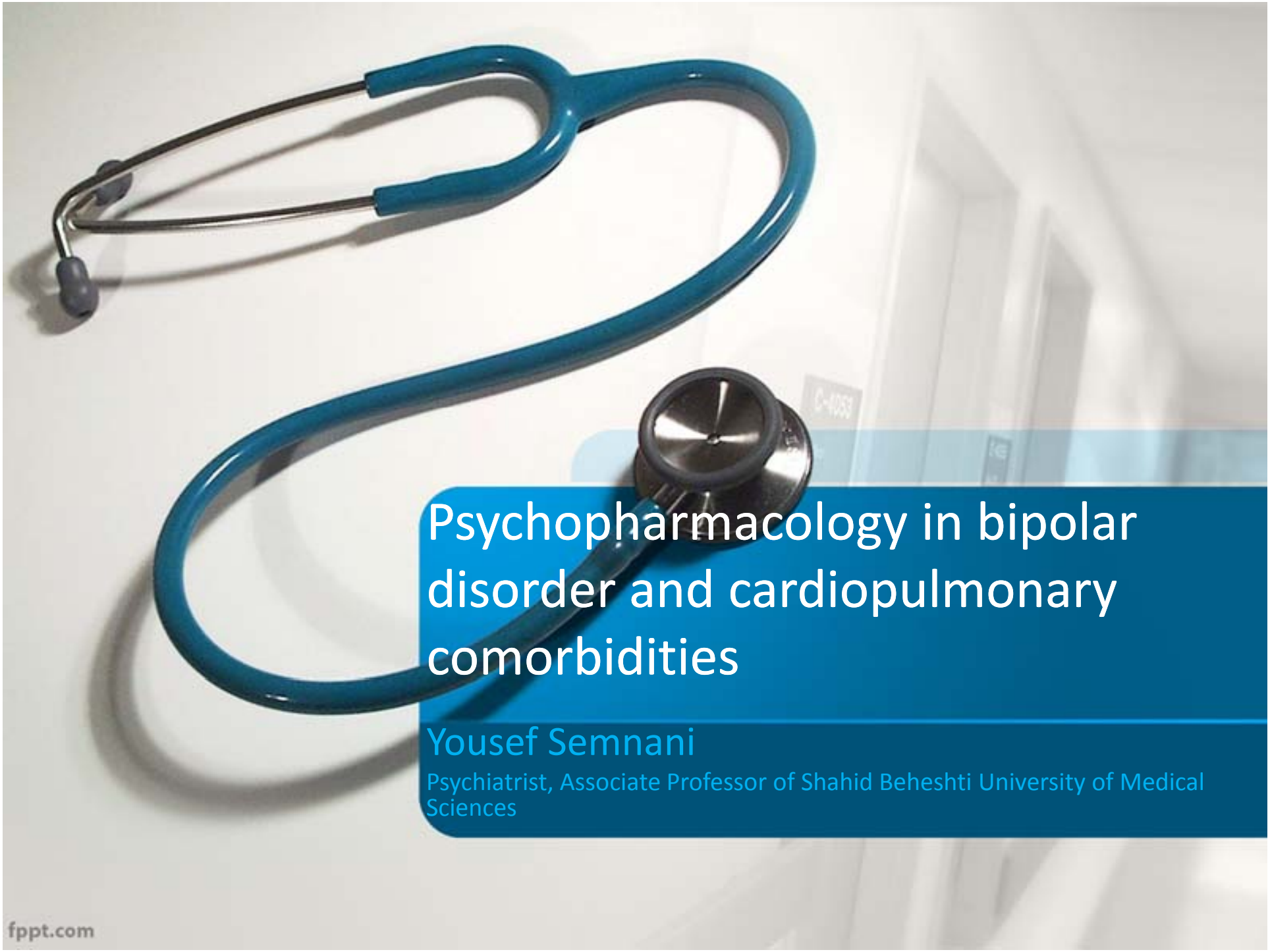

Psychopharmacology in bipolar disorder and cardiopulmonary comorbidities

Yousef Semnani

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Why is it important?

- Individuals with bipolar disorder experience twice the cardiovascular mortality

- The metabolic syndrome is more common in those with bipolar disorder, with a prevalence ratio of 1.6, and includes many traditional cardiovascular risk factors, which may explain much of the elevated risk.


Psychopharmacology in bipolar disorder and cardiac comorbidity
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Which aspects?

- Some bipolar medications exacerbate cardiac problems.
- Some cardiac medications aggravate bipolar disorder.
- Psychotropics and cardiac medications interactions
- ECT and cardiac considerations

Lithium

- Lithium may cause flattening or inversion of T waves that is generally inconsequential and reversible on discontinuation of lithium

- Sinus node dysfunction and first-degree AV block occur infrequently but are the most common cardiac problems secondary to lithium pharmacotherapy

- Symptoms: Dyspnea, paroxysmal tachycardia, dizziness, and fainting, as well as abnormalities in resting pulse.

