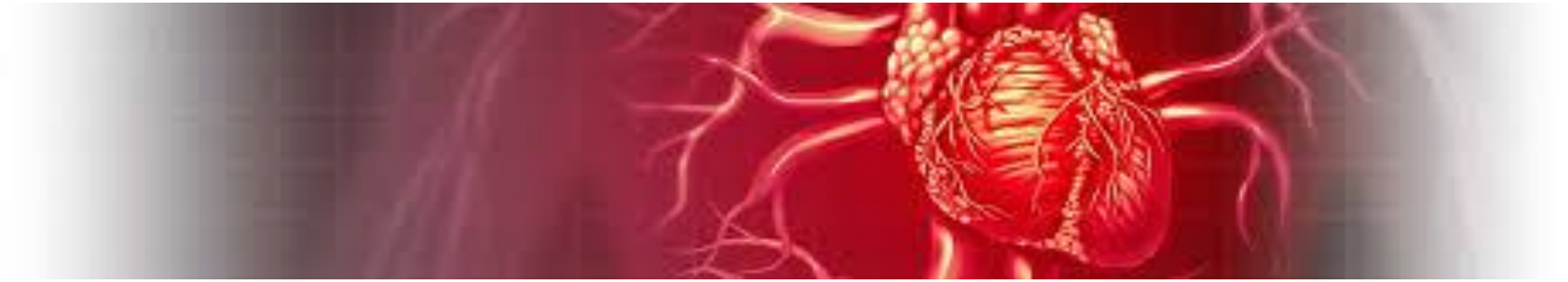
Psychopharmacologic Issues in the Cardiac Patients



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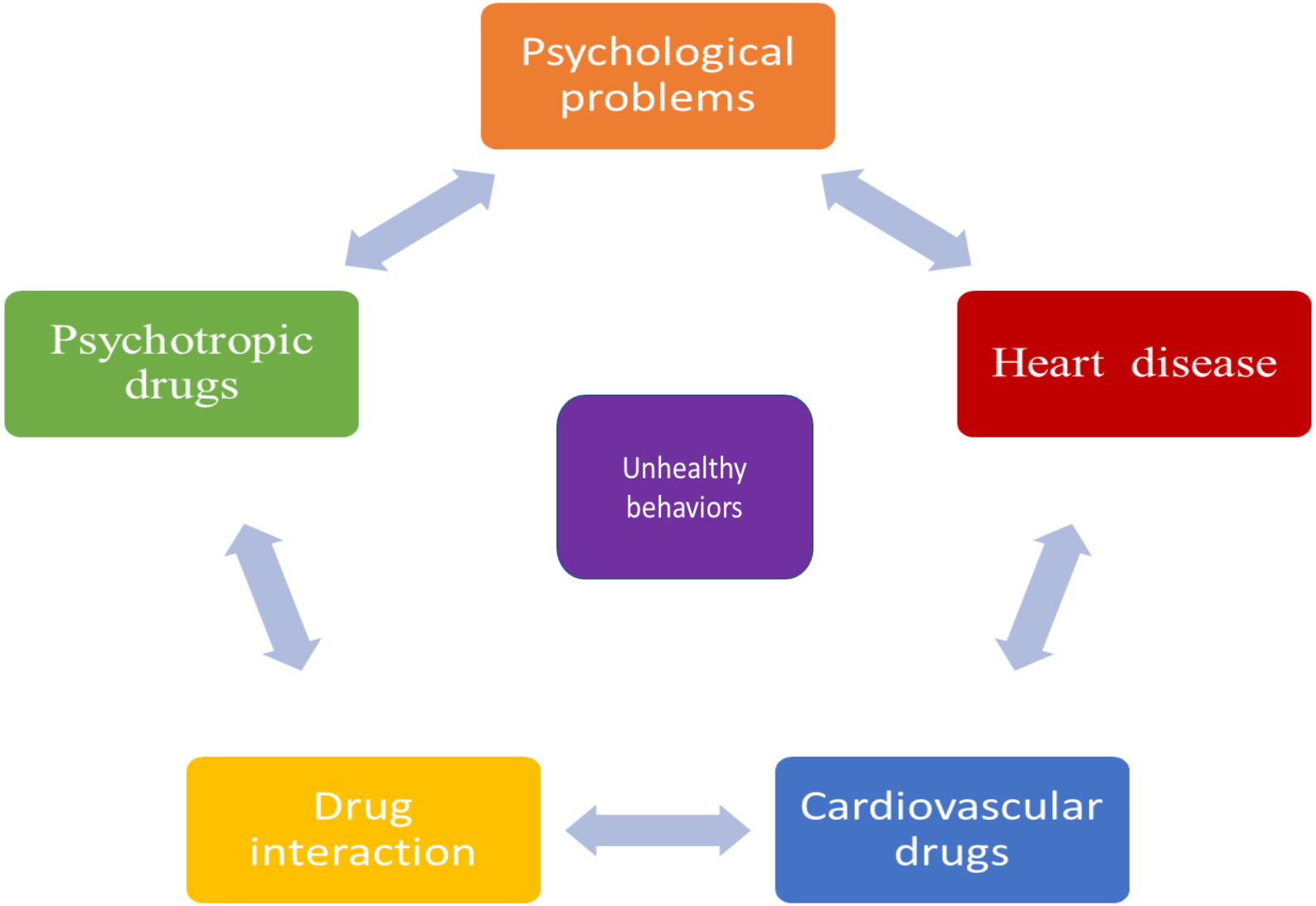
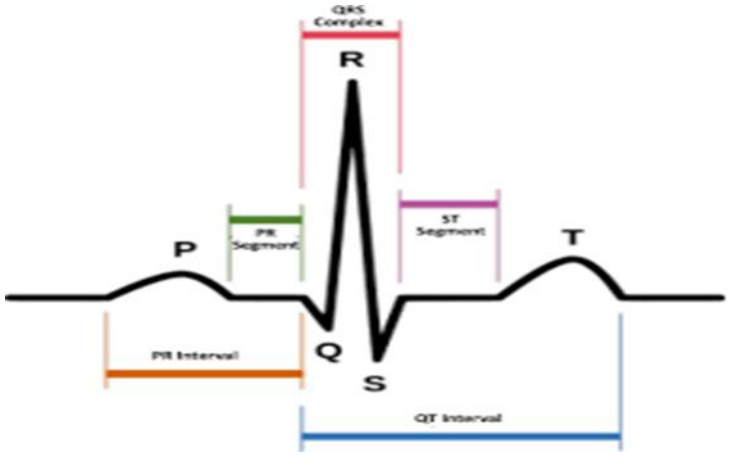
The interface between psychiatry and cardiovascular disease



