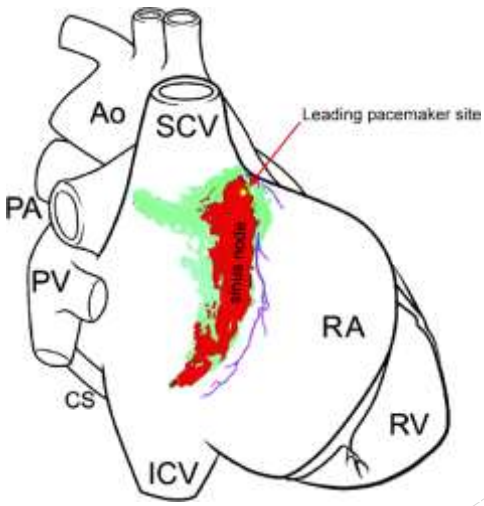
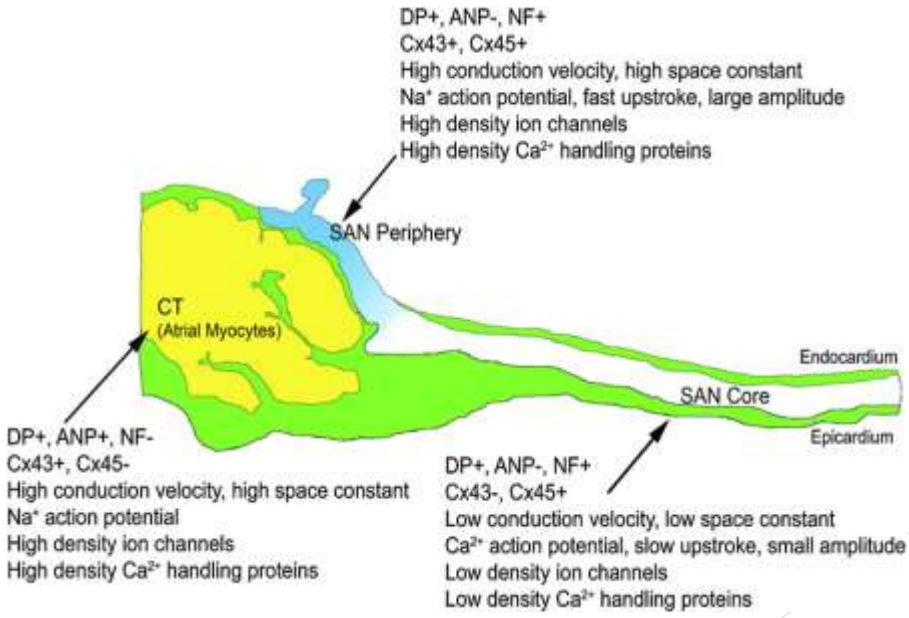
Sinus Node Dysfunction

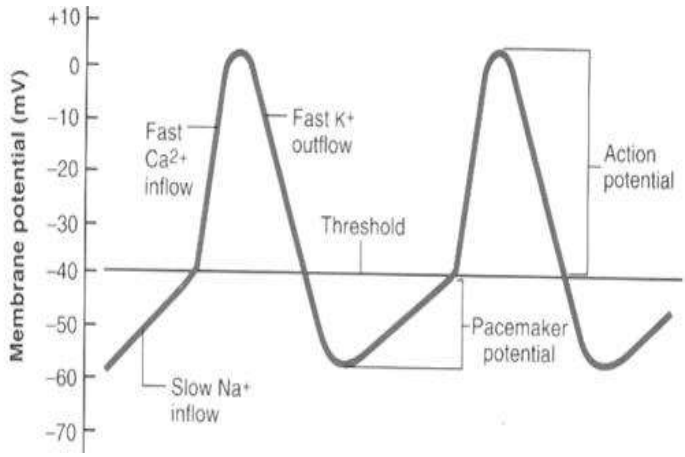
Mohammad Mohsen Morsi
Lecturer Cardiology, Zagazig University

Anatomy

- Located epicardially in the right atrial (RA) sulcus terminalis at the junction of the superior vena cava (SVC) and RA
- Courses downward and to the left, to end subendocardially.
- The sinus node is a spindle-shaped structure with a central body and tapering ends.
- Measures 10 to 20 mm long and 2 to 3 mm wide and thick