Lithium

- special care should be taken with elderly patients and those with preexisting atrial conduction disturbances
- In moderate to severe congestive heart failure, diminished renal blood flow may produce prerenal azotemia secondary to decreased cardiac output. This situation may cause lithium toxicity
- No data suggest that lithium should be stopped after a myocardial infarction It seems most prudent to wait to prescribe medications until a post-MI patient has been stabilized

Lithium & Diuretics

- treatment with a low-sodium diet, thiazide diuretics, or angiotensin-converting enzyme (ACE) inhibitors may elevate the serum lithium level.

- Fewer problems with xanthine derivatives, aldosterone antagonists, loop diuretics??, potassium-sparing diuretics

- Osmotic diuretics increase lithium clearance, the change being proportional to the increased rate of urine flow.

Lithium and antihypertensive

- Calcium channel Blockers
  - Verapamil and diltiazem associated with idiopathic neurotoxicity, despite normal or inconsistently altered lithium levels
  - Lithium clearance is reduced by about 30% by nifedipine

- An interaction of Losartan with lithium has occurred by reduced aldosterone secretion, an effect which is greater with ACE inhibitors than with angiotensin II receptor antagonists.

- reports of neurotoxic symptoms when methyldopa was combined with lithium, both with and without an increase in serum lithium concentration

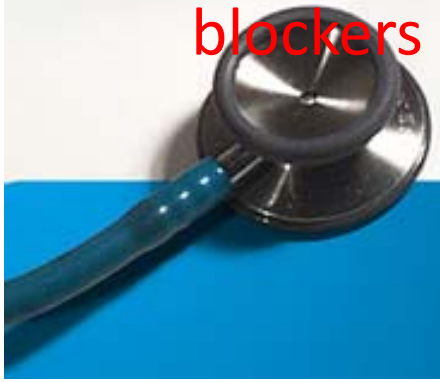
Antiarrhythmic drugs

- Increased risk of arrhythmias with hypokalemia or digitalis toxicity, even at therapeutic serum lithium levels

- β-Blockers with lithium: synergistic bradycardia

Carbamazepine

- A tricyclic structure similar to that of the TCAs and has quinidine-like effects on the heart
- Repeat the ECG after reaching therapeutic serum carbamazepine levels
- Carbamazepine may diminish the effectiveness of antiarrhythmics, antihypertensives, and warfarin
- Neurotoxic effects may be more likely when it is combined with ACE inhibitors or calcium channel blockers



Other mood stabilizers

- Valproic acid does not have adverse cardiac effects
- Lamotrigine , topiramate ,zonisamide , and gabapentin are not cardiotoxic

Antipsychotics

- The principal cardiovascular effects of antipsychotic agents are orthostatic hypotension and QT interval prolongation
- The characteristic tachyarrhythmia is *torsade de pointes, a polymorphic tachycardia*
- Risk factors for torsade:
  - QT interval prolongation of more than 500 msec,
  - family history of sudden death,
  - female sex,
  - hypokalemia,
  - hypomagnesemia,
  - low ejection fraction

- Olanzapine, risperidone, and quetiapine have not been associated with QT prolongation or sudden death

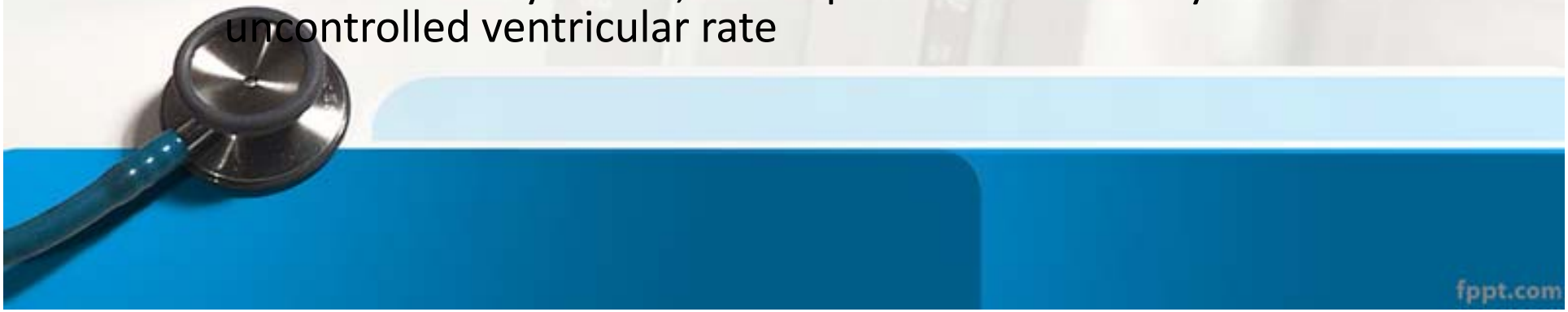
Cardiac medication and bipolar disorder

- ACE inhibitors make mood elevation
- Amiodarone makes mood disorders secondary to thyroid effects