Antidepressants

- Antidepressants are effective in the treatment of depression for patients with cardiac disease.
- SSRIs are now considered the best first-line medications for treating depression in patients with cardiac disease.
- Older antidepressants (i.e., tricyclic antidepressants [TCAs] and monoamine oxidase inhibitors [MAOIs]) have effects that make their use in cardiac patients difficult.

TCAs



- TCAs have cardiovascular effects:
  - Orthostatic hypotension
  - Cardiac conduction delay (bundle branch block or complete atrioventricular nodal block)
  - Ventricular arrhythmias (including potentially lethal ventricular tachycardia and ventricular fibrillation) in overdose.
  - Prolongation of the QT interval

- Nortriptyline and desipramine tend to cause less orthostatic hypotension than tertiaryamine TCAs and are better tolerated by patients with cardiac disease.
- TCAs should generally not be used as first-line agents for treatment of depression in ischemic heart disease patients, although their efficacy may occasionally offset the risk in selected patients.

SSRIs

- SSRIs have little to no cardiac effect in healthy subjects.

➢ Slowing of the heart rate

➢ Sinus bradycardia or sinus arrest, with light-headedness or syncope

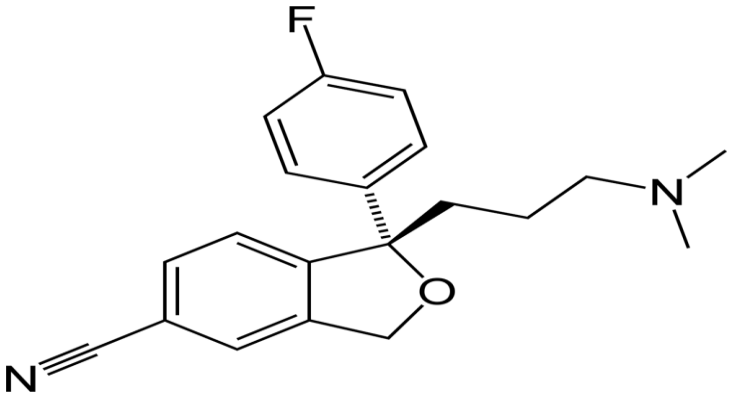
- The combination of beta-adrenergic blockade and SSRIs may result in additive slowing of the heart rate.

