

**THE PiE BOOK
OF
ADVERSE DRUG REACTIONS**



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presented on the occasion of

**Symposia On Side-Effects
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PREFACE

This book marks the culmination of Symposia on Side-Effects (SOS) that happened over three Sundays in March 2019 in Mumbai. This book - '**The PiE Book of Adverse Drug Reactions**' - and its companion book - '**The Day-To-Day Clinical Relevance of The Cytochrome P450 Enzyme Systems**' - attempt to provide a comprehensive review of adverse drug reactions (ADRs) of oral drugs used by physicians.

ADRs and drug interactions kill hundreds of thousands of patients worldwide every year. A majority of the deaths are preventable. This prevention can only occur by empowering the physician with information.

This particular book contains multiple quizzes and short passages of information such that you can open any page and browse usefully.

PiE is an acronym for the **Platform for Intelligent Edutainment**. This Mumbai-based organization was incorporated in 2012 and has strived to disburse knowledge to physicians and medical students in an entertaining format.

The authors thank **Mr. Laxmichand Gada** for making free distribution of this book possible by his generous contributions.

This book would not have been possible without the excellent transcription and editing skills of **Dr. Shruthi Shridhar**. We also thank **Mr. Viren Shah** who printed this book in an extremely aesthetic manner.

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Utmost care has been taken to keep the information here authentic and up-to-date. However, there is no doubt that some mistakes will be found. If you happen to be the one to find them, you know where to find us - on 9820089743 - the PiE phone number.

Please find this book also on www.pie.net.in and www.drtusharshah.com.

THIS BOOK IS NOT FOR SALE!

ALL ANSWERS START WITH 'A'

As the number one antibiotic implicated in DILI (Drug Induced Liver Injury), it causes idiosyncratic hepatic injury in 1 in 2500 prescription. Name it.

Augmentin. Augmentin is the most common antibiotic causing DILI in US & Europe. In India, AKT may be the commoner cause. Fever, nausea, abdominal pain, pruritus, & jaundice are the chief symptoms. Marked elevations of ALP and GGT may occur. DILI can manifest few days into therapy or upto six weeks after completion of therapy. The clavulanate component of Augmentin is hepatotoxic. The maximum dose of clavulanate in adults should not exceed 375 mg per day.

Which drug used in the elderly can cause both hypothyroidism & hyperthyroidism as side effects?

Amiodarone. Each 200 mg tablet of Amiodarone contains about 75 mg of organic iodide. 1 tablet can provide more than 100 times the daily iodine requirement. Hypothyroidism occurs more commonly than hyperthyroidism.

Which cutaneous side-effect does INH share with corticosteroids?

Acne. Acne due to INH occurs more commonly in the younger population. These should not be specifically treated and disappear on cessation of therapy. Those due to steroids occur more on the trunk and upper limbs than on the face and are monomorphic.

A patient on medications for benign prostatic hypertrophy is given ciprofloxacin for UTI. By 5th day the patient develops postural hypotension and has a fall. Name the α -blocker whose levels have risen because of ciprofloxacin-mediated inhibition of CYP enzymes.

Alfuzosin. The other two commonly used alpha blockers, tamsulosin and silodosin, do not have significant drug interactions through the CYP enzymes.

A person on isotretinoin should not receive the tablet Supradyn because of high dose of a vitamin contained in Supradyn. Which vitamin are we talking about?

A. Vitamin A and isotretinoin given together can cause benign intracranial hypertension. For this very reason, doxycycline and isotretinoin should not be given in combination.

A diabetic patient tells you that her episodes of hypoglycaemia recover better with glucose powder than with table sugar. Which drug group that she is taking is responsible for this phenomenon?

α -Glucosidase Inhibitors. A patient on miglitol, acarbose, or voglibose may not be able to breakdown the disaccharide of table sugar and hence may not respond to it quickly in hypoglycaemia.

A visitor to Leh calls you to complain that he has developed severe paraesthesias all over the body. You ask him if he has had Pepsi in Leh and if it tastes different. He is surprised and answers in the affirmative. What drug do you know is responsible for the paraesthesias and the dysgeusia?

Acetazolamide.

Every person on a particular cardiac drug should be asked if he sees glares during night driving. Which drug are we talking about?

Amiodarone. This symptom occurs because of corneal microdeposits.

