about half result in CHF; thus due to CHD, the incidence of CHF is about 0.1-0.2% of all live births.

Ninety percent of all cardiomyopathies in children are of the dilated variety, others being hypertrophic and restrictive type. The reported population incidence of idiopathic DCM in children is 0.6/100, 000 children with recent studies showing 5 year rates of death or transplantation of 46%. More than 50% present within the first year of life. Children with myocarditis as a cause of DCM have a favorable prognosis, with 50-80% showing resolution within 2 years of presentation. The population based studies on childhood cardiomyopathies systematically excluded cardiomyopathies secondary to cancer drug therapy. At least in the past, anthracycline toxicity has accounted for 50% of admissions due to congestive cardiomyopathy in Boston Children’s Hospital.

Prevalence of heart failure in palliated or operated CHD cases is unknown. It has been estimated that 10-20% of operated cases with Mustard/Senning surgery for transposition of vessels and those with Fontan-type operation have symptoms of heart failure.

**Rheumatic fever/rheumatic heart disease** is an important cause of HF in children in developing countries like India. While the incidence and prevalence of RF/RHD are well documented, there are no data on presentation with HF in this group, though a significant majority of acute rheumatic carditis and established juvenile mitral stenosis will present with features of HF. The true incident of HF in children for India is not available but is likely to be enormous considering the huge burden of the problem of critical congenital heart disease in newborns and rheumatic heart disease in older children.

### Clinical features

The clinical features of HF in children vary according to the cause and the age of the child. The presentation of HF in fetus is that of hydrops fetalis and fetal wastage.

An important point to remember is that raised jugular venous pressure, peripheral edema, effusions and chest crepitations are not seen in neonates and are unlikely in young children as a sign of HF. Chest
crepitations in fact suggest the possibility of underlying chest infection, which so often accompanies HF in children especially in high pulmonary flow situations.

Common clinical features of HF in children are given in table 3. Certain features deserve mention:

- The clinical features of HF in a newborn can be fairly non-specific; sometimes the clinical picture resembles that of septicemia. Thus a high index of suspicion is required.
- Unequal upper and lower limb pulses, peripheral bruits or raised/asymmetric blood pressure indicating aortic obstruction (including non-specific aortoarteritis, NSAA), should always be looked for in a child with unexplained HF at any age.
- An interrupted aortic arch or coarctation of aorta (COA) in neonates can have normal femoral pulsations in presence of patent ductus arteriosus (PDA); when the ductus closes, these babies may present with acute shock.
- ACOA usually does not cause HF after one year of age, when sufficient collaterals have developed.
- Central cyanosis, even if mild, associated with HF and soft or no murmurs in a newborn, should always be taken seriously (suggests transposition of great arteries with intact septum, obstructed total anomalous pulmonary venous connection etc).
- An ASD or VSD does not cause HF in first 2 weeks of life; their presence with HF should prompt evaluation for associated TAPVC or COA respectively.
- A premature newborn with significant respiratory distress and a systolic murmur should be evaluated for patent ductus arteriosus causing HF.
- Heart rates above 220/mt are unusual in a neonate even with HF and should always be investigated to rule out tachyarrhythmias as a cause of HF.
- Several children with CHD or cardiomyopathies have associated chromosomal anomalies or extracardiac manifestations which provide clues for diagnosis.
- Older children with TOF physiology can have HF due to complicated course (anemia, infective endocarditis, bicuspid aortic valve with aortic regurgitation) or overshunting from aortopulmonary shunts.

Investigations

The cornerstones for rapid clinical diagnosis of HF in children are chest radiograph and an electrocardiogram.