SSRIs in an acute coronary event and depressed CHF

- **SSRIs** is considered safe in cardiac patients, and may safely prescribe in post-MI patients earlier than 1 month after the MI when indicated by the severity of depression or the follow-up circumstances.
- **Sertraline (t**he SADHART study**)** was more effective than placebo in treating depression in patients with a prior history of depression, but it did not differ from placebo in patients without a prior history.

- **Citalopram, escitalopram, and sertraline** in depressed CHF patients found the drugs to be well tolerated but failed to find a beneficial effect on mood or medical outcomes.
- Dose-dependent QT interval prolongation occurs with **citalopram** treatment, and to a lesser degree with other SSRIs.

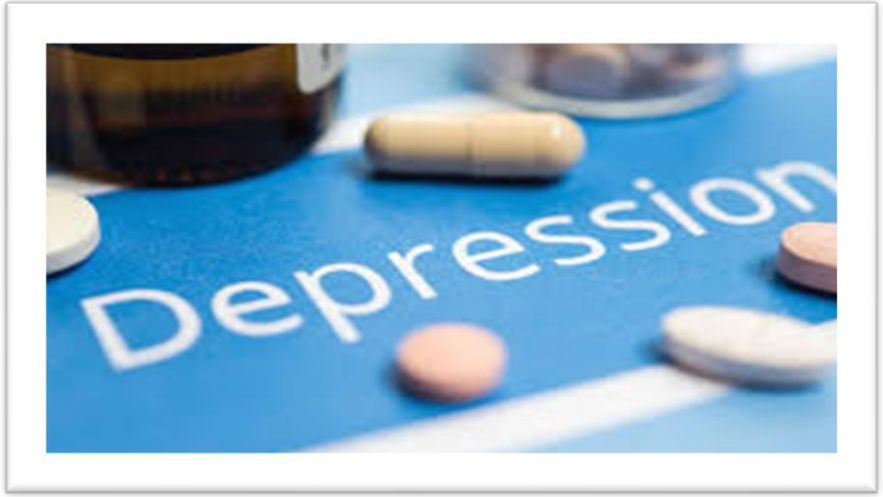
Citalopram



- In 2012, the warning was downgraded to note that **citalopram:**
  - is not recommended at doses >40 mg in the general population
  - is not recommended at doses >20 mg in patients over the age of 65 or with pre-existing liver disease
  - is not recommended for patients with congenital long-QT syndrome
  - should be discontinued in patients with QTc >500 ms
- Many no longer use citalopram as a first-line agent in those with a history of or significant risk factors for heart disease, preferring sertraline instead, given its established safety.

Other antidepressants

- **Venlafaxine** can elevate blood pressure, which may preclude its use as a first-line agent in patients with cardiac disease.
- **Duloxetine** has not been associated with QTc-prolongation or other cardiac side-effects, and may be a reasonable second-line agent.
- **Bupropion** appears to have few cardiovascular effects but may increase blood pressure occasionally. Bupropion, at therapeutic doses, does not have adverse effects on blood pressure, heart rate, or other cardiovascular parameters, and has been shown to reduce rates of smoking.

