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Great Ormond Street Hospital for Children

NHS Trust

Arrhythmias and Cardiac Pharmacology

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Updated: GOSH Cardiac ITU, Troy Dominguez, February 2009

Information for Year 1 ITU Training (basic):

Year 1 ITU curriculum

Pathophysiology:

- Recognition and emergency treatment of life-threatening disorders of cardiac rhythm
- Anti-arrhythmic drugs: classification, indications, side effects and complications
- Arrhythmogenic drugs

Investigations:

- ECG : Arrhythmias : Atrial tachycardia, WPW, SVT, JET, Block.
- ECG changes with ischaemia, pulmonary embolus.

Pharmacology:

- Basic pharmacologic principles covered in "Pharmacology & overdose" module.
- Understand the basic effects & method of action of drugs that act on the heart and cardiovascular system: inotropes, chronotropes, vasodilators, vasoconstrictors, antihypertensives, diuretics.

Reading :

- Key articles are listed in the text
- Article PDF files are stored in the accompanying folder
- CCC Guidelines
- BNF for children
- Chang Wessel Wernovsky, Practice of Cardiac Intensive Care
- GK Siberry and R Iannone The Harriet Lane Handbook. Fifteenth Edition. The Johns Hopkins Hospital 'Techniques to assess cardiac function. Interpretation of the pediatric EKG'

Curriculum Notes for Year 1:

ARRHYTHMIAS

ATRIAL FLUTTER

Defining Characteristics

- Congenital atrial flutter is seen in the perinatal period and usually completely resolves with treatment if the heart is structurally normal.
- Atrial flutter and atrial re-entry tachycardias are seen in patients who have undergone atrial surgery such as repair of ASD, AVSD, Senning, Mustard and Fontan operations. These may occur at any time after surgery including late during medical follow up
- Sinus node dysfunction and Atrial fibrillation can also occur in these patients

Electro-physiology and Typical ECG Changes

Atrial flutter involves a single large circuit of re-entry within atrial muscle, and is one of the most common forms of tachycardia encountered in children with congenital heart disease.

Surface ECG demonstrates abrupt onset of a rapid atrial rhythm that remains quite regular over time. AV conduction pattern is variable (1:1, 2:1)

- The atrial flutter rate in young infants may be up to 350 beats per minute (bpm) and in adolescents may be less than 180 bpm. When atrial impulses are transmitted to the ventricles with a degree of AV block, flutter waves may be visible on the ECG. Hidden p waves may be detected by performing an atrial electrogram or by producing transient AV block with a dose of adenosine. Atrial fibrillation is associated with rate of 350-600 bpm.
- Atrial electrogram may be recorded as follows: Unipolar recording by connection of the leads as for a 12 lead ECG. Connect V1 to the atrial pacing wires. Record ECG and print off the 3 lead tracing of: V1 V5 and AVF. Bipolar recording by connection of the legs as for a 12 lead ECG. Connect lead 1 to one atrial wire and lead 2 to the other. Recording lead 1 will produce an atrial electrogram.

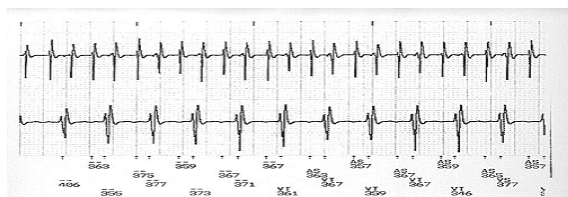
Clinical Features and Treatment

- Atrial flutter or atrial re-entry tachycardias with 1 to 1 conduction require urgent treatment with synchronised cardioversion (0.5 joules per kg). Sinus node dysfunction may follow cardioversion and facilities for temporary pacing should be made available.
- If there is AV block present then the haemodynamics may well tolerate a more time consuming approach and atrial overdrive pacing should be considered. If this is unsuccessful or unavailable, cardioversion (as above) is another good treatment option.
- In cases that are resistant to the above interventions, amiodarone therapy is indicated. This is given as a slow loading dose 25 mic/kg/min for 4 hours followed by 5-15 mic/kg/min. Once the patient is loaded with amiodarone they may revert to sinus rhythm alternatively cardioversion may be successful.

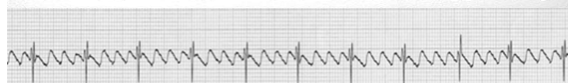
Key References

Lisowski LA, Verheijen PM, Benatar AA, et al. Atrial flutter in the perinatal age group: diagnosis, management and outcome. J Am Coll Cardiol. 2000 Mar 1; 35 (3): 771-7. Retrospective review of 44 neonates. All had atrial flutter either in utero or postnatally. Hydrops was present in 20 of 44. Of neonates who underwent cardioversion, 90% resolved without recurrence.

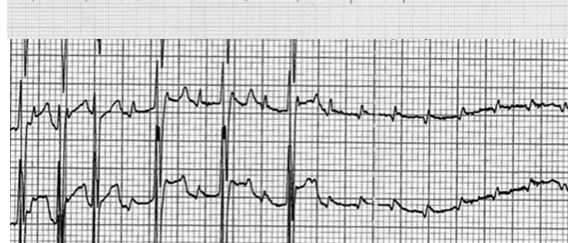
Till JA. Early postoperative arrhythmias. A review of postoperative arrhythmias including details of aetiology, diagnosis and treatment. First section on atrial based arrhythmias.



Atrial Flutter with 2:1 Block



Atrial Flutter with 3:1 Block



Flutter Waves Evident after Adenosine

SINUS NODE DYSFUNCTION

Defining Characteristics

- Acute sinus node dysfunction may occur in post-operative cardiac patients. Typically after the Fontan operation (as a result of atrial distension), repair of sinus venosus ASD, anomalous pulmonary venous drainage repair and Mustard / Senning operation.

Electro-physiology and Typical ECG Changes

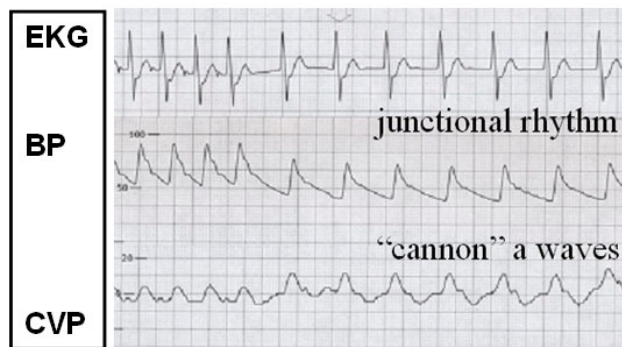
- A slow junctional escape rhythm is seen. This may predispose to atrial flutter and atrial re entry tachycardia.

Clinical Features and Treatment

- Early after cardiac surgery this may (but not always) result in haemodynamic compromise, particularly if it occurs with other adverse factors or in a patient with single ventricle. If intervention is required, the treatment is demand atrial pacing (AAI). Alternatively, isoprenaline infusion may restore sinus rhythm.