Which one of the two causes habituation more commonly - alprazolam or clonazepam?

Alprazolam. The half-life of alprazolam is short. The quick wearing-off of the effect therefore causes craving for another dose. Clonazepam, with its longer half-life has a lesser, though significant, habituation potential.

Neuroleptic Malignant Syndrome is a life-threatening idiosyncratic reaction characterized by fever, altered sensorium, muscle rigidity and autonomic dysfunction. Which group of psychiatric medicines causes NMS?

Antipsychotics. NMS is commoner with traditional antipsychotics like haloperidol than with atypical antipsychotics like quetiapine.

Which antidiabetic drug group is most likely to cause bloating and flatulence?

α -Glucosidase Inhibitors. Metformin too causes GI side-effects in the form of nausea, anorexia, post-meal fullness, and diarrhoea.

The drug of choice for leptospirosis prophylaxis is doxycycline. What is the replacement for doxycycline in pregnancy for this situation?

Azithromycin. The prophylactic dose is 500 mg once a week.

A 40-year-old patient of interstitial lung disease is on oral steroids since a few months. She presents with left groin pain which increases on standing and walking. What complication of steroid therapy should be thought of?

Avascular Necrosis of the Hip. The two commonest causes of AVN are steroid therapy and chronic alcoholism.

A patient of chronic stable angina is given ivabradine to reduce heart rate to 60. After several months of sinus rhythm, the patient suddenly presents with an irregularly irregular pulse of 140/minute. What ADR of ivabradine may have occurred?

Atrial Fibrillation.

ANTICHOLINERGIC SIDE-EFFECTS

The **chief short-term side-effects** occurring due to anticholinergic drugs are -

1. Dry mouth due to decreased salivation and dry eyes due to decreased lacrimation.
2. Blurring of vision due to cycloplegia and precipitation of angle-closure glaucoma.
3. Constipation due to decreased peristalsis and increased sphincter tone.
4. Urinary retention especially in elderly males with BPH.
5. Tachycardia and fluctuations in blood pressure.
6. Drowsiness or delirium.

The **chief long-term side-effect** occurring due to anticholinergic drugs is **dementia**.

Drugs causing anticholinergic side-effects -

1. Antihistamines. First-generation antihistamines like dimenhydrinate (Dramamine), diphenhydramine (Benadryl), chlorpheniramine (Avil) are some examples. Second-generation antihistamines like cetirizine do not have anticholinergic effects.
2. Tricyclic antidepressants of which amitriptyline and doxepin have greatest anticholinergic activity and nortriptyline has the least.
3. First-generation antipsychotics like chlorpromazine, trifluoperazine, and haloperidol are examples.
4. Miscellaneous - Antiemetics like prochlorperazine. The anti-Parkinson drug trihexyphenidyl (Pacitane). Antimuscarinic agents like oxybutynin and tolterodine.

ALL ANSWERS START WITH 'B'

A person with generalised anxiety disorder has tried various SSRIs all of which have caused significant sedation or weight gain. Name the anti-anxiety agent that is relatively non-sedative and weight neutral that might be useful in such a person.

Buspirone.

A 75-year-old male on a holiday calls you to ask for a sleeping-aid that would be available without prescription. You recommend a syrup. He calls a couple of days later saying that he hasn't been able to pass urine since 24 hours. What syrup did you give?

Benadryl. Diphenhydramine or Benadryl is an anticholinergic and can cause acute urinary retention in a person with BPH.

Which nutraceutical is avoided in chronic smokers because it increases the risk of lung cancer in them?

Beta Carotene.

The brand Bambudil by Cipla is an oral tablet that can cause tremors, palpitations and hypokalemia. What is the pharmacologic agent in Bambudil?

Bambuterol (10mg /20mg) is a slow release prodrug of terbutaline.

Hydroxychloroquine and chloroquine can worsen psoriasis. Which antihypertensive drug group can do the same?

Beta-Blockers.

If fexofenadine is category C with respect to pregnancy risk, what category is levocetirizine?

B. Chlorpheniramine maleate (Avil), diphenhydramine (Benadryl), dexpheniramine (Polaramine) are all category B drugs.

Which ocular symptom that lasts two to three hours and disappears spontaneously has been reported with sildenafil but not with tadalafil?