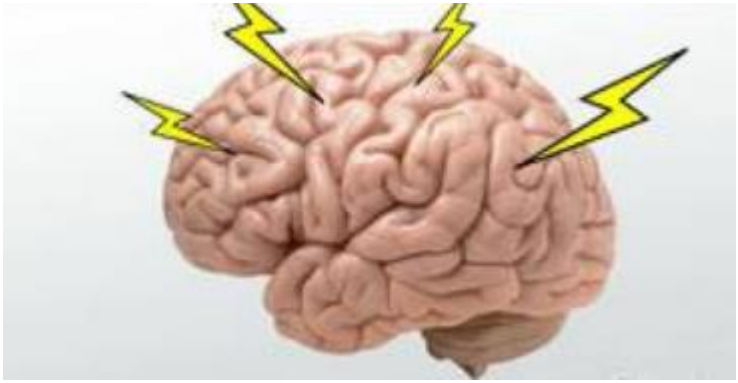


Other antidepressants

- **Mirtazapine** has few effects on cardiac conduction or vital signs, even in overdose. Mirtazapine often has more immediate effects on sleep than do other antidepressants. However, mirtazapine is highly associated with weight gain as a result of its interaction with histamine receptors, limiting its use in patients with cardiac disease.
- **Monoamine oxidase inhibitors** (MAOIs) cause hypotension and orthostatic hypotension; dietary indiscretions leading to high circulating levels of tyramine can cause hypertensive crises. Sympathomimetic agents can increase blood pressure in patients on MAOIs, although hypertensive crises are infrequent. The use of intravenous pressors (epinephrine, isoproterenol, norepinephrine, dopamine, dobutamine) in patients receiving MAOIs requires caution.

Psychostimulants

- Psychostimulants have also been shown to be rapidly acting, efficacious antidepressants in medically hospitalized patients. Clinical response generally occurs within days rather than weeks.
- Stimulants are often used for treatment of depressed medically ill patients, particularly those with pronounced apathy, fatigue, or psychomotor slowing.
- Though they may elevate blood pressure or heart rate, stimulants may be indicated in cardiac patients whose depression requires rapid treatment.
- Stimulants are relatively contraindicated in patients with a history of ventricular tachycardia, recent MI, HF, uncontrolled hypertension or tachycardia.



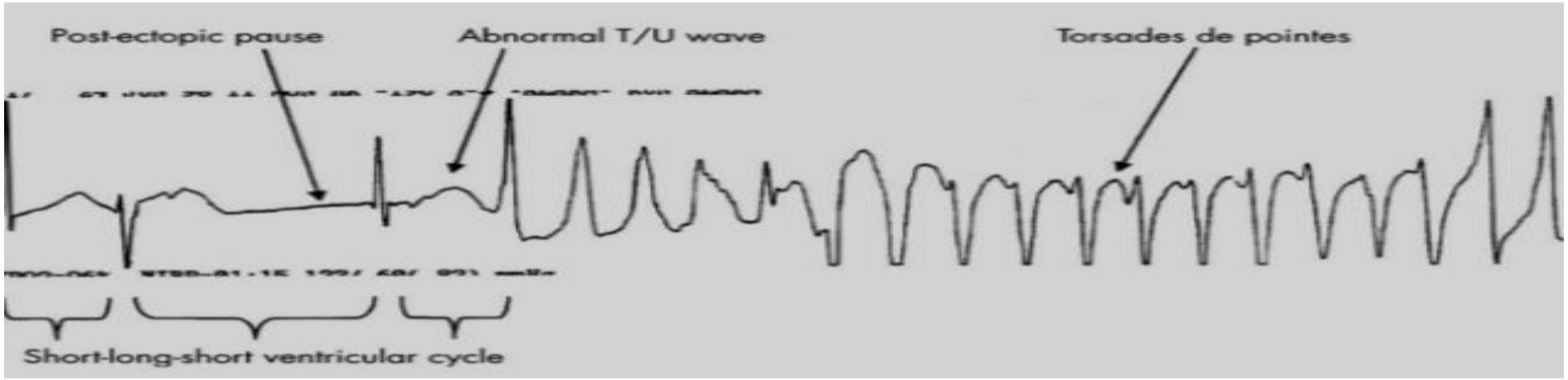

ANTIPSYCHOTIC

Antipsychotics

- First-generation antipsychotics continue to play a role in the management of acute psychotic symptoms in cardiac patients.
- For chronically psychotic patients with heart disease, the choice of antipsychotic is based on side-effect profile.
- The principal cardiovascular effects of antipsychotics are orthostatic hypotension and QT interval prolongation.
- Few data are available on the frequency or clinical significance of orthostatic effects of antipsychotic drugs in patients with heart disease.