Key References

- Till JA. Early postoperative arrhythmias. A review of postoperative arrhythmias including details of aetiology, diagnosis and treatment.



AV BLOCK

Defining Characteristics

- Complete AV block as a result of iatrogenic conduction tissue damage is the most common indication for permanent pacing in childhood. This is more likely when surgical intervention involves sutures or other intervention around the conduction system. Cardiac lesions at risk include perimembranous VSD and subaortic obstruction. In complex abnormal hearts the conduction tissue may have an atypical configuration that renders avoidance more challenging.

Electro-physiology and Typical ECG Changes

- First-degree block is a prolonged PR interval. Normal PR interval depends on heart rate and age (upper limit 0.12 – 0.21 seconds). This can arise after complex intra atrial surgery or interventions around the AV node. (ASD, TAPVD, Tricuspid Atresia, Ebsteins and L-transposition)
- Second-degree block (Wenckebach type 1) is rare and is where the PR interval progresses until a QRS complex is dropped. Most commonly occurs after surgery involving the tricuspid valve annulus and AV junction.
- Third degree or complete AV block can occur in pre-operative patients with L looped transposition and left atrial isomerism. Post-operative block is most common after VSD, L transposition, subvalvar aortic obstruction including Konno procedure, AVSD and tetralogy.

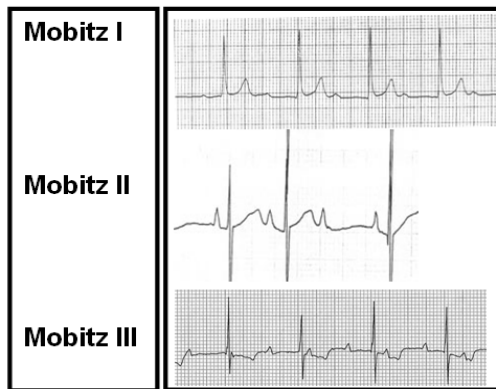
Clinical Features and Treatment

- Fortunately complete block is often transient and recovery usually occurs by the third post-operative day. During the period of block the treatment is pacing, preferably AV sequential. Details regarding pacing are provided below in the pacing section below.
- Prior to introduction of pacemakers; surgically induced heart block had a poor prognosis with up to 50% mortality in the first postoperative year.

Key References

- Weindling SN, Saul JP, Gamble WJ et al. Duration of complete heart block after congenital heart disease surgery. Abstract - J Am Coll Cardiology 1994: 104A A 3 year experience of complete heart block. Complete heart block was observed in 54 of 2698 (2%) cardiac surgery patients. Eventual recovery occurred in 63%. Block persisting

beyond the 10-14th day did not recover. So there is little to be gained by delaying implantation of a permanent pacemaker after this time period.



JUNCTIONAL ECTOPIC TACHYCARDIA OR HIS BUNDLE TACHYCARDIA

Defining Characteristics

- Commonly seen in patients less than one year of age. Acquired post-operatively. Occurs early 6-72 hrs post bypass. Most commonly after repair of Tetralogy, VSD, AVSD, TGA, TAPVC and Fontan.

Electro-physiology and Typical ECG Changes

- JET is classically recognized as a narrow QRS tachycardia (160-260/min) with AV dissociation, and ventricular rate greater than atrial rate.
- Usually occurs 6-72 hours post cardiopulmonary bypass. Nodal inflammation and ischaemia may be present and ventricular function is often diminished.
- Surgery to AV junctional area damages components of the AV node or HIS bundle causing tissue trauma and changes in cell membrane ionic integrity leading to enhanced automaticity.
- JET is driven by a focus within or immediately adjacent to the atrioventricular (AV) junction of the cardiac conduction system (i.e., AV node–His bundle complex), but does not have the features associated with re-entrant tachycardia (e.g., AV node re-entry). The ectopic focus emits impulses at a rapid rate, which are conducted 1:1 down the His-Purkinje system; thus ventricular activation is normal. At the same time the atrium is activated by the normal sinus impulses, at a much slower rate. Thus, there is AV dissociation, except for sinus capture beats resulting from occasional antegrade conduction of a normal sinus impulse, causing the next QRS complex to occur slightly earlier than expected. Such capture beats, since they utilize the same His-Purkinje system as the junctional focus; will occur with an identical QRS morphology to that seen with the underlying JET.
- The tachycardia may or may not have ventriculoatrial (VA) dissociation.
- In young patients, the AV node has the capacity to conduct rapid junctional rates in a retrograde fashion (particularly in the presence of inotropic agents)
- The 2 ECG patterns typically observed are
 - Junctional rhythm with 1:1 retrograde VA conduction
 - Junctional rhythm with retrograde VA dissociation.
- Administration of adenosine results in VA dissociation without termination.
- The tachycardia does not respond to a single extra stimulus and does not convert with programmed stimulation or cardioversion.

Clinical Features and Treatment

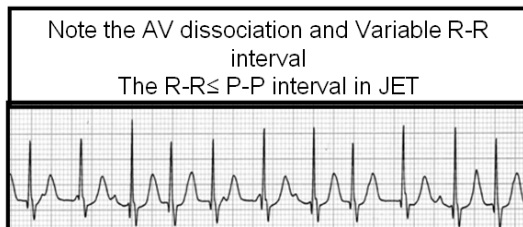
- Tolerance of JET is variable. Not all patients "suffer" from their JET: good haemodynamics may be maintained with volume to assure adequate filling and optimal general critical care. If the patient is compromised, there will be signs of low cardiac output syndrome. Tolerance of JET will be worse if there are residual cardiac lesions of

ventricular dysfunction including diastolic dysfunction. If AV synchrony is restored, the cardiac output and blood pressure will increase. JET usually resolves after a few days of 'healing.'

- Numerous therapeutic options have been used for the treatment of postoperative JET.
- Controlled hypothermia to 34-35°C has been relatively effective in reducing JET rate in early postoperative patients. Other traditional approaches include increase of ventricular preload and reduction of inotropic agents (which are also usually chronotropic) as much as possible. Electrolyte abnormalities, metabolic acidosis must be treated.
- Postoperative JET has been successfully controlled with amiodarone – this inhibits AV conduction and sinus node function. Prolongs action potential and refractory period in myocardium and inhibits adrenergic stimulation.
- Once the JET rate is reduced, the use of atrial or AV sequential pacing can help to restore AV sequence and cardiac output.
- Low magnesium levels have been noted in children who develop JET following cardiopulmonary bypass surgery.
- Occasionally, atrial high-rate pacing to the point of 2:1 AV block can provide a controlled ventricular response while continuing to suppress the JET focus. This finding suggests a relatively high insertion site of the JET focus into the AV conduction system.
- The primary functions of surgical care in postoperative JET are to correct major residual defects that may be contributing to morbidity, to ensure that atrial-based pacing can be achieved, and to provide extracorporeal life support [ECMO] if required.