Blue Vision.

BLACK BOX WARNINGS THE PHYSICIAN SHOULD KNOW

Black Box Warnings are strict and prominent labelling requirements issued by the US FDA warning physicians of serious side-effects.

Some examples of the **important Black Box Warnings** issued by the US FDA are as follows -

- Fournier's gangrene or necrotizing fasciitis of the perineum can occur, albeit rarely, due to **SGLT2 inhibitors**.
- Serious neuropsychiatric side-effects, tendon rupture and dysglycaemia can occur with **fluoroquinolones**.
- A new warning related to **fluoroquinolones** is the rare but serious occurrence of aortic dissection.
- Increased incidence of deaths due to coronary events can occur upto months after a two-week-course of **clarithromycin**.
- Long-term use of **loperamide** can cause serious cardiac events due to QT interval prolongation.
- **Ticagrelor** can cause significant and sometimes fatal bleeding and therefore the concomitant aspirin dose should not exceed 100mg.
- **Oral contraceptives** can increase incidence of strokes if taken by female smokers who are above age 35.
- In February 2019, US FDA released a warning about increased cardiac deaths with **febuxostat** and recommended that it should only be used if allopurinol is contraindicated.
- **Carbamazepine** can cause anaemia and agranulocytosis, thus mandating frequent CBC.

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- Abrupt discontinuation of **beta-blockers** can cause acute coronary syndrome.
- **ACEi** and **ARBs** can cause serious injury or death to the developing foetus.
- Antidepressants, especially **SSRIs**, increase the risk of suicidal thinking in individuals younger than 18 years of age.
- **Atypical antipsychotics** including **quetiapine**, **olanzapine**, and **risperidone** if given in dementia-related psychosis can increase the risk of death.
- Neuropsychiatric side-effects of **mefloquine** can persist long after mefloquine has been discontinued.
- **Pioglitazone** can exacerbate congestive heart failure.
- **Linezolid** can cause the **serotonin syndrome** if given in patients taking serotonergic psychiatric medications like **SSRIs** or **SNRIs**.

An important thing to note is that most black box warnings are issued after discovery of an ADR with the drug already in the market.

ALL ANSWERS START WITH 'C'

SGLT2 inhibitors used for diabetes increase the incidence of urogenital infections because they cause glucosuria. Which organism is the most common cause of these infections?

Candida albicans.

A person on preventive gout medications for six months presents with a respiratory tract infection. You discover a low WBC count. Which your medicine could be the culprit?

Colchicine. Long term colchicine can rarely cause bone marrow depression, peripheral neuropathy, and a coeliac sprue-like enteropathy.

ACEI or ARBs are used in diabetics to prevent or reduce proteinuria. If these cannot be given due to azotaemia or hyperkalaemia, which antihypertensive group can be used to deliver a similar benefit?

Calcium channel blockers namely diltiazem and verapamil (non-dihydropyridines CCBs).

Which ADR is common to iron, calcium, diltiazem, sucralfate, ondansetron, tramadol, tamsulosin, ranolazine, and amitriptyline?

Constipation.

Which drug category related to pregnancy includes drugs that have not been studied adequately and should be used only when benefit is significant.

C. Examples of category C drugs are oxymetazoline nasal spray, tramadol, omeprazole, and Lomotil.

Which antibiotic used for staphylococcal and anaerobic infections and also for falciparum malaria is safe to the foetus in all trimesters of pregnancy?

Clindamycin. Amongst antimalarials, primaquine and doxycycline are category D and are both contraindicated, chloroquine is safe in all trimesters, ACT is safe in 2nd and 3rd trimesters, quinine is safe in 1st and 2nd trimesters while mefloquine for malaria prophylaxis is safe in all trimesters.

Name the drug (other than erythromycin) that, if given to lactating mothers or infants during the first six weeks after birth, may increase the risk of infantile hypertrophic pyloric stenosis.

Clarithromycin. Erythromycin and clarithromycin are unsafe in infants. Azithromycin is safe. However, avoid indiscriminate use of azithromycin in children as it is an important antibiotic for enteric fever.

Which antiviral vaccine other than MMR should not be received for at least three months prior to conceiving a child?

Chickenpox Vaccine.

‘Gamascab’ and ‘Scaboma’ lotions contain lindane. They should not be used as first-line agents against scabies or lice in view of a side effect of lindane. Which?