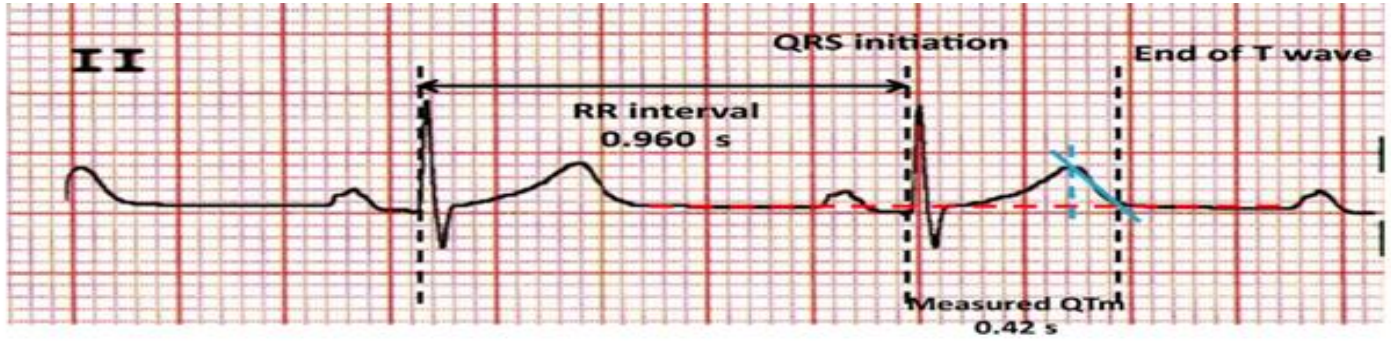
Antipsychotics

- The QT interval normally is less than 450 msec in men and 460 msec in women.
- A QTc interval over 500 msec is generally considered a contraindication to the use of haloperidol and other QT-prolonging agents.
- Intravenous haloperidol is frequently employed in delirious open-heart surgery patients, and although it does have the potential to prolong the QT interval, its use at dosages of up to 1,000 mg/24 hours has been reported without complications.



Antipsychotics and the risk of QT interval prolongation

- Electrocardiographic monitoring is important in intensive care settings and is recommended during antipsychotic treatment when the QTc is greater than 450 msec in men or 470 msec in women.
- Before prescribing drugs that prolong the QT interval, risk factors for TdP should be reviewed. Laboratory values of particular importance are magnesium, calcium, and potassium levels.
- Class IA and III antiarrhythmic drugs, dolasetron, droperidol, tacrolimus, levomethadyl acetate, other antipsychotics, many antibiotics (“floxacins”), and antifungals may increase the risk of TdP.



- The QT interval is measured from the start ofthe QRS to the end ofthe T wave (QTm).
- To determine the end ofthe T wave, a line is drawn from its vertex (blue dotted line) following the slope ofits descending inscription (full blue line) to where itintersects the baseline (dotted line in red).
- Ideally, the QT should be measured in leads with Q waves - DII and V5.

QT Correction with Bazett's Formula:

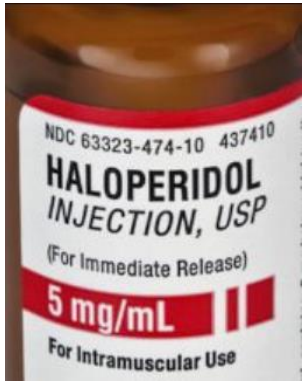
$$\frac{QTm}{\sqrt{RR}} \quad \frac{0.42}{\sqrt{0.96}} \Rightarrow \frac{0.42}{0.9797} = 0.428$$

Antipsychotics and the risk of sudden cardiac death

- A large cohort found that antipsychotic use was associated with a doubling of the risk of sudden cardiac death.
- It seems clear that this risk would be higher in patients with preexisting cardiac disease maintained on antipsychotics.
- Haloperidol, risperidone, olanzapine, and quetiapine as the antipsychotics associated with the highest risk of sudden cardiac death.
- For elderly patients receiving antipsychotics for agitation or behavioral disturbance (e.g., psychotic symptoms in dementia), the risk of death associated with antipsychotics is substantially higher.

