Introduction
Atrial Fibrillation (AF) is an arrhythmia characterized by irregular, disorganized and chaotic electrical activity of the atrium. The ECG classically is represented by low amplitude, variable and irregular base-line undulations corresponding to atrial rate in the range of 400-600/min. The ventricular rate is irregularly irregular (Fig. 1). The mean ventricular rate is usually between 100 to 150/min and is markedly susceptible to acceleration by vagolysis and catecholamines (i.e. standing, exercise).

AF can present as:-

a. Paroxysmal AF- recurrent episodes which terminate spontaneously.
b. Persistent AF – lasts for more than 48 hours and terminates after electric or pharmacologic cardioversion.
c. Permanent AF- fails to terminate despite intervention.

Incidence and Prevalance
Atrial fibrillation was observed in humans as a clinical entity as early as 1909. It is the most common sustained arrhythmia occurring in approximately 0.4% to 1% of the general population. The prevalence of AF increases with age, affecting up to 4% of the population over age 60. Atrial fibrillation accounts for 1/3rd of all patient discharges with arrhythmias as principal diagnosis. More than 50% of the patients with severe rheumatic mitral valve disease have atrial fibrillation. Table 1 enlists the various causes of atrial fibrillation.

Mechanism of AF
Two hypotheses have been proposed:

a. ‘Multiple wavelet’ theory advanced by Moe, in which AF is a result of reentry mechanism in the atrial muscle. Maintenance of fibrillation is favoured by a large mass of atrial tissue.
b. Ectopic focus theory which suggests that AF is due to one or more areas of ectopic automaticity that fires high frequency electric discharges to the neighbouring atria culminating into AF.
Table 1: Etiology of Atrial Fibrillation

I. Cardiac Causes
   1. Valvular heart disease
      i. Rheumatic mitral valve disease
      ii. Mitral valve prolapse- mitral regurgitation
   2. Hypertensive heart disease
   3. Ischemic heart disease
   4. Pericarditis
   5. Cardiac tumors; atrial myxoma
   6. Sick sinus syndrome, WPW syndrome
   7. Cardiomyopathy
      - Hypertrophic
      - Idiopathic dilated
   8. Post coronary bypass surgery

II. Non-cardiac causes-
   1. Pulmonary
      i. Chronic obstructive lung disease
      ii. Pneumonia
      iii. Pulmonary embolism
   2. Hyperthyroidism
   3. Toxic : alcohol (‘holiday heart’ syndrome)

III. “Lone” AF

* “AF begets AF”
AF induces changes in atrial refractoriness that may promote its perpetuation. Brief episodes of AF may shorten atrial refractoriness for several minutes, leading to a heightened tendency for the reinduction of AF after conversion to sinus rhythm. The atria get larger during periods of sustained AF and with restoration of sinus rhythm, the AF is reversible if it has not been present for long. The longer the duration of AF, the more difficult it may be to achieve successful conversion and maintenance of sinus rhythm.

Clinical Presentation
Atrial fibrillation can be an incidental finding in an asymptomatic individual. The patients can present
with variable symptoms like palpitations, fatigue, dyspnoea, angina, reduced sense of well-being, syncope, diaphoresis, dizziness or congestive heart failure. Sometimes, patients can present with embolic stroke resulting from left atrial clot. In some cases, a cognitive disability has been reported presumably due to silent cerebral ischemia.

Complications

1. **Thromboembolism and stroke**
   Sustained or chronic AF presents a considerable risk for thromboembolism; presumably following clot formation in LA, more commonly in LA appendage.

   **Predictors of thromboembolic risk in AF:**
   - Rheumatic heart disease (RHD) - 18-20% stroke/year
   - Hypertension
   - Prior stroke or transient ischemic attack (TIA)
   - Diabetes
   - Congestive heart failure
   - Age > 65 years

   The risk of stroke in high risk patients is 5-8%/year. The echocardiographic risk factors for stroke in patients with AF are presence of LV systolic dysfunction and increased LA size. The importance of non-rheumatic AF as a risk factor for ischemic stroke appears to depend largely on the presence of spontaneous LA contrast on echocardiography.