Convulsions.

Name the nasal spray used to treat acute pain of osteoporotic vertebral fractures whose side effects include flushing, rhinitis, epistaxis, hypocalcaemia, and arguably, an increased risk of cancer.

Calcitonin nasal spray. Before one starts calcitonin nasal spray, one should ensure adequate supplementation with vitamin D and calcium.

In a patient on proton-pump inhibitors, oral calcium carbonate is not well absorbed. Which salt should be used in such patients?

Calcium citrate. Another advantage of calcium citrate is that it can be taken irrespective of meals. Calcium carbonate requires to be taken after meals.

Apart from paracetamol which analgesic belongs to category A of drugs in pregnancy?

Codeine. Tramadol and tapentadol are category C drugs.

Serum levels of which biochemical are reduced by loop diuretics and increased by thiazides?

Calcium. Hydrochlorothiazide and furosemide both cause hyponatremia, hypokalaemia, and hyperuricemia. They have divergent effects on calcium levels.

CORTICOSTEROIDS AND THEIR LONG-TERM MONITORING

In a patient on long-term corticosteroids one must follow the following guidelines.

1. Maintain a total calcium intake 1200 mg/d and vitamin D intake of 800 IU/day.
2. Measure bone mineral density (by DXA) at the initiation of therapy and after one year. Bisphosphonates must be started if T-score < 2.5 or if there is a fragility fracture. Another indication of starting bisphosphonates is a prednisolone dose of $> 7.5\text{mg/day}$ for more than 3 months in any post-menopausal female or a male > 50 years of age.
3. Periodic check for lipid levels and sugar levels is mandatory. Start metformin at the first indication of IFG and IGT.
4. Closely watch blood pressure. If hypertension occurs, avoid diuretics as steroids cause hypokalemia too.
5. Periodic check by ophthalmologist for glaucoma and cataract necessary.
6. Interact with primary prescriber about tapering the dose and/or alternate day dosing.
7. Keep high index of suspicion for osteonecrosis of femoral head if the patient comes with low back pain or hip pain. AVN is often missed.
8. During any acute illness in a person on glucocorticoids, one usually needs to increase dose. Do not make the mistake of stopping steroids if an infection occurs.
9. The risk of GI bleed with steroids is lower than that with NSAIDs. Co-administration can cause significant increase in incidence of GI ulceration/bleed.
10. Single morning dose is preferred in persons with insomnia.

CLOSTRIDIUM DIFFICILE ASSOCIATED DIARRHOEA (CDAD)

CDAD occurs primarily in hospitalized patients. It is one of the most common nosocomial infection. It occurs due to superinfection by *C. difficile* after antibiotics have disrupted the normal gut flora.

The most implicated antibiotics are cephalosporins (especially 2nd and 3rd generation), fluoroquinolones, ampicillin/amoxicillin, and clindamycin.

The risk of developing CDAD seems to be more in patients on proton-pump inhibitors.

Symptoms of CDAD include mild to moderate watery non-bloody diarrhoea, cramps, anorexia, nausea, and fever. Examination reveals lower abdominal tenderness. Neutrophilic leucocytosis is the typical CBC finding. Commonest test used to confirm diagnosis is 'stool for *C. difficile* toxin'.

CDAD can occur 48 hours after hospitalization or anytime upto 3 months after discharge.

Cessation of the culprit antibiotics may be the only treatment necessary if there is mild diarrhoea without fever, abdominal pain or leucocytosis.

In other cases, one may give metronidazole (oral or IV) or vancomycin (oral) for 10 days.

Typical dose of metronidazole is 400 mg tds for 10 days and of vancomycin is 125 mg qds for 10 days.

N.B. *Clostridium difficile* has now been renamed *clostridioides difficile*, a name slightly *difficile* to remember!

ALL ANSWERS START WITH 'D'

Increased serum prolactin levels with galactorrhoea and amenorrhoea may occur with long term use of which drug used commonly in GERD?

Domperidone. This side-effect has been put to use in lactating women to increase milk production.

If a person with proneness to severe motion sickness does not tolerate 'Avomine' and similar antihistamines because of severe drowsiness, what alternative drug maybe used? (Hint - This drug is commonly used in the first trimester of pregnancy.)