Chest radiograph: Should be done in all patients with suspected HF; an echocardiogram is not a substitute for
radiograph. It enables diagnosis of cardiomegaly, quantification of pulmonary blood flow, presence of associated chest infection, pleural effusion etc., as well as being pathognomonic in certain disease states. A cardiothoracic ratio of >60% in neonates and >55% in older children suggest cardiomegaly though expiratory films should be interpreted with caution. A large thymus can also give false impression of cardiomegaly in neonates and infants (Fig. 1). Cardiomegaly with increased pulmonary blood flow (pulmonary plethora), prominent main and branch pulmonary arteries, left atrial enlargement etc. are signs of significantly increased pulmonary blood flow (a finding not appreciable on echocardiogram!) which could cause HF (Fig. 2). Typical radiographs strongly suggestive of certain diagnosis include those with transposition of great arteries (egg-on-side, Fig. 3), obstructed TAPVC (snowstorm appearance, Figure 4), unobstructed TAPVC (Fig. of 8 appearance, Fig. 5), truncus arteriosus (waterfall appearance of hila, Fig. 6), Ebstein’s anomaly (globular cardiomegaly with decreased pulmonary flow), CCP (calcification in RV/AV groove), juvenile mitral stenosis (left atrial appendage enlargement), etc.

Heart Failure in Children: Clinical Aspect and Management

Fig. 1. X-ray chest of a normal neonate with a large thymus.

Fig. 2. Chest radiograph showing cardiomegaly, prominent pulmonary artery segment and increased pulmonary blood flow in a case of large VSD.

Fig. 3. Chest radiograph of a newborn with transposition of great arteries (egg-on-side).

Fig. 4. Chest radiograph of a newborn with obstructed TAPVC showing the ‘snow-storm’ appearance.

Fig. 5. Chest radiograph in an older child with unobstructed TAPVC showing the typical ‘figure of 8’ appearance of mediastinum.

Electrocardiogram: An electrocardiogram is very useful in heart failure for elucidation of cardiac diagnosis. It shows biventricular hypertrophy with volume overload of the left ventricle in the commonest cause of HF in the infant i.e. a large VSD. Tachycardiomyopathy, a
potentially reversible cause of HF, due to incessant supraventricular tachycardias (like ectopic atrial tachycardia) can only be picked up by ECG (Fig. 7). Similarly bradyarrhythmias due to congenital complete heart block are detected on ECG (Fig. 8). Certain patterns on ECG are also virtually diagnostic of specific cardiac pathologies. Thus ALCAPA can present with pathognomonic pathologic q waves in anterolateral leads (Fig. 9). A superior or northwest axis with BVH suggests atrioventricular septal defect as a cause of HF (Fig. 10). In a neonate with unexplained HF, a prolonged QTc interval with terminal T wave inversion

Fig. 6. Chest radiograph in an infant with persistent truncus arteriosus.

Fig. 7. Electrocardiogram of a child presenting with heart failure due to atroventricular re-entrant tachycardia at the rate of 200 beats per minute. Arrows point to P waves. Note that RP interval is shorter than PR interval.

Fig. 8. Holter trace of an infant with bradycardia (ventricular rate of 40 beats per minute) due to congenital complete heart block. Note that there is no relationship between P waves and QRS complexes.

Fig. 9. Electrocardiogram of a child with ALCAPA showing presence of pathologic q waves and ST – T changes (arrows) in lateral leads.

Fig. 10. Electrocardiogram of a child with atrioventricular septal defect showing left axis deviation and right ventricular hypertrophy.

Fig. 11. Electrocardiogram from a child with hypocalcemia showing long QTc interval and bizarre, inverted T waves (white arrow).
Heart Failure in Children: Clinical Aspect and Management

are suggestive of hypocalcemia as the cause of left ventricular dysfunction (Fig. 11).

Echocardiogram: An echocardiogram is invaluable in the diagnosis of heart failure. It confirms the presence of structural heart disease and great vessel anomalies and aids in the acute and long term management strategy. While an echocardiogram is essential for diagnosis of heart disease in HF, as mentioned above, it should always be interpreted in an integrated fashion with clinical, radiographic and ECG findings. Owing to its dependence on operator skills and inherent problems of imaging small children, an echo can miss findings such as TAPVC and aortic arch anomalies. However echo by a skilled echocardiographer is adequate for diagnosis and initial management of practically all diseases causing HF.

Other investigations

B-type natriuretic peptide (BNP): BNP, a cardiac natriuretic hormone, secreted in escalating fashion in ventricular dysfunction and progressive HF, is increasingly used in acute settings for differentiation of HF from pulmonary causes of respiratory distress. While its utility in adults is established, its incremental value in pediatric patients is still investigational. Plasma BNP elevation is a reliable test however for ascertainment of etiology of myocarditis and also constitute evaluation of HF in a newborn. Work-up for hypoxia and sepsis are suggestive of hypocalcemia as the cause of left ventricular dysfunction (Fig. 11).