2. **Congestive Heart Failure (CHF)**

   Patients with organic heart disease such as obstructive hypertrophic cardiomyopathy or chronic stable CHF may decompensate rapidly with the onset of AF due to loss of atrioventricular (AV) synchrony, the uncontrolled ventricular rate and the loss of atrial ‘kick’ i.e. loss of effective atrial contraction with its contribution to cardiac output. Patients with chronic, long standing AF develop rate related cardiomyopathy due to rapid ventricular response, thereby leading to CHF.

Physical Examination and Investigations

1. **Clinical signs**
   - Irregularly irregular heart rate
   - Apex pulse deficit (heart rate by palpation less than that by auscultation)
   - Variable first heart sound
   - Jugular venous pulse may show absent ‘a’ waves or fibrillatory waves may be appreciated and pulse amplitude is variable.

2. **Electrocardiogram (ECG)**

   P waves are absent. Atrial activity is chaotic and fibrillatory (f) waves are present. The baseline of the ECG is often undulating and may occasionally have coarse, irregular activity that can resemble atrial flutter but is not as stereotype from wave to wave as flutter tends to be. The atrial rate is generally in the range of 400-600/min with a ventricular conduction being variable and generally in the range of 100-150/min in the absence of drug therapy.

   Intraventricular conduction of the impulses from fibrillating atria may at times, be associated with phasic aberrant ventricular conduction. Its importance lies in the fact that aberrantly conducted beats may be mistaken for ventricular ectopic beats and this may in uence the physician to withhold digitalis when it is needed or to give antiarrhythmic drugs where they are not needed and may even be contraindicated. Aberration is particularly likely to develop when a lengthening
of ventricular cycle is immediately followed by a short cycle. The beat ending the short cycle shows aberrant conduction. This short-long-short cycle sequence promoting aberration is called as Ashman’s phenomenon.

3. 2D Echocardiography
Role of echo in AF:
- identify structural heart disease
- identify LVH, LV systolic function
- quantify LA enlargement
- detect ‘smoke’ i.e. spontaneous LA contrast/ clot in LA

Most clots are in the left atrial appendage (LAA), but poorly visualised by transthoracic echo. Transesophageal echocardiography (TEE) has a 92% sensitivity and 98% specificity for detecting LAA clot

Management of AF
A flow chart as elaborated in figure 2 seems to be the most practical approach to the management of atrial fibrillation (Fig. 2).
I. Pharmacologic treatment of AF

i. Anticoagulation

The aim of this is to prevent embolic phenomenon. The incidence of systemic embolisation is high in patients undergoing cardioversion and in patients with rheumatic heart disease. (Table 2).

As per SPAF (Stroke Prevention in AF) III randomized clinical trial, adjusted dose warfarin is more efficacious in reducing stroke as compared to low intensity fixed–dose warfarin plus aspirin in high risk patients.

ii. Rate control by drugs

The choice of rate control drugs in atrial fibrillation is outlined in the form of a flow chart in Figure 3. The ventricular response is generally controlled through drugs that slow conduction through the AV node. (Table 3).

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### Table 2: Recommendations of Anticoagulation in Atrial Fibrillation

<table>
<thead>
<tr>
<th>Clinical Background</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rheumatic Heart Disease, age &lt; 75yrs.</td>
<td>Warfarin (INR) between 2.0-3.0</td>
</tr>
<tr>
<td>Lone AF age &lt; 65 yrs</td>
<td>Arpirin 325 mg/day</td>
</tr>
<tr>
<td>High risk, age &lt; 75 yrs</td>
<td>Warfarin (INR 2.0-3.0)</td>
</tr>
<tr>
<td>High risk age &gt; 75 yrs</td>
<td>Warfarin (INR 1.5-2.5)</td>
</tr>
<tr>
<td>Patients with major contradictions to warfarin:</td>
<td></td>
</tr>
<tr>
<td>— Intracranial haemorrhage</td>
<td></td>
</tr>
<tr>
<td>— Poor compliance</td>
<td></td>
</tr>
<tr>
<td>Electric cardioversion</td>
<td>Warfarin (INR 2.0-3.0) 4 weeks before and 4 weeks after cardioversion</td>
</tr>
<tr>
<td>Elective surgery for anticoagulated patients:</td>
<td>Stop warfarin 7 days prior to surgery</td>
</tr>
<tr>
<td>— minor surgery</td>
<td>Daily INR - when &lt; 1.5, start sc heparin 10,000 every 12 hours and follow PT/PTT</td>
</tr>
<tr>
<td>— major Surgery</td>
<td>Stop heparin 12 hours before surgery.</td>
</tr>
</tbody>
</table>