DP+, ANP-, NF+
Cx43+, Cx45+
High conduction velocity, high space constant
Na+ action potential, fast upstroke, large amplitude
High density ion channels
High density Ca2+ handling proteins
SAN Periphery
CT
(Atrial Myocytes)
Endocardium
SAN Core
Epicardium
DP+, ANP+, NF-
Cx43+, Cx45-
High conduction velocity, high space constant
Na+ action potential
High density ion channels
High density Ca2+ handling proteins
DP+, ANP-, NF+
Cx43-, Cx45+
Low conduction velocity, low space constant
Ca2+ action potential, slow upstroke, small amplitude
Low density ion channels
Low density Ca2+ handling proteins


Membrane potential (mV)
+10
0
-10
-20
-30
-40
-50
-60
-70
Fast Ca2+ inflow
Fast K+ outflow
Threshold
Action potential
Pacemaker potential
Slow Na+ inflow

Sinus node dysfunction (SND) refers to a wide range of abnormalities involving sinus node and atrial impulse generation and propagation, which can present from asymptomatic bradycardia to atrial standstill.

So…….. sinus node dysfunction is not always a dysfunction of the sinus node!!!!!

- *> 65 years ….. Prevalence 1: 600*
- *Accounting for ≈ 50% of implant indications in the United States.*
- *Sick sinus syndrome is generally a disease of aging.*
- *In children, after cardiac surgery to correct congenital heart defects.*
- *Whites > Blacks*
- *Greater body mass index, greater height, longer QRS interval ….. Higher incidence*

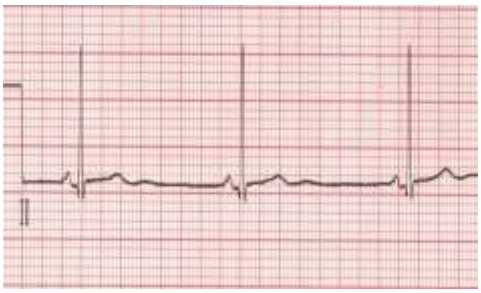
Intrinsic
- Idiopathic/degenerative
- Ischemic heart disease
- Hypertensive heart disease
- Cardiomyopathy
  - Infiltrative diseases
    - Sarcoidosis, amyloidosis
- Surgical trauma
  - Congenital heart disease
    - Mustard procedure
    - ASD closure
  - Cardiac transplant
- Inflammation
  - Collagen vascular disease
  - Rheumatic fever
- Infection
  - Viral myocarditis
  - Lyme disease
- Neuromuscular disorders
- Familial HCN4 & SCN5A

Extrinsic
- Pharmacologic agents
  - Class IA, IC, III antiarrhythmic agents
  - Beta adrenergic blockers
  - Calcium channel blockers
  - Cardiac glycosides
  - Antihypertensives (such as clonidine, methyldopa)
  - Antipsychotics (such as lithium, phenothiazine derivatives)
  - Antidepressants (such as amitriptyline)
- Autonomic
  - Vasovagal syncope (cardioinhibitory)
  - Carotid sinus hypersensitivity
- Metabolic
  - Hypothyroidism
  - Hyperkalemia
  - Hypoxia
  - Intracranial hypertension

Adapted from Vijayaraman P, Ellenbogen K. Bradyarrhythmias and pacemakers. In: Fuster V, Walsh R, Harrington R, eds. *Hurst's the Heart*. 13th ed. New York, NY: McGraw-Hill; 2011.

Sinus bradycardia

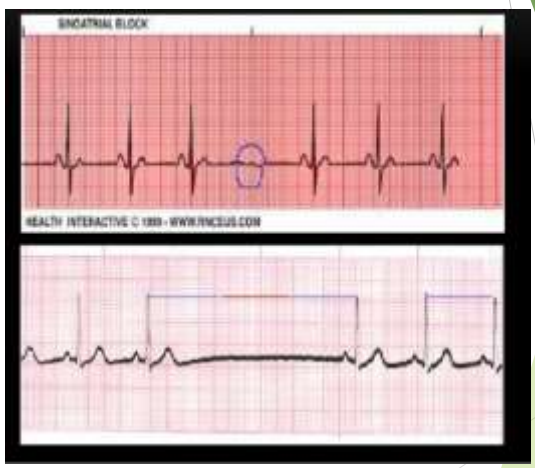
Sinus bradycardia (less than 60 beats/min) is considered abnormal when it is persistent, unexplained, and inappropriate for physiological circumstances (sleep or physical conditioning)is generally considered abnormal.