ECT & cardiovascular problems

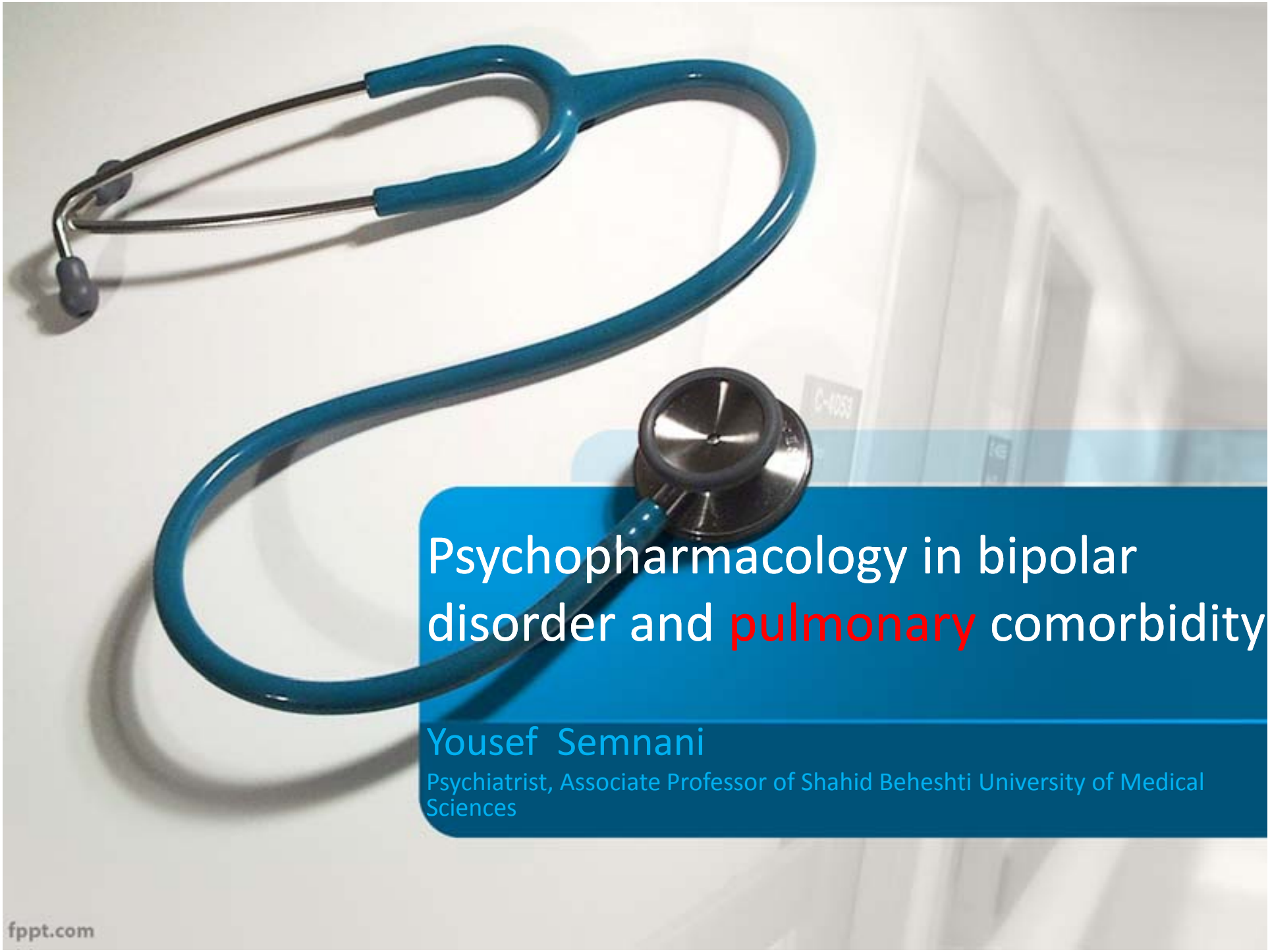
- changes in heart rate and blood pressure typically occur during and immediately after the electrical stimulus and induced seizure

- increased risk with ECT
  - congestive heart failure,
  - severe valvular heart disease,
  - clinically significant cardiac arrhythmias,
  - fragile vascular aneurysms
  - unstable angina or other evidence of active cardiac ischemia
  - uncontrolled hypertension, high-grade atrioventricular block, symptomatic
  - ventricular arrhythmias, and supraventricular arrhythmias with uncontrolled ventricular rate



ECT and cardiovascular problems

- Unstable cardiovascular disease should be stabilized as much as possible prior to ECT.
- Cardiovascular medications should be continued prior to and during the ECT course, including administration of scheduled doses between ECT on treatment days.
- Additional short-acting cardiovascular medications, including anticholinergics, sympatholytics, nitrates, and other antihypertensive agents, should be considered at the time of ECT. Care should be taken to avoid iatrogenic hypotensive effects.
- Whenever possible, systemic lidocaine should be avoided until after the induced seizure



Psychopharmacology in bipolar disorder and pulmonary comorbidity

Yousef Semnani

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Which aspect?