### Table 3: Drugs to Control Ventricular Rate in Atrial Fibrillation

<table>
<thead>
<tr>
<th>Agent</th>
<th>Action</th>
<th>Immediate IV dose</th>
<th>Oral maintenance therapy</th>
<th>Avoid use in</th>
</tr>
</thead>
<tbody>
<tr>
<td>Propranolol</td>
<td>β-blocker</td>
<td>0.5 to 1.0 mg every 5 min up to 5 mg total</td>
<td>80-320 mg/d; hepatic</td>
<td>Bronchosplastic lung disease, CHF</td>
</tr>
<tr>
<td>Metoprolol</td>
<td>β-Blocker</td>
<td>5 mg every 5 min up to 15 mg total</td>
<td>50-200 mg/d; hepatic</td>
<td>Same as propranolol</td>
</tr>
<tr>
<td>Esmolol</td>
<td>β-Blocker</td>
<td>0.5 mg/kg/min load over 1 min plus 0.05–0.3 mg/kg/min</td>
<td>None</td>
<td>Same as propranolol</td>
</tr>
<tr>
<td>Digoxin</td>
<td>Cardiac glycoside</td>
<td>0.5 mg+0.25 mg in 5-6h plus 0.25 mg in 4-6 h</td>
<td>0.125-0.5 mg/d; renal</td>
<td>WPW, HCM</td>
</tr>
<tr>
<td>Diltiazem</td>
<td>Calcium channel blocker</td>
<td>20 mg over 5 min plus 2nd bolus allowed after 20 min +5.10, 15 mg/h infusion</td>
<td>120-360 mg/d; hepatic</td>
<td>WPW, constipation peripheral edema, CHF</td>
</tr>
<tr>
<td>Verapamil</td>
<td>Calcium channel blocker</td>
<td>5-10 mg every 5 min</td>
<td>120-240 mg/d; hepatic</td>
<td>Same as diltiazem, risks with CHF possibly greater</td>
</tr>
</tbody>
</table>

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iii. Rhythm control drugs
The drugs to suppress AF are (Table 4):

- Class 1 agents
  - IA: quinidine, procainamide, disopyramide
  - IC: flecainide, propafenone

- Class III agents
  - Amiodarone, sotalol
  - Ibutilide, dofetilide

The antiarrhythmic therapy proves highly efficacious for some patients, at least initially (< 50% of all patients). It is non-invasive but, this approach is not curative and is associated with high recurrence rate, adverse effects of the drugs with potentially lethal proarrhythmias and a high long term cost.

Rate vs. Rhythm control for AF
With the advent of new pharmacologic and non-pharmacologic therapy for restoration of sinus rhythm in atrial fibrillation, the role of the traditional rate control approach for AF was questioned.

Rationale for rhythm control: Rhythm control would help to achieve an appropriate physiologic rate with regularization of the rhythm. This also restores the atrial contribution to cardiac output. Hopefully, this prevents left atrial dilation, prevents left ventricular dysfunction and reduces the incidence of thromboembolism/ stroke and thus may probably obviate the need for anticoagulation.

In patients with RHD, primarily the valvular anomaly should be corrected following which the