Key References

- Dodge-Khatami et al. Surgical substrates of postoperative JET in congenital heart defects, JTCVS, 2002; 123:624-30. JET occurred most frequently after repair of tetralogy of Fallot (n = 25; 21.9%), 6 after repair of VSD (3.7%), and 6 after repair of AVSD (10.3%). Stepwise logistic regression revealed that resection of muscle bundles, higher bypass temperatures and relief of right ventricular outflow tract obstruction through the right atrium significantly and independently predicted postoperative JET. Relief of RVOT obstruction appeared to be more important in the causation of JET than VSD closure, which probably explained the higher incidence of this complication after tetralogy of Fallot repair. Muscular resection seems to be more arrhythmogenic than is simple division. Increased traction through the right atrium for relief of right ventricular outflow tract obstruction would fit the hypothesis that enhanced automaticity of the His bundle, the morphologic substrate for JET, may result from direct trauma or infiltrative haemorrhage of the conduction system.
- Hoffman TM et al. Postoperative JET in children: incidence, risk factors, and treatment. Ann Thorac Surg. 2002 Nov; 74(5): 1607-11. A nested case-cohort analysis of 33 patients (5.6%) who experienced JET from 594 consecutively monitored patients who underwent cardiac operations. Univariate and multivariate analyses to determine factors associated with the occurrence of JET. The age range was 1 day to 10.5 years (median, 1.8 months). Univariate analysis revealed that dopamine or milrinone use postoperatively, longer cardiopulmonary bypass times, and younger age were associated with JET. Multivariate modelling elicited that dopamine use postoperatively and age less than 6 months were associated with JET. Only 13 (39%) of the patients with JET received therapeutic interventions.



VENTRICULAR TACHYCARDIA

Defining Characteristics

- Serious ventricular arrhythmias are uncommon in young patients but occur later in teenagers and adults with congenital heart disease (TOF, Aortic stenosis). They also occur in children with cardiomyopathy of all ages and may be a first sign of rejection after orthotopic heart transplant. Serious ventricular arrhythmias such as VT and VF are a cause of sudden cardiac death in these patient groups.
- Ventricular tachycardia is seen rarely as a congenital abnormality in neonates. This is thought to relate to rare tumors of the Purkinje cell.

Electro-physiology and Typical ECG Changes

- Note: Isolated premature ventricular complexes occur after congenital heart surgery in the setting of hypokalemia and are benign.
- Sustained wide complex tachycardia should be treated as VT and managed as an emergency. If an atrial electrogram is available, this will demonstrate either AV dissociation or passive retrograde P waves (VA association). A dose of adenosine may be useful to clarify this and uncover AV dissociation. Adenosine will be therapeutic if the rhythm turns out to be SVT (the other differential diagnosis).
- Monomorphic VT is ventricular tachycardia with a single dominant QRS complex appearance. This type of VT arises from re-entry through a damaged or scarred area of myocardium.
- Torsade is a type of VT that is caused by repolarisation abnormalities. There is a varying QRS morphology that seems to twist around the isoelectric baseline of the ECG. Torsade is associated with pre-morbid prolongation of the QT interval or 'long QT syndrome'. Normal QT interval varies with heart rate and should be corrected ($QT_c = QT \text{ in seconds} / \text{square root of the RR interval in seconds}$). $QT_c > 0.45 \text{ seconds}$ is abnormal. Torsade may also occur as a complication of therapy with anti arrhythmic drugs from class 1A and 3. Torsades can be potentiated by hypokalemia, hypocalcaemia and hypomagnesaemia.

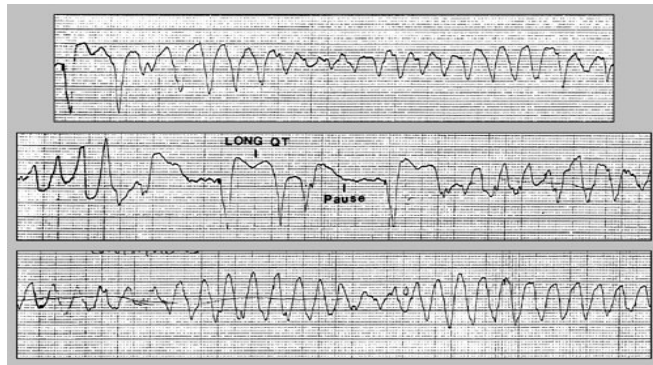
Clinical Features and Treatment

- Compromised patients with sustained VT should receive immediate synchronised cardioversion with 1-2 joules per kg.
- Stable patients with sustained VT should be treated with an anti arrhythmic drug. The choice of agent should be discussed with a consultant cardiologist. At GOSH the first line therapy is amiodarone 25 mic/kg/min for 4 hours followed by 5-15 mic/kg/min. In the USA the first line therapy is lidocaine 1 mg/kg followed by 20-50 mic/kg/min.
- Intermittent episodes of Torsades should not be cardioverted. The first line of treatment is magnesium sulphate 25 mg/kg. This may be followed by anti arrhythmic drugs including lidocaine and / or esmolol. The choice of therapy should be discussed with a consultant cardiologist.
- Long-term prevention of symptomatic VT remains a major therapeutic challenge. As well as medical therapy options include implantation of an internal defibrillator or catheter ablation.

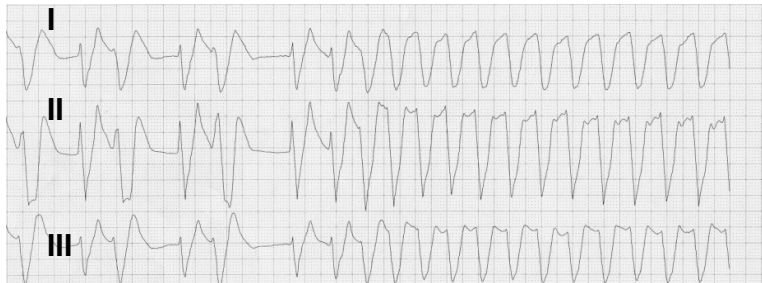
Key References

- Gatzoulis MA, Balaji S, Webber SA, Siu SC, Hokanson JS, Poile C, Rosenthal M, Risk factors for arrhythmia and sudden cardiac death late after repair of tetralogy of Fallot: a multicentre study. Lancet. 2000 Sep 16; 356 (9234): 975-81. This study followed up 793 patients late after repair of tetralogy. 33 died suddenly of ventricular arrhythmia. Risk of sudden death was increased with widening of the QRS over time. QRS widening was associated with the degree of pulmonary regurgitation.
- Case CL. Substrates for sudden cardiac death. Pediatric Clinics of North America 51 (2004) 1223-1227. This reviews the pathophysiology of serious ventricular arrhythmia leading to sudden cardiac death.

Torsades de pointes



Monomorphic VT



VENTRICULAR FIBRILLATION

Defining Characteristics

- Predominant arrhythmia that results in sudden cardiac death. VF is uncommon in young patients but occurs in teenagers and adults with congenital heart disease. Occurs in children with cardiomyopathy of all ages and may be a first sign of rejection after heart transplant.
- In a post-operative cardiac patient, VF may be a sign of myocardial ischaemia and substrate for this should be assessed and treated immediately.
- May occur in 'normal' patients after blunt chest trauma, electrocution and severe hypothermia.