Hemoglobin is important in diagnosis of HF in children; while protracted values around 5 gm/dl can cause HF even with a normal heart, hemoglobin of 7-8 gm/dl can cause decompensation in cases with underlying heart disease but no HF. Electrolytes like serum calcium, phosphorous and blood glucose should be routinely measured in all children with HF, especially neonates, where their abnormalities are an uncommon but reversible cause of ventricular dysfunction. Similarly screening for hypoxia and sepsis also constitute evaluation of HF in a newborn. Work-up for ascertainment of etiology of myocarditis and cardiomyopathy is exhaustive and detailed elsewhere. ASO (anti-streptolysin O) and CRP (C-reactive protein) are invaluable in work up for diagnosis of suspected primary attack of rheumatic fever (RF) or recurrence of RF in cases with rheumatic heart disease.

Staging the severity of Heart Failure

While several systems exist for grading severity of HF in adults, including universally known New York Heart Association Class, it is difficult to grade HF or apply these classifications in children especially infants. A common system followed is that advocated by Ross for classification of heart failure (Table 4) and scoring its severity (not shown).

Table 4. Ross Classification of Heart Failure in Infants

<table>
<thead>
<tr>
<th>Class</th>
<th>Description</th>
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<tbody>
<tr>
<td>I</td>
<td>No limitations or symptoms</td>
</tr>
<tr>
<td>II</td>
<td>Mild tachypnea or diaphoresis with feeding in infants</td>
</tr>
<tr>
<td>III</td>
<td>Marked tachypnea or diaphoresis with food or exertion</td>
</tr>
<tr>
<td>IV</td>
<td>Symptoms at rest with tachypnea, retraction, grunting or diaphoresis</td>
</tr>
</tbody>
</table>

Management of Heart Failure

The management of HF in children can be divided into following categories:

1. CHD presenting with acute shock, where immediate treatment (pharmacologic, percutaneous, or surgical) is required

In neonatal period several causes of HF can present with acute circulatory collapse or progress to shock if not recognized early. These can be due to

- A closing ductus where antegrade systemic flow is compromised, for e.g., tight COA, interruption of aortic arch, critical AS, HLHS, and TGA with intact septum and restrictive inter-atrial communication. These disorders require maintenance of duct patency with prostaglandin infusion till the time more definitive treatment can be employed. This consists of percutaneous procedures for critical AS (valvuloplasty), TGA (balloon atrial septostomy) as well as surgical procedures for neonatal COA, HLHS etc. In cases where surgery for COA is not possible due to severe comorbid conditions, a balloon dilatation is performed, although the restenosis rates are likely to be higher.

- Conditions like mitral atresia (requiring emergency atrial septostomy) and obstructed TAPVC (requires emergency surgery) can cause severe elevations in pulmonary venous pressure and have similar consequences.

- Non-cardiac cause of neonatal HF, tachyarrhythmias and neonatal myocarditis can also rapidly progress to shock if not managed early.

- Lesions like AS, PS and COA, if associated with corresponding ventricular dysfunction or heart failure should undergo urgent relief of obstruction, irrespective of magnitude of gradient at baseline.

Because these children are very sick, they should be transferred to tertiary centers with expertise in their care, after initial resuscitation and prostaglandin infusion (if required). They require intensive monitoring because of frequent co-morbidities and likely
requirement of ventilation (due to pulmonary edema, chest infections or due to apnea as an adverse effect of prostaglandin therapy)

2. CHD awaiting surgery where medical treatment is applied for stabilization and alleviation of symptoms- short-term medical therapy

This is a very common group because except some VSDs and PDA in premature babies (which may close spontaneously), most of CHDs causing HF require surgical intervention. These children present with HF and frequently have co-morbidities like sepsis or chest infection. They tolerate repeated bouts of HF and chest infection (which enters into a vicious cycle with HF) poorly and should undergo surgery or nonsurgical catheter intervention promptly after stabilization of medical condition. These conditions include

- Large VSD/PDA/AVSD/Persistent truncus arteriosus with uncontrolled CHF or history of life threatening infection
- Severe AS or COA
- TGA with IVS and prepared LV
- Uneobstructed TAPVC.