Doxylamine which is available in combination with pyridoxine as 'Doxinate'.

A diabetic patient gives you a history of idiopathic pancreatitis in the past. Which oral anti-diabetic drug group should you avoid in this patient?

DPP4 inhibitors.

Many patients undergoing PCI are given 'Brilinta' or ticagrelor. Which ADR should the patient be aware of other than bleeding?

Dyspnoea on exertion.

Which basal insulin has a lower risk of hypoglycemia - Degludec (Tresiba) or Glargine (Lantus)?

Degludec. This is why degludec can be pre-mixed with a short acting insulin while glargine cannot.

Impulse Control Disorder is the ADR of which group of neurologic drugs?

Dopaminergics like pramipexole, levodopa, ropinirole. Symptoms of impulse control disorder include excessive shopping, compulsive gambling, sexual compulsion etc.

Name a side-effect that is common to orlistat, colchicine, metformin, magnesium-containing antacids, and sertraline.

Diarrhoea.

A lactating mother has waded through dirty water. Name the single dose preventive medicine that can be given safely and is the first-choice drug.

Doxycycline. Though doxycycline is contraindicated in pregnancy and in children below age 8, a small 200 mg single dose consumed by the mother is safe. Absorption of doxycycline thus ingested by the breastfeeding child is inhibited by the calcium in breastmilk.

Methyldopa given in pregnancy for hypertension should be switched to another drug immediately postpartum even if tolerated very well. This is to prevent which complication?

Depression. Continuation of methyldopa after delivery is associated with an increase in the incidence of post-partum depression.

Which ADR is common to metronidazole, olmesartan, acetazolamide, and eszopiclone?

Dysgeusia.

To which drug is oral atropine added to reduce its addictive potential?

Diphenoxylate which is an opioid and is therefore used as an antimotility agent for diarrhoea. One brand containing diphenoxylate and atropine is Lomotil. Lomotil is contraindicated in children as it can cause respiratory depression.

What does the acronym DRESS in DRESS syndrome stand for?

Drug Rash with Eosinophilia and Systemic Symptoms. DRESS is a severe, idiosyncratic, multisystem reaction to a drug characterized by fever, skin rash, lymphadenopathy, haematological abnormalities and internal organ involvement. Medicines most commonly associated with DRESS are anticonvulsants, beta-lactam antibiotics, and allopurinol. The estimated mortality of DRESS is 10%.

DO'S AND DON'TS IN GERIATRIC PRESCRIPTION
(a partial selection from the STOPP/START Criteria & Beers Criteria)

CARDIOVASCULAR SYSTEM -

- Do not use warfarin for first uncomplicated DVT for longer than six months.
- Do not use warfarin for first uncomplicated pulmonary embolus for more than 12 months.
- Do not use aspirin in a dose greater than 150mg/day.
- Do not use calcium channel blockers in patients with chronic constipation.
- Do not use aspirin for primary prophylaxis even in diabetics.
- Do prescribe antihypertensive therapy when systolic BP is consistently above 160 mm Hg.
- Do not hesitate to give statins when indicated if life expectancy is greater than 5 years.

CENTRAL NERVOUS SYSTEM -

- Do not use tricyclic antidepressants with dementia, glaucoma, constipation, and cardiac conductive abnormalities.
- Do not use first-generation antihistamines for more than one week.
- Do not hesitate to prescribe antidepressants in the presence of moderate to severe depressive symptoms lasting at least three years.

GASTROINTESTINAL SYSTEM -

- Do not use prochlorperazine (Stemetil) or metoclopramide (Perinorm) with parkinsonism.
- Do not use loperamide, diphenoxylate or codeine for treatment of severe infective gastroenteritis.

RESPIRATORY SYSTEM -

- Do not use theophylline as monotherapy for COPD.
- Do consider continuous home oxygen therapy in patients with severe COPD.
- Do not use oral corticosteroids for a long duration in COPD or asthma.

ALL ANSWERS START WITH 'E'

The incidence of ocular toxicity due to this drug is < 1% on a dose of 15 mg/kg/d. But rises to 5% on a dose of 25 mg/kg/d. Which drug are we talking about that can cause dyschromatopsia (abnormal colour perception) or blurring of the centre of the reading vision (due to optic neuritis)?