Electro-physiology and Typical ECG Changes

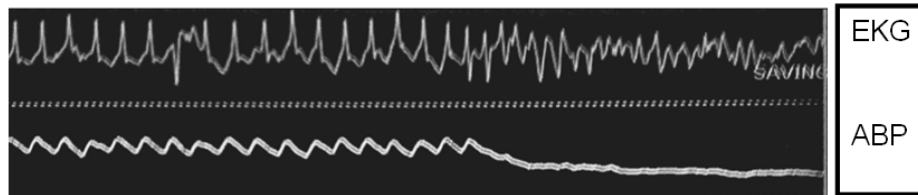
- May arise if a critically timed depolarization occurs during the vulnerable period of terminal re-polarisation.
- May occur as the terminal event in a critically ill patient with multiple organ dysfunction and circulatory failure.
- Myocardial scar, ischaemia, metabolic derangement and drugs cause regional alterations in the action potential and refractoriness.

Clinical Features and Treatment

- Chaotic ventricular rhythm that results in pulse-less cardiac arrest.
- Treatment is cardioversion with 2-4 joules per kg as per APLS Guidelines.
- Correct electrolyte imbalance such as hyperkalaemia, acidosis and hypocalcaemia.
- Placement of an automatic internal cardiac defibrillator may be indicated (AICD) in patients with known predisposition or history of VT / VF.

Key References

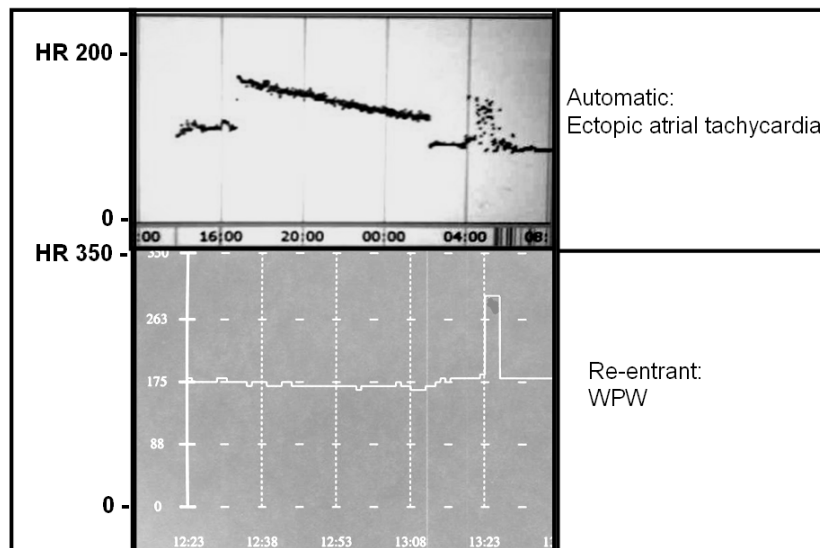
- FA Fish. Ventricular fibrillation: basic concepts. Pediatric Clinics of North America 51. 2004 1211-1221



SUPRAVENTRICULAR TACHYCARDIA

Defining Characteristics

- Narrow complex tachycardia.
- Commonest sustained tachyarrhythmia in children.
- “Supraventricular” implies the tachycardia is originating in the atria, AV node, or through an accessory pathway between the atrium and ventricle.
- These tachycardias may be classified by mechanism:
 1. **Re-entrant:** PAROXYSMAL with a FIXED, fast heart rate that DOES respond to vagal maneuvers.
Examples include Atrial flutter, Wolf-Parkinson-White syndrome, AV node re-entrant tachycardia, etc.
 2. **Automatic:** INCESSANT with a VARIABLE, fast to moderately fast heart rate that DOES NOT respond to vagal maneuvers.
Examples include sinus tachycardia, junctional ectopic tachycardia, atrial ectopic tachycardia etc.



Electro-physiology and Typical ECG Changes

- Narrow complex tachycardia that is supraventricular in origin, most commonly caused by accessory AV connection or AV node re-entry.
- Accessory connection or ‘orthodromic SVT’ is associated with the Wolff-Parkinson-White syndrome. The impulse travels forward down the AV node to the ventricles then returns up the accessory pathway back to the atrium. The surface ECG in WPW shows a widened QRS and short PR interval or delta wave. WPW patients are prone to atrial flutter and other more malignant ventricular arrhythmias. The risk of sudden death is 1% every 10 years. The SVT will have a narrow QRS and may have a retrograde P wave.
- A rare type of SVT ‘antidromic SVT’ occurs when the impulse travels forward down the accessory pathway and back up the AV node. This is associated with a widened QRS that may appear similar to VT.

- Atrioventricular node re-entry uses two functionally and physiologically distinct AV node components; the slow and fast pathways. Typical node re-entry uses the slow pathway in the antegrade direction and fast pathway in the retrograde direction. This is the opposite way in the atypical AV node re-entry SVT.
- Mechanisms of SVT in patients vary with age. In fetuses and the newborn SVT is exclusively caused by accessory pathways, by 10 years of age AV nodal mechanisms play an increasing role.

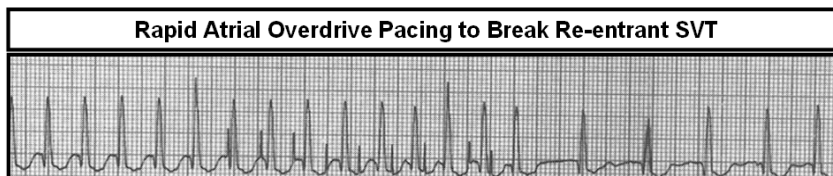
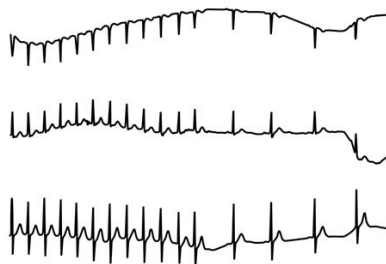
Clinical Features and Treatment

- The prognosis depends upon age of onset. 93% of infants with SVT in the first 2 months of life have resolved by the 8th month. Children who have SVT at age 5 years or older will continue to suffer episodes in 78% of cases.
- Syncope in a WPW patient should be treated with radiofrequency ablation of the accessory pathway.
- Adenosine, vagal manoeuvres, amiodarone and flecainide may all break the SVT circuit of a re-entrant tachycardia at the level of the SA node. Additionally, rapid atrial overdrive pacing via atrial wires or an oesophageal electrode may break the re-entrant circuit.
- In rare situations, a refractory SVT with severe haemodynamic compromise requires full ICU support including mechanical support with ECMO.
- Automatic tachycardias do not usually respond to vagal manoeuvres, cardioversion, or adenosine.