Sinus pauses

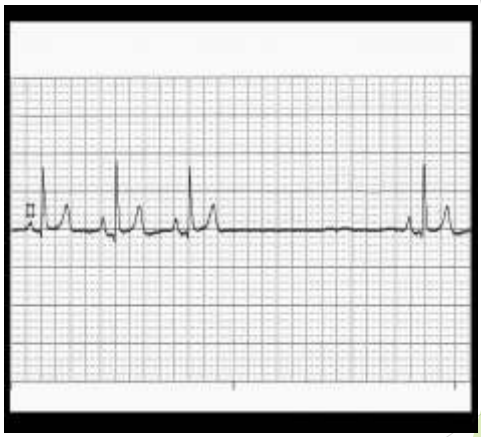
Sinus arrest *and* ***sinoatrial exit block*** *can result in sinus pauses*

They are definite evidence of SND.



Sinus arrest

- *Total cessation of impulse formation within the sinus node.*
- *The pause is not an exact multiple of the preceding P-P interval but is random in duration.*
- *Asymptomatic pauses of 2 to 3 seconds can be seen in up to 11% of normal individuals and in one third of trainedathletes,*
- *Pauses longer than 3 seconds are usually caused by SND*



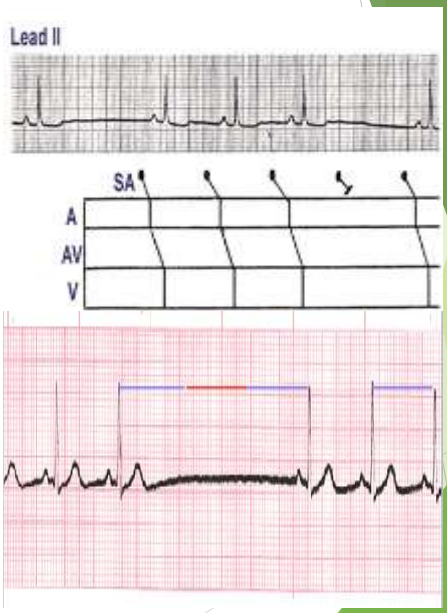
Sinus exit block

- *Normally generated sinus impulse fails to conduct to the atria because of delay in conduction or block within the sinus node itself or perinodal tissue.*
- *Exit block is classified into three types, analogous to those of AV block:*

I. *First degree: All sinus impulses are conducted to the atrium but with fixed delay. Concealed on ECG.*

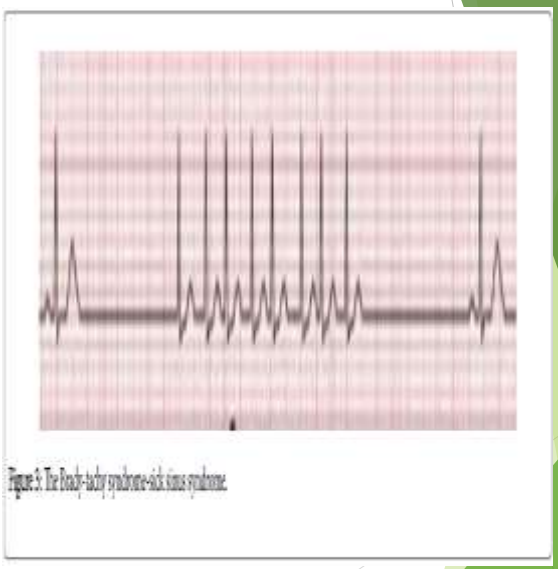
II. *Second degree: Type I (Wenckebach)------ Type II (one, two or more sinus impuses are blocked).*

III. *Third degree: (Complete) absent P waves with long pauses & escape rhythm.*



Tachycardia –Bradycardia Syndrome

- The syndrome of alternating bradycardia and tachycardia was originally described in 4 patients by Short in 1954. These patients had periods of atrial flutter or fibrillation with periods of sinus pauses at termination of the atrial arrhythmia leading to syncope.
- In 1968 Ferrer described the sluggish return of sinus node function following electrical cardioversion



Tachycardia –Bradycardia Syndrome

- The tachycardia-bradycardia syndrome, although frequently referring to the combination of atrial tachyarrhythmia alternating with pauses, could be applied to any combination of tachycardia with bradycardia.