Ethambutol. Every patient on first line AKT should be informed about the following side effects -

- Red urine.
- Nausea / vomiting. Pyrazinamide and INH cause the most nausea and should be taken after food. Therefore, fixed drug combinations that must be taken empty stomach may cause more gastritis. Gastritis typically occurs in the very first week of therapy. AKT-induced jaundice usually occurs after two weeks of therapy.
- New fever / rash.
- Joint pains which may be due to pyrazinamide.
- Visual loss and change in colour perception.

Statin-induced myopathy is dose dependent. Which drug, if given with a statin, can help keep the dose of the statin low.

Ezetimibe.

Which vitamin is considered useful in preventing the progression of NAFLD but may increase the incidence of prostate cancer if given for a long duration?

E.

Which is the only first line AKT oral drug that is not hepatotoxic?

Ethambutol.

Spirolactone causes gynaecomastia. Which aldosterone antagonist does not cause gynaecomastia?

Eplerenone. The disadvantage of eplerenone is its higher cost and the fact that it is a substrate of CYP3A4 enzyme. Thus, CYP3A4 inhibitors can cause rise in level of eplerenone and hyperkalaemia.

Which drug used for treatment of acute migraine headaches is a category X drug?

Ergotamine. Migranil and Vasograin are common ergot brands. Ergotamine is also contraindicated in patients with coronary artery disease. A category X drug used for migraine prophylaxis is valproate.

Beta-blockers are undeserved recipients of major blame for this side-effect. Hydrochlorothiazide is the most likely antihypertensive to cause this side-effect. ACEi and ARBs do not cause this side-effect. This symptom is often a nocebo effect related to Google searches made by hypertensive patients. What side-effect are we talking about?

Erectile Dysfunction. Nebivolol has the greatest 'safety profile' amongst beta-blockers with respect to erectile dysfunction.

Which extremely effective therapy for severe depression has fallen out of favour because of troublesome retrograde amnesia caused by it?

Electroconvulsive Therapy.

Which cardiac anomaly is caused by the use of lithium in early pregnancy?

Ebstein Anomaly.

ERRORS IN PRESCRIPTIONS AND HOW TO AVOID THEM

These are tips from the consulting paediatrician Dr. Tushar Maniar on how to avoid adverse reactions of a badly written prescription.

1. Improve handwriting by writing in CAPITAL LETTERS. An even better option is to use a software to print prescriptions.
2. Telephonic advice is liable to many mistakes including mistaken identity, dosage and frequency errors, as well as not remembering other medications and pre-existing conditions. Avoid telephonic consultations as far as possible.
3. If consulting over the phone, give only basic symptomatic medication and ask the patient to reach a doctor or a hospital. Always text the medicine names.
4. Memorize the dosage for a 10 kg child and multiply for different body weights. Remember the maximum dose in an overweight child is the adult dose.
5. Have a list of lookalike and sound-alike medicines used by you. Avoid using multiple compositions and strengths of a particular brand name.
6. Avoid short forms. Write generic names at least for the unusual products.
7. Always write 0.5 ml and not .5 ml.
8. Explain the route of administration clearly. For example, drops are not only oral but can be aural and tablets can be inserted vaginally.
9. De-prescribe whenever possible.
10. Check for drug interactions.
11. Read out your prescriptions loudly to the patient.

ALL ANSWERS START WITH 'F'

Which cardiovascular drug often used in high doses in nephrology may cause ototoxicity?

Furosemide. Torsemide on the other hand does not accumulate in tissues and has less propensity to cause ototoxicity.

Name the drug of choice added to folic acid to treat severe mucositis due to methotrexate.

Folinic Acid (Leucovorin).

Name a drug used in BPH that can cause erectile dysfunction and gynaecomastia.

Finasteride. Both finasteride and dutasteride can cause these ADRs.

What ADR must a patient be forewarned about when starting carbimazole or methimazole?

Fever. Methimazole and its prodrug carbimazole can cause bone marrow depression, a side-effect not significantly seen with propylthiouracil. Despite this fact, propylthiouracil is not used except in the first trimester of pregnancy because it has significant hepatotoxicity.

Below what GFR should you not give SGLT2 inhibitors?

Forty-Five. On the other hand, metformin should not be given below a GFR of 30.