Key References

- Hoffman TM, Wernovsky G, Wieand TS et al. The incidence of arrhythmias in the paediatric cardiac intensive care unit. Paediatric Cardiology 2002 Nov-Dec; 23 (6): 598-604. SVT was the second most common arrhythmia seen in the CICU.
- Till JA et al. Adenosine: safety and efficacy in the treatment of SVT in infants and children. Heart 1989; 62: 204-211

Conversion of SVT to Sinus Rhythm with Adenosine



MYOCARDIAL ISCHAEMIA

Defining Characteristics

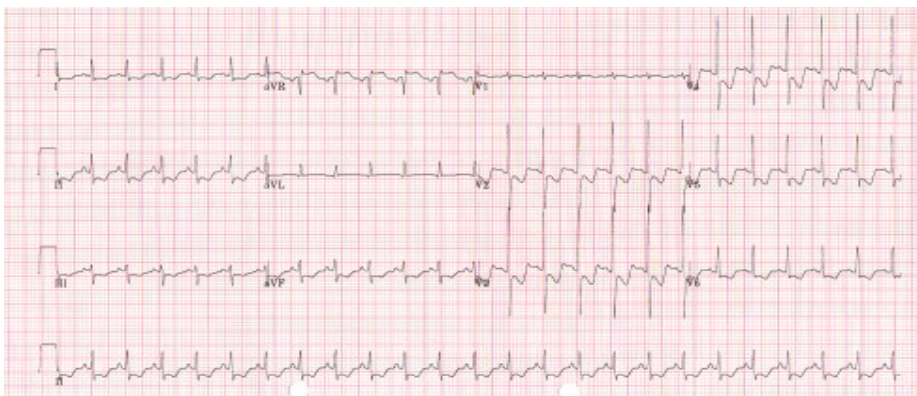
- Insufficient coronary flow due to obstruction of the vessel or inadequate perfusion pressure.

Electro-physiology and Typical ECG Changes

- ST depression in the relevant territory: left or right. There may be reciprocal elevation in the opposite leads.

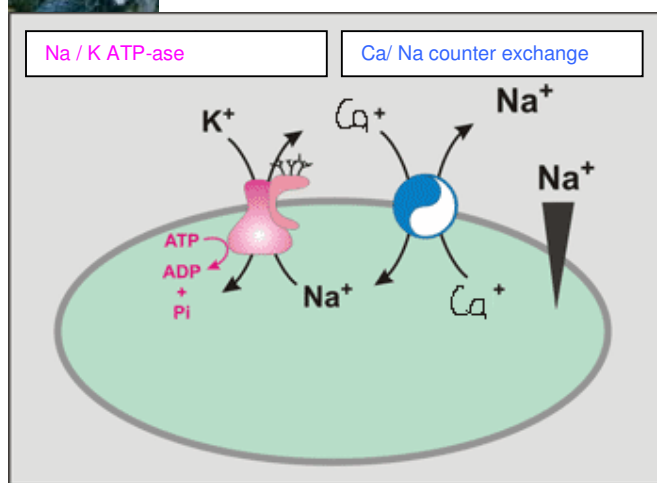
Clinical Features and Treatment

- Treat the cause as a matter of urgency.



PHARMACOLOGY

Cardiac glycosides



Cardiac glycosides act directly on the heart to increase the force of contraction; they also slow the heart rate by an indirect effect. The two most important cardiac glycosides are digoxin and digitoxin, which are present in the leaves of the foxglove (*Digitalis* sp.) and have been used for their effect on the heart for over 200 years.

The cardiac glycosides produce their effects by inhibition of sarcolemmal Na^+ , K^+ -ATPase. Cardiac muscle cells normally have a resting potential of approximately -60 to -80mV , this is achieved by the action of Na^+ , K^+ -ATPase, which pumps three sodium ions out of the cell in exchange for two potassium ions. By competing with potassium for binding to the enzyme, the cardiac glycosides inhibit the action of the pump and therefore reduce the resting membrane potential and increase the intracellular concentration of sodium. This reduces the gradient for the $\text{Na}^+/\text{Ca}^{2+}$ counter exchange channel to work, increasing intracellular calcium, and increasing force of contraction.

There is also an effect on the autonomic nervous system, increasing vagal activity, slowing the heart rate and allowing more time for diastolic filling.

Most commonly used for the treatment of heart failure or SVT.

Caution digoxin toxicity causes hypokalemia, arrhythmias, bradycardia, AV block, and bigeminy. Care must be taken to monitor drug levels.

Digoxin

Pharmacokinetics

Onset 30-120 mins after ingestion. Peak 2-6 hours. $T_{1/2}$ 30-40 hours. High protein binding (25%). Renal excretion.

Diuretics

Help in cardiac failure by reducing fluid overload - pulmonary and peripheral oedema. By optimising intravascular volume, diuretics can reduce workload.

Commonly used drugs include:

Loop diuretics: e.g furosemide work by inhibiting Na^+ reabsorption from the loop of Henle, thereby increasing tubular Na^+ , and therefore Na^+ and water loss.

Adverse effects: Hypovolemia, hyponatremia, hypokalemia

Furosemide:

Pharmacokinetics

P.O : Onset 1 hour after ingestion. 60% bioavailability. Peak 1-2 hours. Duration of action 6-8 hours. $T_{1/2}$ 30 mins. High protein binding (98%). Renal excretion mainly.

I.V. Onset 5 mins. Peak action 30 mins. Duration of action 2 hours.

Thiazides e.g metolazone increase distal tubular Na^+ and K^+ by inhibiting absorption in ascending loop of henle, promoting electrolyte and fluid loss. More effective than other thiazides or loop diuretics in renal failure.

Metolazone

Pharmacokinetics

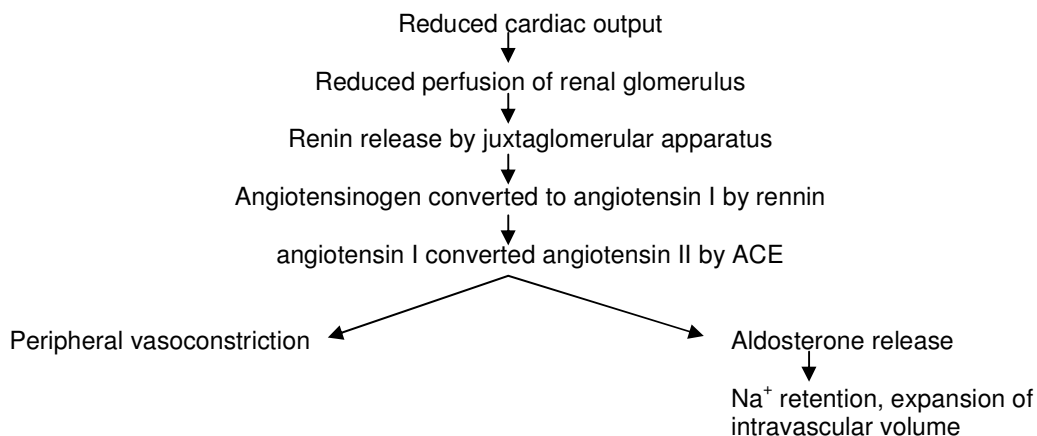
Peak 2-4 hours. $T_{1/2}$ 8 hours. Protein bound (33%), plus 70% bound to erythrocytes.. Renal excretion by filtration and active tubular excretion..