- The clinical implication of the combination of tachycardia and bradycardia is the limitation imposed on the use of negative chronotropic agents without the concomitant use of cardiac pacing.

Chronotropic Incompetence

Present in 20-60% of patients with SND

Although the resting heart rate can be normal, these patients can have the inability to increase their heart rate during exercise or have unpredictable fluctuations in the heart rate during activity.

The definition is not agreed on, but it is reasonable to designate it as an abnormally low heart rate response to exercise manifesting as:

- Less than normal increase in the sinus rate at each stage of exercise, with a plateau at less than 70% to 75% of the age-predicted maximum heart rate (220 − age)
- Inability to achieve a sinus rate of 100 to 120 beats/min at maximum effort.

Atrial standstill

Atrial standstill is a condition characterized by the absence of electrical and mechanical atrial activity.

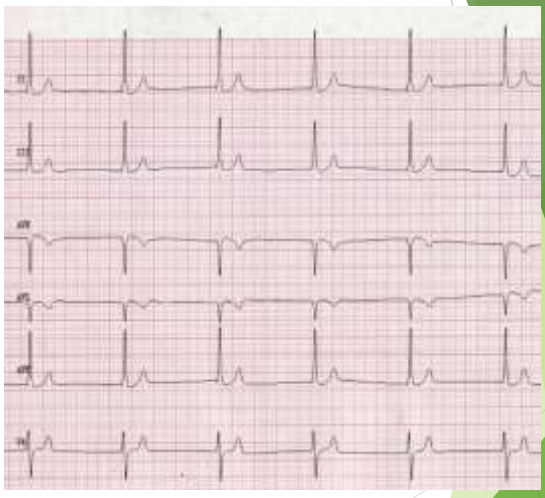
The diagnostic criteria include:

1) the absence of P waves in the ECG and of A waves in the intracardiac recordings

2) narrow QRS complexes

3) evidence of atrial paralysis (absence of A waves in the jugular venous pulse, in the atrial pressure recording and in the mitral Doppler recording)

4) inability to stimulate the atria



Atrial standstill

- *Atrial standstill can be partial or total --- intermittent or permanent.*
- *Intermittent (Digitalis sor quinidine intoxication, hyperkalaemia, hypoxia, or myocardial infarction)*
- *Permanent atrial standstill is characterized by severe morphological changes with fibrosis and cell death,and accompanied by reduced expression of atrial natriuretic peptide.*

Atrial standstill

- *After valve replacement - organic heart disease -systemic muscular disease--after longstanding atrial fibrillation -* ***Fibrotic atrial cardiomyopathy.***
- ***Atrial standstill poses extremely high risk of thrombo-embolism.***

Principles of management

- Total survival and the risk of sudden cardiac death of patients with sick sinus syndrome (SSS) (irrespective of symptoms) are similar to that of the general population.
- systemic thromboembolism is common in untreated patients with SND systemic embolism occurred in 15.2% of unpaced SSS patients, compared with 1.3% in age-matched controls.

Principles of management

- the incidence of atrial fibrillation (AF) in unpaced patients was 8.2% at initial diagnosis and increased to 15.8% during a mean follow-up of 38 months.
- Slow progression (over 10 to 30 years) is expected.
- The prognosis largely depends on the type of dysfunction and the presence and severity of the underlying heart disease.

Principles of management

- The worst prognosis is associated with the tachycardia-bradycardia syndrome and atrial standstill (mostly because of the risk for thromboembolic complications).
- The incidence of advanced AV conduction system disease in patients with SND is low and, when present, its progression is slow. At the time of diagnosis of SND, approximately 17% of the patients New AV conduction abnormalities develop at a rate of approximately 2.7% per year. The incidence of advanced AV block during longterm follow-up is low (approximately 1% per year)

Principles of management

- Correlation of symptoms with evidence of SND is the essential part of the diagnostic strategy.

Electrocardiogram and Ambulatory Monitoring

- The diagnosis of SND as the cause of the symptoms is rarely made from the ECG.
- In patients with frequent symptoms, 24- or 48-hour ambulatory Holter monitoring can be useful.
- Cardiac event monitoring or implantable loop recorders in patients with less frequent symptoms.
- Documentation of symptoms in a diary by the patient while wearing the cardiac monitor is essential for correlation of symptoms with the heart rhythm at the time.

