

# Psychiatric Medications in the Medically III

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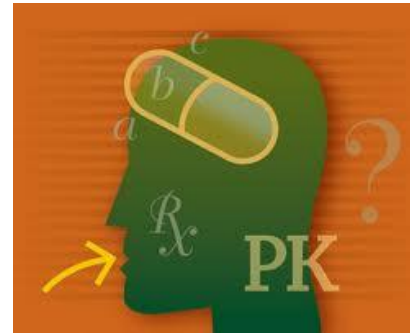
# Outline



- Pharmacokinetics and pharmacodynamics
- Prescribing in patients with:
- Gastrointestinal disorders
  - Renal disease
  - Cardiovascular disease
  - CNS disease
  - Endocrine disease
  - Respiratory disease

# Pharmacokinetics

- Absorption
- Distribution
- Metabolism
- Elimination
- Determines plasma levels and availability at biologically active sites
- Altered by disease of the gastrointestinal tract, liver, heart and kidneys



# Drug-drug Interactions



- Hepatic cytochrome P450 enzyme system catalyses most phase I reactions and is involved in metabolizing more than 80% of all prescribed drugs
- Inhibitors
- Inducers
- Genetic polymorphism
- CYP interactions are continually updated in publications and websites
- [www.drug-interactions.com](http://www.drug-interactions.com)

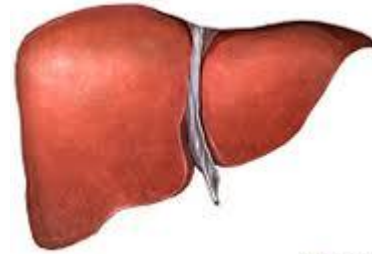
# General Prescribing Principles in the Medically III

- Make a clear diagnosis
- Document rationale for prescribing
- Assess target symptoms
- Measure response with appropriate rating scales
- Explore use of non-medical measures
- Avoid medications that significantly inhibit or induce CYP enzymes



# Gastrointestinal Disorders

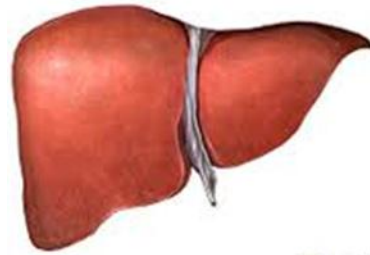
## Hepatic Insufficiency



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- **Reduced capacity to metabolise** biological waste and drugs- hepatic encephalopathy
- **Reduced ability to synthesise** plasma proteins and clotting factors- protein binding, bleeding
- **Reduced hepatic blood flow-** reduced first pass metabolism and elevated plasma levels

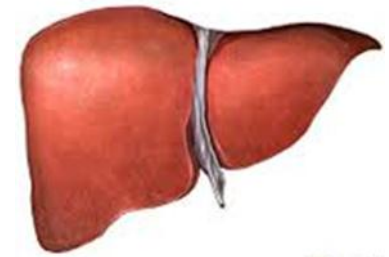
# Prescribing Principals



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- Prescribe as few drugs as possible
- Use lower starting doses
- Longer dosing intervals
- Avoid drugs that are very sedating
- Avoid drugs that are constipating
- Avoid drugs that are hepatotoxic in their own right such as MAOIs and chlorpromazine
- Weekly LFTs

# Drug Induced Hepatic Damage

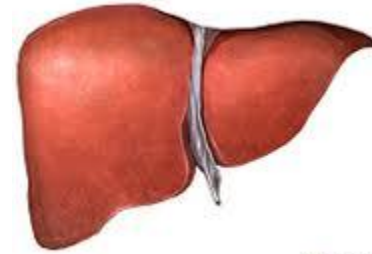


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- **Hepatotoxicity**= ALT > 3 times the upper limit of normal combined with a serum bilirubin more than 2 times the upper limit of normal
- **Risk factors**: increasing age, female gender, alcohol consumption, obesity, pre-existing liver disease, genetic predisposition, co-prescribing of enzyme-inducing drugs