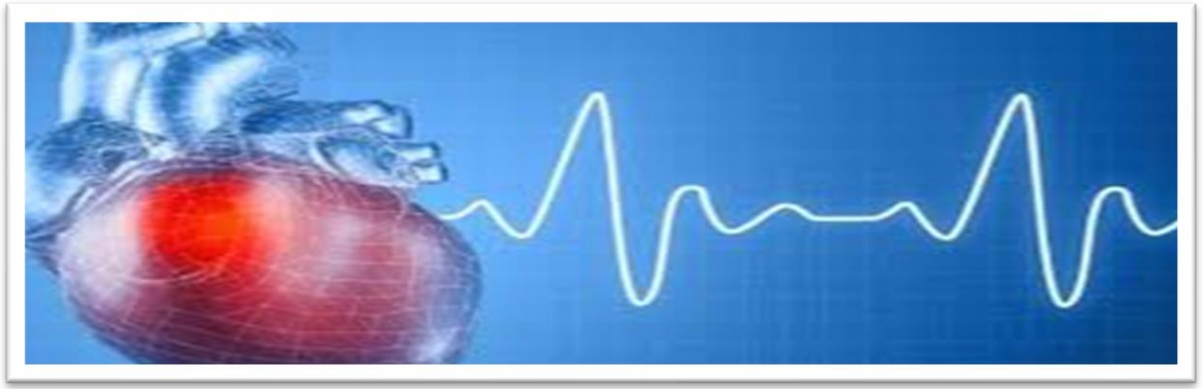
Antipsychotic medications in the delirious cardiac patient

- IV haloperidol remains the “gold standard” for managing delirium. Most patients require standard doses of haloperidol (2 to 10 mg).
- Potassium and Magnesium should be checked, and Abnormalities should be Corrected.
- If an agitated, delirious patient is or becomes unable to receive IV haloperidol (e.g., because of QTc prolongation), there are a number of other options.
- In most cases of delirium, it is often reasonable to schedule a low dose of IV haloperidol or an oral atypical antipsychotic at bedtime.



Other cardiovascular side effects of the Antipsychotics

- **Polymorphic ventricular tachycardia** can also occur in the absence of a long QT interval.
- **Brugada syndrome** is a rare disorder characterized by a history of syncope and risk of sudden death due to polymorphic ventricular tachyarrhythmias. Phenothiazines might increase risk.
- Second-generation antipsychotics also increase cardiovascular disease risk indirectly through promotion of the **metabolic syndrome.**
- **Myocarditis** has been estimated to occur in 0.01%–1.0% of patients treated with clozapine, generally within the first few weeks of treatment.
- **Cardiomyopathy** has also been reported, with onset up to a few years after starting clozapine, even without prior acute myocarditis.



Anxiolytics

Anxiolytics

- **Benzodiazepines** have no specific cardiac effects.
- Reduction of anxiety tends to reduce sympathetic nervous system activation and, therefore, to slow heart rate, decrease myocardial workload, and reduce myocardial irritability.
- Among patients with myocardial ischemia or infarction, benzodiazepines reduce catecholamine levels and decrease coronary vascular resistance.
- Benzodiazepines may inhibit platelet aggregation and raise the ventricular fibrillation (VF) threshold.
- Benzodiazepines are generally well tolerated by the general hospital population.
- Benzodiazepines also appear to be safe even in seriously ill patients, with low rates of adverse events.

Anxiolytics

- The risk of benzodiazepine dependence in the acute care setting is minimal.
- Benzodiazepines may even have beneficial effects on cardiovascular outcomes in specific populations, such as those with cocaine-induced chest pain.
- They can exacerbate confusion and paradoxically worsen agitation in patients with delirium or dementia.
- Oxazepam, lorazepam, and temazepam may be better tolerated by patients with heart failure with hepatic congestion.
- **Buspirone** has no cardiovascular effects.

Anxiolytics

- Benzodiazepines are often the agents of choice for the anxious cardiac patient.
- In general, these agents can be discontinued on discharge from the hospital if they were only used on a short-term basis.
- Benzodiazepines may not be the agents of choice for patients with acute or chronic organic brain syndromes, tenuous respiratory function, or a history of substance dependence. For these patients antipsychotics or gabapentin are often useful.

Other Agents in the acute treatment of anxiety

- **Antidepressants** often take several weeks to work and are best used to treat primary anxiety disorders, such as PD, GAD, or PTSD.
- **Antipsychotics** have the additional beneficial effects of symptomatically treating co-morbid delirium, and they do not cause the paradoxical disinhibition that is sometimes associated with benzodiazepines.
- The anticonvulsant **gabapentin** has been used in the acute treatment of anxiety. Gabapentin is also used at times to treat post-operative pain and alcohol withdrawal.