Autonomic Modulation

- *Carotid sinus massage (pause longer than 3 seconds)*
- *Heart rate response to the Valsalva maneuver (normally decreased) or upright tilt (normally increased) can also be used to verify that the autonomic nervous system itself is intact.*
- *Complete pharmacological autonomic blockade is used to determine the intrinsic heart rate .(Complete autonomic blockade is accomplished by administering atropine, 0.04 mg/kg, and propranolol 0.2 mg/kg)*
- *The normal intrinsic heart rate is age-dependent and can be calculated using the following equation: intrinsic heart rate (beats/min) = 118.1 − (0.57 × age)*

Exercise Testing

- *To assess chronotropic incompetence in patients with exertional symptoms.*
- *Failure to achieve 80% of the maximum predicted HR (220 minus age) at peak exercise is considered evidence of a blunted HR response.*

Electrophysiological Testing

- *Noninvasive testing is usually adequate in establishing the diagnosis of SND and guiding subsequent therapy. However, invasive EP testing can be of value in symptomatic patients in whom SND is suspected but cannot be documented in association with symptoms.*
- *The most useful measures of the overall sinus node function are a combination of the responses to atropine and exercise, and the sinus node recovery time (SNRT).*

- *Interval between the end of a period of pacing-induced overdrive suppression of sinus node activity and the return of sinus node function.*
- ***Sinus Node Recovery Time**. SNRT is the longest pause from the last paced beat to the first sinus return beat at a particular pacing CL. Normally, the SNRT is less than 1500 milliseconds ± 250 milliseconds.*
- ***Corrected Sinus Node Recovery Time**. Corrected SNRT equals SNRT minus the baseline sinus CL. Normal values of corrected SNRT have been repor.ted from 350 to 550 milliseconds*

- Sino-atrial conduction time :
- Signal averaged ECG.
- Direct recording in the EP lab.
- Indirect methods (Strauss – Narula techniques).

- The primary limitations of EP assessment in SND are the low sensitivity of the tests.
- The sensitivity of the SNRT and SACT are about 50% alone and approximately 65% combined.
- The combined specificity is better at approximately 88%.
- If abnormalities are found, EP testing may support the diagnosis of SND but cannot be used to exclude sinus node disease in view of the limited sensitivity.

Indication for pacing in patients with persistent bradycardia

Recommendations	Class[a]	Level[b]	Ref.[c]
1) Sinus node disease. Pacing is indicated when symptoms can clearly be attributed to bradycardia.	I	B	1,6–9
2) Sinus node disease. Pacing may be indicated when symptoms are likely to be due to bradycardia, even if the evidence is not conclusive.	IIb	C	-
3) Sinus node disease. Pacing is not indicated in patients with SB which is asymptomatic or due to reversible causes.	III	C	-

Recommendations for permanent pacing in SND

Class I Pacemaer indicated
- SND with documented symptomatic bradycardia.
- SND as resulting from essential long-term drug therapy.
- Symptomatic chronotropic incompetence.

Class IIa Pacemaker reasonable
- SND with heart rate <40 bpm when a clear association between symptoms consistent with bradycardia and actual presence of bradycardia has not been documented.
- Syncope of unexplained origin when clinically significant abnormalities of sinus node function are found during EP studies.

Class IIb Pacemaker considered
- Minimally symptomatic with chronic heart rate <40 bpm while awake.