3. CHD requiring long term medical therapy

Several causes of HF in children require prolonged medical therapy because of tendency for spontaneous resolution or a cure for the condition in long term or due to the fact that the surgical treatment is problematic.

- Ventricular septal defect is one of the commonest causes for HF after the neonatal period, in infancy. About 10% of non-restrictive VSD die in 1st year of life, primarily due to CHF. However up to 30-40% of small or moderate sized defects close spontaneously (mostly by 3-5 years of age) and 25% decrease in size. A minority of VSD with large L-R flow can also close spontaneously. Thus at least some VSD presenting in infancy with less than severe HF can be judiciously followed on medical therapy and watched for spontaneous closure. Similarly, small PDAs in term babies until 3 months of age, and those in premature babies not in HF (with or without the use of indomethacin) may be observed for spontaneous closure.

- Myocarditis in children is a potentially reversible cause of HF provided the acute phase is cared for with the best available medical care (ventricular assist devices, if necessary). Similarly some uncommon causes of cardiomyopathies (e.g. carnitine deficiency associated) can be treated effectively with supplementation.

- Some conditions like congenital mitral stenosis are problematic to manage in infancy and it is prudent to defer surgery till later if the child is growing normally.

4. Long-term therapy in cases with irreversible myocardial dysfunction or where no other definitive therapy can be offered.

Finally, there is the group of conditions causing HF where there is established myocardial dysfunction. This can be due to cardiomyopathies (primary and secondary), decompensated systemic ventricle (SV physiology, cTGA), and following palliative surgeries. This group displays the whole spectrum from asymptomatic ventricular dysfunction to decompensated HF and requires long term medical therapy. HF therapy is also required long term in residual defects following surgery and in valvular diseases where the risk-benefit ratio is not in favour of surgery.

**Drugs for Treatment of Heart Failure**

Management of CHF in children is complex because of frequent presence of structural heart disease (on which medical treatment has little effect) and variable presentation and spontaneous resolution of some diseases. On the other hand, advances in medical science have ensured a wide variety of evidence-based and emerging therapies for treatment or palliation of HF (Table 5). There are several newer agents, the roles of which are still investigational, in adults and in children. These include natriuretic peptides (e.g., nesiritide), calcium sensitizers (e.g., levosimendan), vasopressin antagonists (e.g., tolvaptan), renin inhibitors (e.g., aliskiren), endothelin antagonists (e.g., sitoxentan) etc. Some like oral phosphodiesterase inhibitors, anti-inflammatory molecules, nitric oxide agonists, and neuropeptidase antagonists have not proven useful or found to have excess side-effects.

Most of this evidence base has been generated in adults in whom randomized trials usually happen

**Table 5. Treatment Options for Chronic Heart Failure**

<table>
<thead>
<tr>
<th>Established Pharmacotherapy</th>
<th>Investigational Treatments</th>
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<tbody>
<tr>
<td>ACE Inhibitors</td>
<td>Angiotensin receptor blocker</td>
</tr>
<tr>
<td>Beta-blockers</td>
<td>Nesiritide</td>
</tr>
<tr>
<td>Digoxin</td>
<td>Levosimendan</td>
</tr>
<tr>
<td>Aldosterone antagonists</td>
<td></td>
</tr>
<tr>
<td>Anticoagulants (with severe ventricular dysfunction)</td>
<td></td>
</tr>
<tr>
<td>Cardiac transplantation</td>
<td></td>
</tr>
<tr>
<td>Surgery</td>
<td></td>
</tr>
<tr>
<td>Definite (for structural disease)</td>
<td>Ventricular remodeling</td>
</tr>
<tr>
<td>Ventricular assist devices</td>
<td>Cardiac resynchronization therapy</td>
</tr>
<tr>
<td>Extracorporeal membrane oxygenation</td>
<td>ICD</td>
</tr>
<tr>
<td>Intermittent ionotrope infusion (weekend pulsed dobutamine)</td>
<td>Stem cell therapy</td>
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</table>
earlier. Conducting such trials in children has been difficult on account of ethical issues and logistical problems. While treatment of HF in children is often extrapolated from that in adults, this may not be accurate owing to different pathophysiology and etiology of HF in children. These dilemmas are exemplified by the recently published randomized controlled trial for carvedilol in children with HF, where beta-blockade did not improve outcomes over those with placebo. While smaller uncontrolled studies earlier had shown significant benefit with carvedilol, the neutral results of this trial were presumably due to inadequate sample size (due to high rate of spontaneous improvement in placebo group) and heterogeneous effect of drug on type of systemic ventricle (beneficial in systemic left ventricle only). Tables 6-8 outline the treatment of heart failure in children and dosages of common drugs used for treatment in acute and chronic settings.