Name the drug used for migraine prophylaxis that can cause weight gain and drug-induced parkinsonism.

Flunarizine

NSAIDs are category B/B/D which mean that they are category B and B in the 1st and 2nd trimesters and D in the 3rd trimester. Which foetal organ do they adversely affect in the 3rd trimester?

Foetal Ductus Arteriosus. They cause premature closure of foetal ductus arteriosus if given in the 3rd trimester.

An asymptomatic child on first line AKT has increased levels of transaminases. At what level would you label the child as having hepatotoxicity?

Five times upper limit of normal since the patient is asymptomatic. SGOT and SGPT elevation of three times ULN is considered indicative of hepatotoxicity if the patient is symptomatic. A bilirubin level of 1.5 gms/dL is also considered a sign of hepatotoxicity.

Which inhaled corticosteroid used in asthma has a greater first-pass metabolism than beclomethasone and is therefore less-likely to produce systemic side-effects?

Fluticasone.

FALL RISK IN THE ELDERLY DUE TO DRUGS

The following drugs are associated with a high risk of falls -

1. Benzodiazepines
2. Nonbenzodiazepine sedatives
3. Opioids
4. Hypoglycaemics
5. Antipsychotics

The following drugs are associated with a moderate risk of falls -

1. Antidepressants
2. Antihypertensives
3. Other cardiac drugs including antianginals and antiarrhythmics

The following drugs are associated with a low but definite risk of falls -

1. Diuretics
2. Antihistamines and other drugs with anticholinergic side-effects.
3. Alpha blockers

ALL ANSWERS START WITH 'G'

Pirfenidone is an antifibrotic agent used in mild to moderate IPF where it appears to slow the progression of fibrosis. Which organ system suffers ADR most commonly?

Gastrointestinal. Anorexia and vomiting are common side-effects which increase with an increase in dose. Further, one must monitor liver enzymes in patients on pirfenidone.

A patient of yours goes to the dentist who refers him back to you asking for a change in antihypertensive medication. What oral pathology has the dentist seen?

Gingival Hypertrophy. The dentist wants you to change, amlodipine (or cilnidipine or s-amlodipine) which has caused the gum disease.

Name the expectorant present in brands like syrup Mucinex and Ascoril Plus. Expectorants should not be used in the first trimester because of greater incidence of birth defects.

Guaifenesin.

A breastfeeding mother was given primaquine. Her baby developed mild jaundice but severe pallor. What deficiency in this boy could you have predisposed him to this side-effect?

G6PD deficiency.

Patients on warfarin should not be taking the supplement brand Revital. Which content of Revital can increase the risk of bleeding due to warfarin?

Ginkgo Biloba.

What hepatobiliary side-effect may occur with the parenteral antibiotic ceftriaxone?

Gallbladder sludge or Gallstones. This complication is usually asymptomatic.

DRUGS CAUSING GYNAECOMASTIA

- **ANTIANDROGENS -**

Patients of prostate cancer may be given bicalutamide or flutamide. Usually gynaecomastia appears during the first year of antiandrogen therapy in 40-70 % of patients.

- **5 ALPHA - REDUCTASE INHIBITORS -**

Patients of BPH on dutasteride or finasteride are prone to gynaecomastia because of increased circulating testosterone that is converted to oestrogen.

- **SPIRONOLACTONE -**

Used in various conditions including cirrhosis and heart failure, spironolactone can induce gynaecomastia after only one month of treatment. The occurrence is dose-dependent. Eplerenone does not cause gynaecomastia.

- **PROTEASE INHIBITORS IN ART -**

Drugs such as saquinavir and lopinavir used in antiretroviral therapy can cause gynaecomastia.

Many more drugs have been listed as 'possibly causing' gynaecomastia. These include high doses of antipsychotics, androgens which are abused by athletes, and even omeprazole.

GROUPISMS AND GROUP-SCHISMS

The word **schism** refers to the **difference between two members of the same group**. For example, the schism in the Samajwadi Party of U.P. led to a father temporarily expelling his son from the party.

Here are examples of **Medical Group-Schisms** with respect to side-effects.

1) Spironolactone and eplerenone are both aldosterone antagonists used in disorders like CCF and portal hypertension.

Spironolactone causes gynaecomastia while eplerenone does not. On the other hand, eplerenone has drug interactions related to CYP450 enzymes while spironolactone does not.