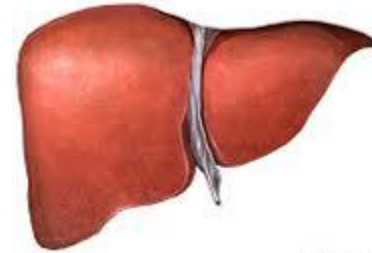
# Antidepressants



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- Anticholinergic TCAs can exacerbate hepatic encephalopathy
- Citalopram, paroxetine, sertraline, and fluoxetine have all been used safely in patients with hepatitis C
- Hepatotoxicity is a rare side effect of many antidepressants
- **Imipramine (25mg), paroxetine (10mg), citalopram (10mg)** recommended in hepatic impairment
- Citalopram- monitor QTc

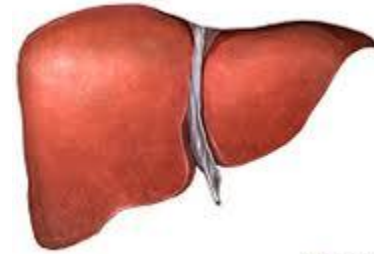
# Antipsychotics



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- Haloperidol most commonly chosen agent
- Sulpiride/amisulpiride safe options
- Avoid chlorpromazine
- Clozapine is contraindicated in active liver disease, progressive liver disease and hepatic failure
- Avoid low potency medications
- Hepatotoxicity from SGAs is rare

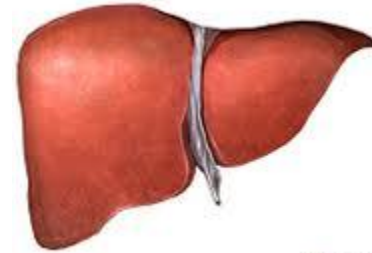
# Anxiolytics



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- Lorazepam, oxazepam, and temazepam are metabolized by phase II conjugation and have short half lives with no active metabolites
- Preferred agents in patients with hepatic disease
- All benzos should be avoided in patients at risk of developing hepatic encephalopathy

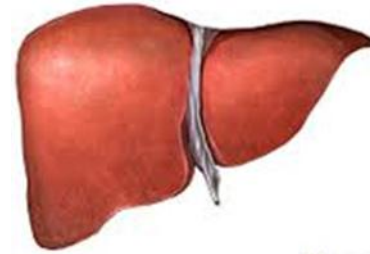
# Mood Stabilizers



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- Carbamazepine and valproate relatively contra-indicated
- Gabapentin is renally excreted
- Lithium may require dosage adjustment because of fluid shifts associated with ascites
- Lamotrigine dose should be reduced according to severity of hepatic impairment

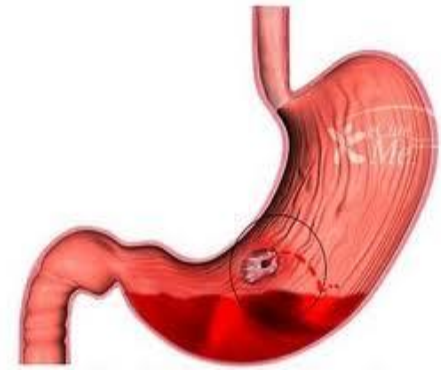
# Anti-dementia Drugs



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- Donepezil, galantamine, rivastigmine should be used with caution
- Memantine mainly renally eliminated no dose reduction required

# Gastrointestinal Disorders: Gastric Bleeding



- **Antidepressants:** SSRIs interfere with platelet aggregation through depletion of platelet serotonin stores, gastric irritation
- Absolute effects are modest and about equal to low dose ibuprofen
- Elderly and those with a history of GIT bleeding at higher risk
- SSRIs and warfarin increase risk of non-GIT bleeds 3.5 fold