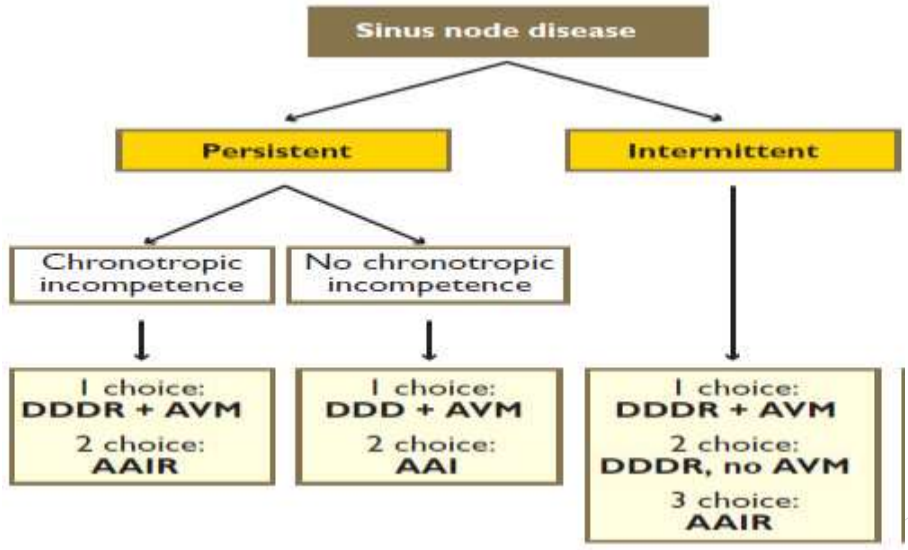
Class III Pacemaker not indicated
- Asymptomatic patients.
- Symptoms suggestive of bradycardia clearly documented to occur in the absence of bradycardia.
- Symptomatic bradycardia due to non-essential drug therapy.

Adapted from ACC/AHA/HRS. 2008 Guideline for device-based therapy for cardiac rhythm abnormalities. *Heart Rhythm*. 2008;5:e1-e62.

Table 8 Outcome of randomized controlled trials of dual-chamber versus ventricular pacing

Outcome	References	Dual-chamber benefit over ventricular pacing	Notes
All-cause deaths	2, 11–15	No benefit	
Stroke, embolism	2, 11–15	Benefit (in meta-analysis only, not in single trial)	HR 0.80.[15] Benefit higher in SSS.
Atrial fibrillation	2, 11–15	Benefit	HR 0.81[12] and 0.76.[13] Benefit higher in SSS.
HF, hospitalization for HF	2, 11, 12, 14, 15	No benefit	
Exercise capacity	15	Benefit	Overall standardized mean improvement of 35%. Not significant compared to VVIR.
Pacemaker syndrome	11–13, 15	Benefit	Documented in up to 25% of VVI patients.
Functional status	11, 12, 15	No benefit	
Quality of life	11–13, 15	Variable	Consistent direction of effect on quality of life, but the size cannot be estimated with confidence.
Complications	2, 11–13, 15	More complications with dual-chamber	Higher rate of lead dislodgment (4.25 vs. 1.4%) and inadequate pacing (1.3 vs. 0.3%).

HF = heart failure; HR, hazard ratio; SSS = sick sinus syndrome.



Choice of pacing mode/programming in patients with persistent bradycardia

Recommendations	Class [a]	Level [b]	Ref. [c]
7) Sinus node disease. **7A)** Dual-chamber PM with preservation of spontaneous AV conduction is indicated for reducing the risk of AF and stroke, avoiding PM syndrome and improving quality of life.	I	A (vs. VVI)	2, 3, 11–13, 15–17
		B (vs. AAI)	
7B) Rate response features should be adopted for patients with chronotropic incompetence, especially if young and physically active.	IIa	C	-

3) Reflex asystolic syncope. Pacing should be considered in patients ≥40 years with recurrent, unpredictable reflex syncopes and documented symptomatic pause/s due to sinus arrest or AV block or the combination of the two.	IIa	B	5, 18, 19
4) Asymptomatic pauses (sinus arrest or AV block). Pacing should be considered in patients with history of syncope and documentation of asymptomatic pauses >6 s due to sinus arrest, sinus-atrial block or AV block.	IIa	C	-

Choice of pacing mode

Recommendations	Class [a]	Level [b]	Ref. [c]
6) Intermittent documented bradycardia. Preservation of spontaneous AV conduction is recommended.	I	B	16, 17
7) Reflex asystolic syncope. Dual-chamber pacing with rate hysteresis is the preferred mode of pacing in order to preserve spontaneous sinus rhythm.	I	C	-

To conclude ……..

- Sinus node dysfunction is not uncommon disease.
- It entails a wide range of disorders ranging from asymptomatic bradycardia to atrial standstill.
- Prognosis is generally good, risk of sudden death is similar to general population …. Risk of thromboembolism & traumatic syncope to be considered.
- Pacing does not improve survival & is only indicated for symptomatic cases.
- DDD (R) is the preferred mode of pacing.
- In AF (tachy- brady) & atrial standstill never forget anticoagulation.