Vasodilators

Reduce afterload, and reduce cardiac work.

ACEI.

Angiotensin converting enzyme inhibitors block conversion of angiotensin I to angiotensin II, thereby causing peripheral arteriolar vasodilatation and reducing systemic afterload.



Captopril

Lowers systemic vascular resistance and systemic blood pressure without increase in heart rate. In paediatric cardiac intensive care it is an effective oral continuation therapy for children who have been receiving infusions of Nitroprusside or hydralazine.

Complications Hypotension, (hence small test dose). Also can enhance renal failure.

Pharmacokinetics

Peak 1 hour. Presence of food may reduce absorption (upto 40%). Duration of action 2-6 hours. $T_{1/2}$ 3 hours. Liver metabolism and excreted unchanged by kidneys.

Calcium channel blockers

Nifedipine cause vasodilatation by inhibiting calcium influx in smooth muscle cells, causing muscle relaxation. **USE CALCIUM CHANNEL BLOCKERS WITH EXTREME CAUTION IN INFANTS.**

Pharmacokinetics

Onset <20 mins after ingestion. 60% bioavailability. Peak 1 hour (longer with slow release). $T_{1/2}$ 2-5 hours. High protein binding (98%). Liver metabolism to inactive compounds. Renal excretion.

Phosphodiesterase inhibitors.e.g milrinone.

Inhibitors of phosphodiesterase are known to reduce the degradation of cyclic nucleotides and therefore increase tissue concentrations of cAMP and cGMP. The heart, however, possesses a specific subtype of the enzyme called phosphodiesterase III, the inhibition of which results in an elevation of cAMP only. As cAMP is the second messenger for β_1 -adrenoceptors in the heart, elevation of its concentrations by use of selective phosphodiesterase III inhibitors such as enoximone and milrinone mimics the effects of β_1 -adrenoceptor stimulation. These drugs are therefore useful for increasing the force of contraction of the heart in cardiac failure. Additionally, this class of drugs affect the sarcoplasmic reticulum and increase the rate of Ca^{+} reabsorption, which allows for better diastolic relaxation (lusitropic action). Milrinone increases cardiac contractility, and causes peripheral vasodilation thus increasing cardiac output without increasing myocardial oxygen demand.

Milrinone

Pharmacokinetics

I.V. Onset 2-5 mins. Peak 10 mins. $T_{1/2}$ 2-4 hours. 70% plasma protein bound. Liver metabolism. Renal excretion of both metabolites and active drug (around 80% may be excreted unchanged).

Catecholamines act on beta adrenergic receptors on myocardium (via cAMP) to increase cardiac output by an increase in contractility, but carry a penalty of generally increasing cardiac oxygen consumption.(Also risk of tachydysrhythmias and increased afterload.)

| Drug | Alpha | Beta1 | Beta 2 | DA 1+2 |
|---------------|-------|-------|--------|--------|
| Dopamine | ++ | ++ | + | ++ |
| Dobutamine | + | +++ | + | |
| Adrenaline | +++ | +++ | +++ | |
| Isoproterenol | | +++ | +++ | |

Beta 1 receptors increase heart rate, AV conduction velocity and ventricular contractility. **Beta 2** receptor activation produces peripheral vasodilation and bronchial dilation. **Alpha** receptor activation produces peripheral vasoconstriction including constriction of the skin, gut and renal arteries. **DA** receptor activation gives renal, coronary, gut and cerebral artery dilation.

| | Action | Pharmacology | Drawbacks |
|---------------------------------|---|--|--|
| Dopamine | Increase in contractility, vasodilate coronary arteries, chronotrope. Get increase in cardiac index. Peripheral vasoconstrictor | Agonist at adrenergic beta (and alpha receptors at higher doses), and dopaminergic receptors. (30% protein bound)Half life 2mins, renal, liver and Monoamine Oxidase metabolism | Tachycardia, vasoconstriction at higher doses (>10 mcg/kg/min) |
| Dobutamine | Inotrope, and peripheral vasodilator | Predominantly a beta 1 agonist. Synthetic sympathomimetic amine. Half life 2mins, liver metabolism | Tachycardia at higher doses |
| Epinephrine / adrenaline | Inotrope, chronotrope | Agonist at alpha, and beta receptors. Half-life 2 mins Liver metabolised, but also uptake by neurones, and metabolised by MAO, and COMT. | Marked vasoconstrictor effect at higher doses, leading to peripheral ischaemia |
| Isoproterenol | Chronotrope, some inotropy. Peripheral vasodilator. Predominantly used as chronotrope e.g post cardiac transplant | Synthetic sympathomimetic amine. Beta 1 agonist. Half-life 2-5mins, Conjugated mainly in liver and lungs. | Contraindicated on HOCM (may exacerbate) |

Information for Year 2 ITU Training (advanced):

Year 2 ITU curriculum

Pathophysiology and Investigation:

- Principles of cardiac pacing.
- Use of temporary pacing
- Trans-venous pacing, Oesophageal pacing, internal pacing
- Management of pacing box failure

Reading :

- Key articles are listed in the text
- Article PDF files are stored in the accompanying folder
- CCC Guidelines
- BNF for children
- Chang Wessel Wernovsky, Practice of Cardiac Intensive Care

Curriculum Notes for Year 2:

PACING

Adapted from CCC Guidelines on Pacing by Aparna Hoskote

INITIAL ASSESSMENT

- Steps to achieve successful and non-stressful manipulation of the temporary pacing system:
 - What is the native underlying rhythm?
 - What are the modes of pacing available?
 - What you would like to accomplish?
- Patients with symptomatic tachycardia > than 170/min are rarely helped by manipulating the standard temporary pacemaker - Cardioversion (whether electrical or pharmacological) should be the mainstay of therapy.
- [Note: A word of caution, those patients susceptible to JET (TOF, VSD, etc.) with unstable tachycardia are quite likely to fare as poorly with unfettered electrical cardioversion, as with sub optimal approach to pacing. It may, in fact, be quite beneficial to overdrive pace these patients at rates of 180 to 200. The bedside guidance and advice of a cardiology or intensive care consultant should be considered.]
- All other patients have a sufficient underlying rhythm to allow for a methodical and reasoned approach to the patient.

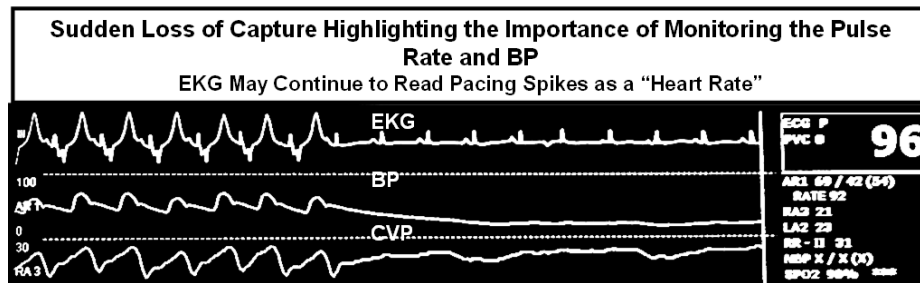
CHECKING THE UNDERLYING RHYTHM IN A PATIENT WHO IS ALREADY PACED

- The appropriate way to examine the patient's underlying rhythm is to gradually reduce the pacing rate, allowing the intrinsic rhythm to emerge.
- These underlying rhythms are overdrive suppressed by pacing and may not appear in a timely fashion after the abrupt termination of pacing. The threshold to recapture the heart after such a manoeuvre may be significantly higher than it was before pacing inhibition (the Wodinsky effect).