# Renal Disease



- Renal disease alters absorption, distribution and protein binding
- Reduced capacity to excrete drugs
- **Drugs requiring dose reduction:** lithium, gabapentin, pregabalin, memantine, paliperidone, paroxetine, desvenlafaxine, topiramate, and venlafaxine
- General rule 2/3 dose
- **Drugs removed by dialysis:** lithium, gabapentin, pregabalin, valproate, topiramate, and levetiracetam

# Prescribing Principals



- Classify stage of impairment using GFR
- Assume elderly patients have renal impairment
- Avoid nephrotoxic drugs
- Avoid extensively renally cleared drugs  
(sulpiride, amisulpiride, lithium)
- Avoid long acting drugs
- Avoid drugs with anticholinergic side effects
- Avoid drugs that prolong QTc interval
- Be vigilant for NMS



# Antidepressants



- Virtually all antidepressants can be used
- SSRIs first line: sertraline, citalopram
- Nortriptyline preferred TCA
- Dose reduction required for venlafaxine, desvenlafaxine, bupropion, paroxetine and reboxetine

# Antipsychotics



- All antipsychotics can be used
- First line: haloperidol 2-6mg, olanzapine 5mg
- Avoid amisulpiride and sulpiride
- Reduce dose of risperidone and paliperidone
- Avoid highly anticholinergic agents

# Anxiolytics and Sedative Hypnotics



- Avoid barbiturates, cause osteomalacia and sedation
- Monitor for excessive sedation
- Lorazepam, oxazepam, zopiclone preferred agents
- Dose reduction required in ESRD

# Mood Stabilizers



- Lithium entirely excreted by kidneys, contraindicated in acute renal failure but not chronic renal failure
- Lithium completely dialysed, give single oral dose after dialysis, check levels 2-3 hours after dialysis
- First line: valproate, carbamazepine, lamotrigine, start low dose increase slowly

# Anti-dementia Drugs



- Limited data
- Rivastigmine first line
- Avoid galantamine in moderate to severe renal insufficiency
- Reduce dose of memantine

# Cardiovascular Disease



Potential cardiovascular side effects:

- Orthostatic hypotension
- Changes in heart rate
- QTc prolongation
- Conduction disturbances
- Arrhythmias

At risk patients:

- Unstable coronary artery disease, conduction abnormalities, orthostatic hypotension, CCF

# Antidepressants TCAs



- Avoid in patients with cardiac disease
- Increase heart rate, cause postural hypotension, slow cardiac conduction and have class1 antiarrhythmic activity
- Cardiotoxic in overdose

# SSRIs



- Fluoxetine: mild bradycardia in elderly with pre-existing arrhythmias
- Citalopram: dose dependant QT interval prolongation, avoid doses  $> 40\text{mg}$
- Escitalopram: similar profile
- **Sertraline: drug of choice in post MI depression**



# Other Antidepressants



- Venlafaxine, duloxetine: may affect blood pressure or heart rate
- Trazodone: reports of orthostatic hypotension, arrhythmias, QT prolongation
- Bupropion: Elevates blood pressure
- **Mirtazepine: no significant effects post MI**
- **Mianserin: low cardiotoxicity**

# Antipsychotics



- CCF: Avoid agents that cause postural hypotension  
(low potency, clozapine, quetiapine)
- Increased risk of sudden cardiac death
- Highest risk of prolonging QTc: pimozide, thioridazine, droperidol, sertindole, ziprasidone, quetiapine, haloperidol
- Lowest effect on QTc: aripiprazole, paliperidone, clozapine, olanzapine, risperidone, sulpiride
- Clozapine: myocarditis, cardiomyopathy
- ECG in at risk patients

# Anxiolytics and Sedative Hypnotics



- Benzos are safe
- IVI administration causes hypotension
- Buspirone safe

# Mood Stabilisers



- Lithium: non specific ECG changes, uncommon: sinus node dysfunction, AV block, QTc prolongation, decreased clearance in CCF
- Valproate is safe
- Carbamazepine: cardiotoxic, AV conduction disturbances
- Lamotrigine: clinically insignificant PR prolongation