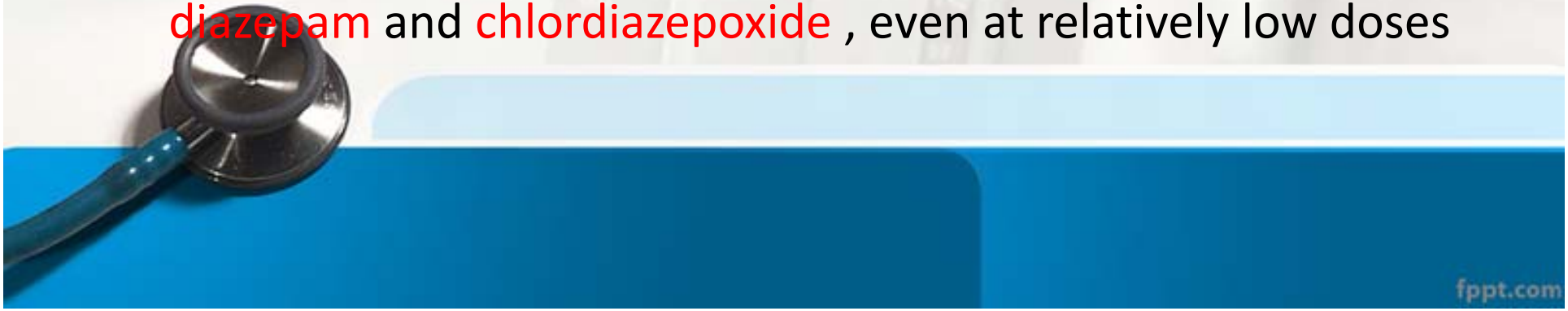
- Bipolar medications aggravate pulmonary problems
- Pulmonary medications exacerbate bipolar disorder
- Psychotropics and pulmonary medications interactions
- ECT & pulmonary problems

Benzodiazepines

- Increased PCO2 normally drives breathing. Many COPD patients are chronically hypercapnic and lose their sensitivity to increased PCO2. As a result, their drive to breathe becomes more dependent on low oxygen saturation (hypoxia) than on PCO2.

- Benzodiazepines can blunt the ventilatory response to hypoxia, thereby inducing more hypercapnia.

- Patients with moderate to severe COPD are particularly at risk for CO2 retention with long-acting benzodiazepines such as diazepam and chlordiazepoxide , even at relatively low doses



Benzodiazepines

- For short-term treatment of acute anxiety in the setting of COPD, lorazepam is the benzodiazepine of Choice

- The anxiolytic effects of a neuroleptic may be helpful. None causes respiratory depression.

Antipsychotics

- Typical neuroleptics such as haloperidol at high doses may cause laryngospasm, akathisia, and paradoxical intercostal muscle movements that, in turn, may cause restlessness and interfere with breathing.

- Tardive dyskinesia sometimes affects the diaphragm, larynx and other muscles used in breathing, and in severe cases, this effect can result in respiratory insufficiency

- Tartrazine (FD&C Yellow #5), a dye contained in several psychotropic drugs, can provoke severe bronchospasm for up to several hours after ingestion.

- Susceptible individuals may have a history of sensitivity to aspirin and bronchospasm from foods colored yellow or orange, such as soft drinks or candy

Lithium

- Renal lithium clearance is increased and serum lithium concentrations are reduced by theophylline and aminophylline

- Valproic acid may increase prothrombin time and INR in patients taking warfarin

- The incidence of steroid psychosis is dose-related, seen in less than 1% of patients taking 40 mg or less of prednisone per day versus 28% taking 80 mg daily

- Isoniazid
  - Schizophreniform psychosis, delirium, euphoria, agitation, paranoia, auditory and visual hallucinations (Commonly given with vitamin B6 or nicotinamide to prevent)

ECT & pulmonary

- Patients with chronic obstructive pulmonary disease should receive pretreatment with any prescribed bronchodilators as well as preoxygenation at each ECT treatment

- Theophylline should be discontinued or levels should be kept as low as clinically feasible to minimize the risk of prolonged seizures

- Patients with asthma should have bronchodilators available for use both before and after each ECT treatment