WIRES, LEADS AND CONNECTIONS

- By convention, atrial wires are the rightmost, with ventricular wires closer to the midline – regardless of whether there is an abnormality in the position of the heart (dextrocardia) and chambers within the heart (heterotaxy).
- In case not sure, record an electrocardiogram from the wires to decide which chamber they are originating from.
- If convention not followed then they should be labelled between the exit point and metal connection pins.
- Pacing cables and the headers they are connected to are colour coded as **blue for atrial** and **white for ventricular**.
- The connections and cables are all electrically identical and are easily interchangeable – can lead to unexpected and potentially dangerous pacing behaviour.

- The headers on the pacing generator are designed to accept one end of the pacing cable but can be connected to the pins of the pacing wires if necessary.
- Check that the header is actually closed and engaged on the pacing cable.
- The polarities (+ and -) on the pacing cables and pacing generator - **The physics of pacing has electrons leaving the generator thro' the negative (-) terminal, entering the heart and then returning thro' the positive (+) terminal.** Rarely, one may find that the only one PW has contact with the heart. In this situation, reversing the polarity of the system may be useful. This is most easily accomplished by turning the pacing cable around on the headers at the top of the pacing generator.
- If single lead, the heart lead should be connected to the (-) terminal and the subcutaneous lead is connected to the (+) terminal.
- Temporary pacing wires are usually reliable for periods of more than 2 weeks
- If rapid or progressive increases in threshold are noted, new wires or early implant of a permanent pacemaker would have to be considered if the patient is pacemaker dependent.
- The threshold of pacing wires can be increased in the presence of **ANY** acidosis (metabolic or respiratory) **note: therefore, be cautious for sudden loss of capture and bradycardia in pacing dependent patients with unrecognised acidosis (blocked ETT tube, low cardiac output, anaemia, etc.)**



THE PACING GENERATOR – CHOICES

- PACE - can pace and sense both atrium and ventricles
- Medtronic – old – can pace both atrium and ventricle but can sense only the ventricle
- Single chamber high rate devices

THE PACING GENERATOR CONTROLS SENSING

- **Amount of energy it takes for the pacemaker to recognize that a native complex or depolarisation has occurred.** Degree that pacemaker detects impulse, lower mV = more sensitive.
- Note the numbers on the sensing panel represent the minimum size of the ventricular signal that the pacemaker will recognise thus higher numbers are less sensitive.
- Sensing problems are often the root cause of abnormal pacing behaviour. **If the pacemaker is putting out pacing spikes “on top of” the patient’s underlying rhythm, it could be that the sensitivity number needs to be reduced. For example, reducing the sensitivity from 2mv to 0.5mv means that, now, the pacemaker will detect electrical activity down to 0.5mv as the patient’s underlying native activity. On the other hand, lower numbers for sensitivity also may mean that the pacemaker could be fooled by the patient’s muscle activity, tremors, or bedside care into thinking that real underlying heart beats are occurring, when, in fact, all that is going on is arm or chest movement.**
- Just as systole is only as good as diastole, pacing is as good as sensing.
- Sensing ranges from 0.1 to 20 mV.
- Inappropriate sensing may be the cause if there is possibility of competition of the patient’s rhythm.

OUTPUTS (ATRIAL AND VENTRICULAR)

- The current is delivered (during a fixed pulse width) through the wires to the heart. Most patients need at least 1mA to capture (see thresholds below) and some will have either

skeletal or diaphragmatic capture, particularly thro' the atrial leads, at outputs above 10mA. **Note: High output to the atrial wires may capture the ventricle.**

- Threshold - Minimum stimulus needed to consistently capture.

RATE – VENTRICULAR

- Determines the number of milliseconds from the previous ventricular event (whether sensed or paced) that the pacemaker waits before the ventricular channel fires.
- Max rate on PACE is 180.
- Rapid rate pacing under special parameters for overdrive pacing.

AV INTERVAL

- Determines the number of milliseconds **after an atrial signal (paced or sensed) that the pacemaker will wait for native ventricular activity, before going on to put in its own ventricular pacing spike** (regardless of what the atria are doing).

PACING – CONFIGURING THE CONTROLS SENSING

- The ventricular and atrial outputs to a min of 0.1 mA and
- Ventricular rate to a minimum of 30
- The ventricular sensitivity to the lowest number 1.0mV
- Turn on the pacemaker
- See the display and the patient's ECG
- Turn the sensitivity up until the sensing R no longer flashes up in time with the QRS or you begin to see the V flashing or both
- The maximum value at which there is consistent sensing defines the sensing threshold.
- Usual practice is to have a sensing margin of at least 2 times – e.g. if the pacemaker senses at 8, set it at 4 or less.

VENTRICULAR THRESHOLD

- Once you have established that the pacemaker is sensing safely, you can move on to determining the ventricular threshold without concern about asynchronous pacing and pro-arrhythmia
- Turn the vent rate up to a number above the patient's own rate, until you see the V flashing consistently
- Note that your ventricular output should still be at 0.1 mA and thus no change should be evident on the ECG.
- Now, while watching the ECG (not the pacemaker) increase the vent output until you see both a change in QRS morphology and a change in the rate to what you set
- The minimum value when you see a consistent pacing defines the pacing threshold.
- Usual practice is to have a pacing safety margin of at least 2 times (or 3 times if the patient has an unstable escape rhythm) – if the pacing threshold is 3, set at 7 (or 10).
- **Note that pacing temporary wires at unnecessarily high outputs may lead to premature carbonisation of the leads and degradation of wire function.**

ATRIAL THRESHOLD

- This is most easily done in the patient with intact AV nodal conduction
- Patients with slow or unstable rhythms should be configured in ventricular pacing initially, and then the atrial output adjusted as described in AV sequential pacing.
- With the pacemaker sensing safely the ventricular and the vent output at a minimum
- Set the rate to a number above the patient's own rate
- Now watching the ECG, (not the pacemaker) increase atrial output until you see a change in the rate to what you set
- You should also see each atrial pacing spike, usually followed by a p wave then a narrow QRS after a brief delay at the AV NODE
- If you are pacing the atrium and the QRS complex becomes abruptly wide without a P wave or AV interval then what you believe to be your atrial wires may not be. **but also, because atrial wires are often placed near the purse-string suture used to close the right atrial bypass cannulation site, it is quite possible for higher output atrial pacing to be easily captured by the patient's ventricle. if one checks an anatomically correct picture or specimen, one can see the right atrial appendage lies over the anterior surface of the right ventricle.**