Mood Stabilizers

Lithium

- Lithium occasionally causes sinus node dysfunction and even sinus arrest.
- Generally, even in patients with reduced cardiac output, lithium can be safely used by adjusting the dosage downward.
- Because renal function is sometimes impaired in advanced heart failure, lithium dosing requires further reduction.
- Caution is necessary for patients taking ACE inhibitors, angiotensin II receptor blockers, and/or diuretics, especially thiazides, and for those on salt-restricted diets.
- In patients with acute CHF exacerbations and acute coronary syndromes, rapid electrolyte and fluid balance shifts can occur; lithium is best avoided during such episodes because of the difficulty managing fluctuations in lithium levels as cardiac therapy (especially diuretics) is adjusted.
- Lithium has been reported to provoke Brugada syndrome.

Other Mood Stabilizers

- **Valproic acid** and **lamotrigine** have no cardiovascular effects.
- **Carbamazepine** resembles TCAs in having quinidine-like class IA antiarrhythmic effects and may cause atrioventricular conduction disturbances.
- Carbamazepine has been reported to provoke Brugada syndrome.

Cholinesterase Inhibitors and *N*-Methyl-D-Aspartate Receptor Antagonists

- The procholinergic effect of **cholinesterase inhibitors** may cause vagotonic effects, including bradycardia or heart block.
- For the *N*-methyl-D-aspartate (NMDA) receptor antagonist **memantine**, hypertension is the only cardiac effect described by the manufacturer on the basis of premarketing controlled trials.

Selected cardiac side effects of psychotropic drugs

Drug/class	Cardiac effects
Lithium	Sinus node dysfunction and arrest
SSRIs	Slowing of heart rate; occasional sinus bradycardia or sinus arrest
TCAs	Orthostatic hypotension; atrioventricular conduction disturbance; class IA antiarrhythmic effect; proarrhythmia in overdose and in setting of ischemia
MAOIs	Orthostatic hypotension
First-generation Antipsychotics	Orthostatic hypotension (especially low-potency drugs); QT interval prolongation; torsade de pointes
Second-generation Antipsychotics	Variable; QT interval prolongation; ventricular arrhythmias; metabolic syndrome
Clozapine	Effects listed above plus orthostatic hypotension; myocarditis
Carbamazepine	Class IA antiarrhythmic effects; atrioventricular block; hyponatremia
Cholinesterase inhibitors	Decreased heart rate

Note. MAOIs=monoamine oxidase inhibitors; SSRIs=selective serotonin reuptake inhibitors; TCAs=tricyclic antidepressants.

Electroconvulsive Therapy

- For elderly patients or those with known coronary disease, monitoring the ECG is essential, and treatment with intravenous beta-blockers is sometimes required.
- ECT has been used safely in patients with ischemic heart disease, heart failure, and heart transplants.
- Acute MI or recent malignant tachyarrhythmias are relatively strong contraindications.
- Takotsubo cardiomyopathy has been reported after ECT; a case of successful reintroduction of ECT after prior Takotsubo cardiomyopathy response to ECT has also been reported.

Drug interactions

Cardiac–Psychiatric Drug Interactions

- A few drug interactions between psychotropic and cardiovascular drugs are worth noting.
- Many psychotropic drugs lower blood pressure; their interaction with antihypertensives, vasodilators, and diuretics may potentiate hypotension.
- TCAs and antipsychotics that prolong the QT interval may interact with antiarrhythmics such as quinidine, procainamide, moricizine, and amiodarone and result in further QT prolongation or atrioventricular block.
- Although SSRIs may increase the risk of bleeding, most do not appear to have a clinically significant effect on the international normalized ratio (INR) in patients treated with warfarin.
- Over the long term, however, concomitant SSRI use approximately doubles the risk of bleeding associated with antiplatelet agents and warfarin alone.

Psychotropic drug interactions with cardiovascular drugs

Psychotropic agent	Cardiovascular agent	Effect
SSRIs	Beta-blockers	Additive bradycardic effects
	Warfarin	Increased bleeding risk, especially with paroxetine and fluoxetine, despite little effect on INR
MAOIs	Epinephrine, dopamine	Hypertension
TCAs	Class IA antiarrhythmics, amiodarone	Prolonged QT interval, increased AV block
Lithium	ACE inhibitors, angiotensin II receptor blockers	Increased lithium level
	Thiazide diuretics	Increased lithium level
Phenothiazines	Beta-blockers	Hypotension

Note. ACE=angiotensin-converting enzyme; AV=atrioventricular; INR=international normalized ratio; MAOIs=monoamine oxidase inhibitors; SSRIs=selective serotonin reuptake inhibitors; TCAs= tricyclic antidepressants.


Thank You
For Your Atten