Table 4: Drugs for Rhythm Control in Atrial Fibrillation

<table>
<thead>
<tr>
<th>Drug</th>
<th>Oral Dose</th>
<th>Useful In</th>
<th>Avoid In</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class IA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Quinidine gluconate</td>
<td>300-600 mg every 6-8 hr; sustained release preparations: 324-972 mg every 8-12 hrs.</td>
<td>Chronic renal failure</td>
<td>CHF, liver failure</td>
</tr>
<tr>
<td>Procainamide</td>
<td>0.5-1.5g every 12 hr</td>
<td>CHF, joint disease</td>
<td></td>
</tr>
<tr>
<td>Disopyramide</td>
<td>200-400 mg every 12 hr</td>
<td>Older men at risk for urinary retention, CHF, glaucoma, renal failure</td>
<td></td>
</tr>
<tr>
<td>Class IC</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Flecainide</td>
<td>75-150 mg every 12 hr</td>
<td>Failure of Class IA drugs</td>
<td>CHF, CAD</td>
</tr>
<tr>
<td>Propafenone</td>
<td>150-300 mg every 8 hr</td>
<td>Failure of Class IA drugs</td>
<td>CHF</td>
</tr>
<tr>
<td>Class III</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sotalol</td>
<td>80-240 mg every 12 hr</td>
<td>Failure of IA or IC drug; may be used with mild-moderate LV dysfunction</td>
<td>Where beta blockade is contraindicated</td>
</tr>
<tr>
<td>Amiodarone</td>
<td>1200 mg OD for 5 days followed by 400 mg OD for 1 month then 200-400 mg OD. Many alternative dosing regimens</td>
<td>Severe LV dysfunction, failure of other drugs. CHF, renal failure</td>
<td>Pulmonary disease.</td>
</tr>
</tbody>
</table>
aim should be to maintain the patient in normal sinus rhythm using rhythm control drugs. As per ‘CRRAFT’ (Control of rate versus rhythm in rheumatic atrial fibrillation trial) study done at KEM hospital, Mumbai, it was shown that rhythm control approach was better than rate control for rheumatic AF. The other trials like AFFIRM and RACE did not show any change in mortality with use of rhythm control drugs as compared to rate control drugs.

AFFIRM
AFFIRM investigators conducted a randomized, multicenter comparison of rate versus rhythm control treatment strategies in patients with atrial fibrillation and a high risk of stroke or death. The primary end point was overall mortality. A total of 4060 patients (mean age – 70 years) were enrolled in the study.

In this trial rate control regime appeared to be as good as rhythm control approach and in fact with a tendency to higher mortality in the latter group though not statistically significant. The implications of this study seem relevant for the elderly patient and cannot be extrapolated to the younger patient population. Also the means for achieving sinus rhythm were left to the discretion of the physician and therefore multiple rhythm control strategies were used and this by itself may have led to poor outcomes.

II. Non-pharmacologic treatment of AF
Understanding the limitations of the drug therapy for AF, last decade has shown many novel non-pharmacologic treatment modalities (Table 5).

Table 5: Non-pharmacologic therapy

<table>
<thead>
<tr>
<th>Type of AF</th>
<th>Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Paroxysmal AF</td>
<td>Pacemaker therapy- overdrive atrial pacing or dual site right atrial or biastral pacing.</td>
</tr>
<tr>
<td>2. Persistent AF</td>
<td>Atrial defibrillation- internal cardioversion of the atria via percutaneously directed transvenous devices.</td>
</tr>
<tr>
<td>3. Permanent AF</td>
<td>I) Radiofrequency ablation:</td>
</tr>
<tr>
<td></td>
<td>a) Palliative- atrio-ventricular node ablation with implantation of rate responsive pacemaker (VVIR pacing) - advisable in tachycardiomyopathy setting.</td>
</tr>
<tr>
<td></td>
<td>b) Curative-</td>
</tr>
<tr>
<td></td>
<td>i) Pulmonary vein isolation and ablation of the ectopic focus</td>
</tr>
<tr>
<td></td>
<td>ii) Catheter ‘maze’ procedure</td>
</tr>
<tr>
<td></td>
<td>II) Surgical ‘maze’</td>
</tr>
</tbody>
</table>

Pulmonary vein isolation (Figure 4)
There is a suggestion that many patients with atrial fibrillation have the foci of the arrhythmia in the pulmonary veins. Isolation of these foci followed by their radiofrequency catheter ablation is a new, effective curative procedure, which is still under investigation. Its success rate is about 50-70% with a recurrence rate of 20-30%, with complications like pulmonary vein stenosis, pericardial effusion occurring in about 10% of the patients.

Conclusion
Atrial fibrillation continues to be a menacing problem, however, the recent advance in the non-drug therapy is promising to overcome it, hopefully in the near future. Till such time, the traditional approach of rate control with anticoagulation seems to be the mainstay of therapy for most patients.
References

Fig. 4 : Pulmonary vein isolation