# Anti-dementia Drugs



- Cholinesterase inhibitors: vagotonic effects avoid in patients with conduction abnormalities and unexplained syncopal episodes
- Memantine: rarely causes bradycardia

# Psychostimulants



- Increase heart rate and blood pressure
- Methylphenidate and dextroamphetamine no significant cardiovascular effects in low doses
- Contraindicated: structural cardiac abnormalities, cardiomyopathy, coronary artery disease, cardiac rhythm abnormalities
- Modafinil increases BP in non cardiac patients
- Atomoxetine increases heart rate, blood pressure in non cardiac patients, avoid in cardiac patients

# Central Nervous System CVA



- Lower threshold for CNS side effects
- Risks of orthostatic hypotension
- Co-morbid disorders: cardiac, diabetes

# CVA: Antidepressants



- Prophylaxis: nortriptyline, fluoxetine, mirtazepine, escitalopram, sertraline
- Existing depression: nortriptyline, trazodone, mirtazepine, fluoxetine, sertraline, citalopram, escitalopram
- Most studied **fluoxetine, citalopram, nortriptyline**
- Citalopram agent of choice in patients taking warfarin
- Amitriptyline for post stroke pain



# Central Nervous System Seizures



- High psychiatric comorbidity
- Psychosis and depression risk factors for seizures
- Antidepressant and antipsychotics: hyponatraemia, lower seizure threshold
- More sedating agents more likely to induce seizures
- Anticonvulsant drugs associated with new-onset depression and psychosis
- Be aware of drug-drug interactions

# Central Nervous System Seizures



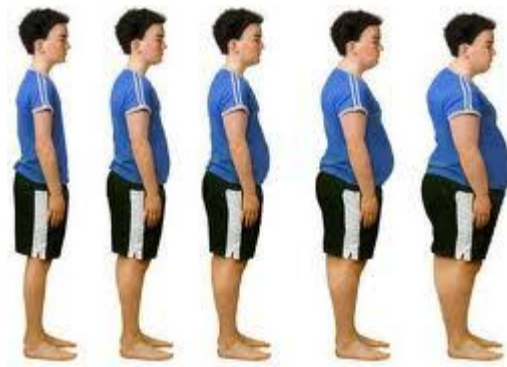
- **Antidepressants** First line: SSRIs
- Avoid: TCAs, bupropion
- Caution: Mirtazepine, venlafaxine, duloxetine
- **Antipsychotics** First line: Haloperidol, trifluoperazine, sulpiride
- Avoid: Clozapine, chlorpromazine
- Caution: Risperidone, olanzapine, quetiapine, amisulpiride

# Parkinson's Disease



- **Antidepressants:** SSRIs first line, low risk of worsening motor symptoms, caution when combined with selegeline (serotonin syndrome), avoid TCAs
- **Antipsychotics:** Clozapine effective without aggravating the disease, quetiapine well tolerated, avoid risperidone and FGA

# Diabetes Mellitus



- **Antidepressants:** SSRIs first line
- Fluoxetine and sertraline reduce HbA1c
- Avoid TCAs
- SNRIs used in the treatment of diabetes neuropathy
- **Antipsychotics:** Be aware of the metabolic complications
- Minimal weight gain for ziprasidone and aripiprazole

# Respiratory Disease



- **Antidepressants:** generally safe
- **Benzodiazepines:** respiratory depressant
- Oxazepam, temazepam, lorazepam agents of choice in COPD
- All benzos contraindicated in sleep apnoea
- Non benzodiazepine hypnotics, ramelteon, buspirone are safer
- **Antipsychotics:** concern- laryngeal dystonia, tardive dyskinesia. Clozapine: respiratory arrest and depression, allergic asthma



## Conclusion



- General medical conditions are common among patients with psychiatric illness
- Psychotropic prescribing is complicated by the underlying disease process, current medications as well as drug-drug interactions
- Medications with proven efficacy and safety and the lowest potential for drug interactions should be chosen
- Initial dose, titration speed and end dose may need to be adjusted and regular monitoring of side effects and clinical response is needed