**Table 6. Treatment Algorithm for Acute Heart Failure in Neonates**

<table>
<thead>
<tr>
<th>Supportive measures</th>
<th>Avoid hypothermia and hypoglycemia, check for hypocalcemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maintenance of adequate oxygenation</td>
<td>Monitoring of blood gases if perfusion is poor Ventilate, if required, with modest PEEP to achieve PaO2 of 50-60 mmHg and SaO2 of 75-85% to avoid pulmonary congestion</td>
</tr>
<tr>
<td>Adequate hydration</td>
<td>Stop oral feeds if severe tachypnea</td>
</tr>
<tr>
<td>Intravenous access for shock</td>
<td>I/V and CVP lines (umbilical vein cannula)</td>
</tr>
<tr>
<td>Milrinone</td>
<td>Ionotrope and vasodilator</td>
</tr>
<tr>
<td>Diuretics</td>
<td>Load with 25-50 mcg/kg/min. maintain at 0.25-1 mcg/kg/min</td>
</tr>
<tr>
<td>Vasodilators</td>
<td>Captopril 0.1-1 mg/kg/day PO q 8hrly Sodium nitroprusside 0.5-4 mcg/kg/min IV</td>
</tr>
<tr>
<td>Prostaglandin infusion for ductus-dependent lesions</td>
<td>Start at 0.1 mcg/kg/min (uptil 0.4 mcg/kg/min if no response), taper to lowest dose possible (0.005 mcg/kg/min) Monitor for apnea, keep minimum required dose</td>
</tr>
</tbody>
</table>

**Management of Heart Failure: Important Issues in children**

- Treatment of HF in children, like in adults, should consist of treatment of the cause, precipitating factors (like anemia, infective endocarditis, infections, acute rheumatic fever, non-compliance with drug or diet, arrhythmias, etc), and treatment of the congested state.
- Digoxin has a very narrow safety window in children and adults alike. It should be avoided in premature babies, those with renal compromised state and cases with acute myocarditis. Electrolytes (K⁺, Ca++, Mg++) should be carefully monitored to avoid potentiation of toxicity and development of arrhythmias (which are more often bradyarrhythmias in children).
- Generally initial total digitalization is not performed. One can start directly to oral maintenance dose at 10 mcg/kg/day (The available digoxin elixir has 50 mcg/ml, hence the dose is 0.1 ml/kg twice daily).
- Continuous infusion of diuretics is recommended in cases of acute decompensated heart failure (ADHF). Monitoring and supplementation of K⁺ is necessary at higher doses, as deficiency is associated with increased arrhythmic death.
- During early infancy supplementation of potassium is usually not required uptil 2mg/kg of dose for furosemide or equivalent. In these cases we...
give the parental preparation of furosemide orally for logistic reasons as furosemide syrup is not available in our country. In other cases requiring higher doses and in older children, we usually give a combination of loop diuretic and spironolactone (or other potassium sparing diuretics). In cases requiring chronic therapy, development of diuretic resistance is quite common. Addition of low dose dopamine may help in this situation by increasing renal blood flow.

- ACE Inhibitors should be avoided in HF caused by lesions having pressure overload physiology e.g. in aortic stenosis, as they might interfere with compensatory hypertrophy. The incidence of ACE Inhibitor induced cough is much less in children as compared to adults.

- Beta blockers should not be administered in acute decompensated heart failure. They should be started once child is stable at low dose, and slow up-titrations (once every two weeks through 4 levels according to pediatric carvedilol study group trial) should be done as this determines the occurrence and degree of side effects. In case up-titration is not tolerated, lower doses should be continued rather than discontinuing the drug. In the carvedilol trial, overall about 20% children had worsening of HF in both carvedilol and placebo population, of which 11% each withdrew from the study due to this.