- The minimum atrial output that consistently captures the atrium and conducts to the ventricle defines the pacing threshold

AV INTERVAL

- Threshold may vary at different AV Intervals

PHYSIOLOGY OF PACING

- Mechanical contraction of the ventricles is most efficient when depolarisation occurs via the normal His-Purkinje system. In a patient with sinus bradycardia and intact AV conduction, atrial pacing is more efficient than either dual chamber or ventricular pacing.
- In a patient with AV block, dual chamber pacing that maintains AV synchrony is superior to ventricular pacing alone. Optimal AV delay (PR interval) for dual chamber pacing in a very young paediatric patient tends to be short (70 to 120 milliseconds); longer AV delays can result in atrial cannon waves and elevated filling pressures.
- **The benefit of AV sequential pacing may not be manifest in increase in BP but rather augmentation in cardiac output and a decrease in left and/or right atrial line pressures ("filling pressures").**

MODES OF PACING

EMERGENCY VENTRICULAR PACING (VOO) –

- Used in complete heart block or other cause of severe bradycardia.
- Set mode on VOO, turn vent output to 20mA, change mode to asynchronous.
- Adjust the ventricular rate.
- If no capture, try reversing the polarity of the pacing cables, and check integrity of connections.
- Note that many of these patients may have other confounding problems (ischaemia or acidosis) and their capture thresholds are quite high until their circulation or myocardium is resuscitated by other means.
- Pacemaker dependent patients with poor thresholds or safety margins should have an alternative modality of pacing immediately available. Note that if you are asynchronously pacing, if the patient develops their own rhythm or significant ectopy there is a risk of inducing ventricular tachycardia or fibrillation.
- Usually patients sick enough to require VOO pacing are sick enough to justify the presence of a defibrillator at the bedside – if one is not yet present, take the time now to bring it over. Most defibrillators also have the ability to do transcutaneous pacing – another good reason to have it available.

DEMAND VENTRICULAR PACING (VVI)

- To be used in patients who need a backup in case of sudden unexpected bradycardia or in patients with identified AV conduction block in whom AV synchrony is not thought to be necessary or achievable (e.g. if no atrial wires are placed). Note that this mode requires the establishment of satisfactory ventricular sensing. Once this is done, you can easily establish a ventricular capture threshold and then set a minimum rate at which you wish the pacemaker to start pacing.

ATRIAL PACING

- Used in patients with sinus bradycardia or sinus arrest, but who have intact AV conduction. Also useful in junctional tachycardia.
- **AOO** – advantage of simplicity but may require ongoing adjustment if the patient's underlying rhythm changes. It is asynchronous in the atrium, and thus carries the risk of inducing an arrhythmia (usually not ventricular, but still potentially haemodynamically embarrassing).
- Turn the ventricular output and sensing all the way to minimum (minimum output and asynchronous).
- Set the AV interval to 0msec, which serves as a reminder to others that you are not AV pacing, and does not influence pacemaker behaviour in this mode.

- Select your pacing rate using the 'ventricular rate' adjustment then gradually increase the atrial output until you see evidence of capture.
- **AAI** – advantage of adding the atrial systolic contribution to the cardiac output
- Check atrial sensitivity
- Check threshold and set voltage

DVI – (AV sequential)

- Usual indication is AV conduction block.
- First establish a satisfactory VVI pacing mode – hopefully will stabilise the hemodynamics somewhat and then give time to adjust the remainder of the set up.
- While VVI pacing, set the AV interval to a high number – 200msec
- Watching the ECG, gradually increase the atrial output until you see evidence of atrial capture (P waves following the A pacing spike)
- You should see evidence in the invasive pressure tracings that you have achieved hemodynamic AV synchrony
- Cannon waves should disappear from CVP, RA and LA lines and if there was beat-to-beat variation in arterial pressures, it should have vanished too.
- Note that many patients with AV block in the CCU will have an underlying sinus tachycardia 'hiding' in the ECG baseline
- Thus in order to achieve AV Synchrony, you must be pacing faster than the underlying sinus tachycardia. Usually the sinus rate is measurable from the wire study you should have already done to establish the diagnosis of AV Block. Once you have established AV synchrony you can adjust the AV interval to achieve the most favourable hemodynamics.

DDD – (AV Universal)

- Paces and senses the atrium and ventricle and can act in different modes depending on the underlying rhythm
- If AV conduction is intact, but the rate is slow, the pacemaker may appear as an AAI system, pacing the atrium but allowing AV conduction to result in intrinsic QRS complex.
- In the presence of AV block but an adequate atrial rate, the pacemaker can track the atrial rate, time out a programmed AV delay in the pacemaker (generally anywhere from 70 to 240 milliseconds) and pace the ventricle when an intrinsic ventricular event is not sensed in the allotted AV delay time interval
- The DDD mode in AF or A Fib can result in a rapid ventricular rate depending on programmed timing cycles.

RAPID OVERDRIVE PACING

- Only applicable for re-entrant SVT including atrial flutter
- Applied for short time – 3-5 seconds, rate 10-40 bpm higher than the tachyarrhythmia
- Risk of accelerating ventricular rhythm

OTHER PACING AVAILABLE

Permanent pacing

- This is required in children with persistent high grade AV block. The choice of pacing system takes account of the child's size, presence of intra-cardiac shunt and myocardial performance. In small infants a single-chamber pacing box is indicated if ventricular function is good. When function is poor a dual-chamber box is required. Where there is right-left shunting, epicardial pacing wires are placed to reduce the risk of embolus associated with transvenous wires.

Transcutaneous pads

- This method makes use of the defibrillator machine. This method may be used for emergency pacing for heart block after congenital heart surgery when the pacing wires have failed. Transcutaneous pads are placed on the sternum and apex as for defibrillation. These are connected to the defibrillator and the machine is switched to 'Pace' mode. The rate and output may be adjusted in order to achieve capture. This mode

of pacing requires high outputs. It will achieve VOO mode pacing only. It is painful and the patient should be ventilated, sedated and muscle relaxed. It is a temporising measure for use only until cardiothoracic surgery input can be obtained to revise pacing wires.

Transvenous

- The transvenous approach is used in adults and adolescents to achieve right ventricular access for VOO pacing in cases of heart block or severe bradycardia. The indications include ischaemic heart disease with sinus node dysfunction, Lyme disease and drug overdoses. A temporary wire is placed via the internal jugular vein into the right ventricle by a cardiologist in the cardiac catheter laboratory. When a return to normal sinus rhythm occurs and the wire can then be withdrawn from the heart. If a long-term device is required for permanent pacing this can be arranged electively.

Oesophageal

- This method provides temporary pacing and is most useful in small children in who the tissue depth between the oesophagus and the heart is low. The indications include failure of transthoracic pacing wires in heart block or severe bradycardia and non-sinus tachycardias requiring overdrive pacing. If used for long period at high outputs the electrode may generate a burn in the oesophageal mucosa. A temporary oesophageal electrode is placed to the depth of the mid sternum and attached to a single output high-rate pacing box.