- Persistently high heart rates (>180/min in older children) with absence of normal variability during sleep or exercise should always be investigated to rule out tachycardiomyopathy as the cause of HF.

**Myocarditis/Cardiomyopathy**

Acute myocarditis and pediatric cardiomyopathy deserve a special mention as despite intensive research they still are an enigma and a challenge to clinicians. Many clinicians view acute myocarditis and cardiomyopathy in children as a continuum; indeed a large study in North America found myocarditis as the most common cause of cardiomyopathy (46%) 8. This however increases the ambiguities in the diagnosis of myocarditis especially the relevance and indications of tissue diagnosis by endomyocardial biopsy. Several small studies have been conducted with immunoglobulin and immunosuppressive therapy in children with acute myocarditis. However robust trials are few, with the outcome that there still is no consensus on use of these therapies 16, 17. Of note, studies in myocarditis indicate a high prevalence of resolution of cardiomyopathy in 2 years to the tune of 50-80% 18. Children with fulminant myocarditis with a high chance of recovery, do well when put on extracorporeal membrane oxygenation (ECMO) and ventricular assist devices 19, 20. These findings suggest that a diagnosis of myocarditis is a positive prognostic factor in children with HF even if requiring mechanical support. Therefore circulatory assist devices, if available, should be used aggressively in these children.

**Cardiac transplantation**

Heart transplantation has been used for treatment of end-stage heart disease in children for nearly 4 decades with first infant transplant done in late 1960s. Around 350 pediatric cardiac transplantations are done annually, representing about 10% of total cardiac transplantations. Majority of the transplantations are carried out for end-stage heart disease due to cardiomyopathies. Other causes include congenital heart diseases like hypoplastic heart syndrome and other complex CHD, single ventricle, palliated heart disease, etc. One year survival has approached 90% and estimated conditional graft half-life is about 17.5 years in younger children (in comparison immediate waiting list mortality is about 20%18). However, given the fact that the surgery is done in few centers globally and the available donor hearts have remained static over last many years to few hundreds, it is clear that heart transplantation can be a solution for a minority only.

**Stem Cell Therapy**

A heightened interest has developed in stem cell therapy for heart failure. Several trials have been completed, or are ongoing in adults with HF, predominantly due to ischemic heart disease. Stem cell therapy has been also used for non ischemic cardiomyopathy at our center 21, and is being investigated worldwide under experimental settings, including our center, for children with refractory heart failure who are not candidates for transplantation.

**CONCLUSION**

HF in children is a complex syndrome with heterogeneous etiology and presentation. Unlike adults, HF in children is commonly due to structural heart disease and reversible conditions, thus lending it amenable to definitive therapy or short term aggressive therapy. Thus the overall outcome with HF is better in children than that in adults. Clinical presentation of HF in younger children can be non-specific requiring heightened degree of suspicion. In particular, some conditions that can present with acute shock are important to recognize, as they can be effectively treated or palliated on an urgent basis. While the general principles of management are similar to those in adults, there is a dearth of evidence base in pediatric heart failure. It would require a judicious balance of extrapolation from adult medicine (thus avoiding...
generation of redundant evidence) and development of children specific treatments (thus recognizing the inherent differences in HF of children and adults) to optimize the outcomes in this challenging field.

REFERENCES

1. Ramakrishnan S, Kothari SS, Bahl VK. Heart Failure-Definition and Diagnosis. Indian Heart J 2005; 57:13-20
17. Hia CP, Yip WC, Tai BC, Quek SC. Immunosuppressive therapy in acute myocarditis: an 18 year systematic review. Arch Dis Child 2004;89:580-584
18. Canter CE, Shaddy RE, Bernstein D et al. Indications for Heart Transplantation in Pediatric Heart Disease: A Scientific Statement from the American Heart Association Council on Cardiovascular Disease in the Young; the Councils on Clinical Cardiology, Cardiovascular Nursing, and Cardiovascular Surgery and Anesthesia; and the Quality of Care and Outcomes Research Interdisciplinary Working Group. Circulation 2007;115:658-676