2) Hydroxychloroquine and chloroquine have both been used as DMARDs. The former is now preferred because it causes lesser ocular toxicity than chloroquine.

3) Some adverse drug reactions are **class specific**. For example, all fluoroquinolones can cause tendon rupture. Moxifloxacin, however, causes more QTc prolongation than the other quinolones.

4) Clonidine and moxonidine are both centrally-acting antihypertensive drugs. Moxonidine stoppage causes less rebound hypertension than clonidine stoppage. Moxonidine probably causes less dryness of mouth than clonidine.

ALL ANSWERS START WITH 'H'

Excessive use of oral or inhaled salbutamol may cause muscle cramps or cardiac arrhythmias due to which biochemical abnormality?

Hypokalaemia.

If an uncontrolled hypothyroid is given HCTZ for hypertension, what electrolyte disturbance may be precipitated?

Hyponatraemia.

What endocrine disorder is caused by long term use of lithium?

Hypothyroidism.

What endocrine disorder is caused by second-generation long-term antipsychotics?

Hyperglycaemia. SGAs like risperidone, quetiapine, and olanzapine can also cause dyslipidaemia.

Which complication may occur if an antimotility agent like loperamide is given in bloody diarrhoea due to Shiga-toxin producing E. Coli?

Haemolytic Uremic Syndrome.

Risk of this complication increases if ACEi are given simultaneously with NSAIDs.

Hyperkalaemia. A triple whammy occurs when ACE inhibitors are given with potassium-sparing diuretics and NSAIDs.

Name the drug used as a DMARD that can cause reversible corneal deposits and serious macular toxicity if taken over years in a cumulative dose of 1000g.

Hydroxychloroquine. A person taking hydroxychloroquine 400mg/day will reach the cumulative dose of 1000g in about eight years.

A teenaged girl is advised by her family physician to wait in the clinic for fifteen minutes after an injectable vaccine. The physician wants to watch for syncope. Which vaccine has been given?

HPV Vaccine. Gardasil or Cervarix.

HYPONATRAEMIA DUE TO DRUGS

Drug induced hyponatraemia and hospitalization due to the same is not uncommon in the elderly. Here are a few take home messages on the subject.

1. Diuretic therapy in the elderly with indapamide, thiazides, or loop diuretics should be monitored closely for electrolyte imbalance. Hospitalization may be required for profound hyponatraemia defined as serum sodium levels less than 125 mEq/L.
2. SSRIs can cause hyponatraemia. This is more common in the older population, especially older women. SNRIs can cause hyponatraemia too.
3. NSAIDs can cause exertional hyponatraemia in athletes participating in endurance sports.
4. Both carbamazepine and oxcarbazepine can cause hyponatraemia with the latter being more commonly the culprit.

DRUGS CAUSING DYSGLYCEAMIA

ANTIBIOTICS -

Fluoroquinolones can cause hypoglycaemia especially in diabetics. Hyperglycemia may occur too.

ATYPICAL ANTIPSYCHOTICS -

Of the three common second-generation antipsychotics, olanzapine is the most likely to cause hyperglycaemia.

BETA-BLOCKERS -

Beta-blockers can cause both hyperglycaemia and hypoglycaemia unawareness.

THIAZIDE AND THIAZIDE-LIKE DIURETICS -

Amongst antihypertensives, thiazides and thiazide-like diuretics are most likely to cause hyperglycaemia. Thus indapamide, hydrochlorothiazide, chlorthalidone, and metolazone can all cause hyperglycaemia.

CORTICOSTEROIDS -

All corticosteroids can worsen diabetes or cause first-time hyperglycaemia.

STATINS -

Long-term use of statins can cause new-onset diabetes, especially in the obese. It seems that this occurrence is irrespective of the molecule used and the dosage of the statin.

ALL ANSWERS START WITH 'I'

Pyridoxine or vitamin B6 needs to be given with this drug in adults but not in children. Which drug are we talking about?

INH which does not cause peripheral neuropathy in the paediatric age group because of lower doses.

Which nebulized drug given four times a day in COPD may cause acute urinary retention in a patient with BPH?

Ipratropium. The longer acting tiotropium can cause the same ADR because of anticholinergic effect.

Which therapeutic modality for pain-relief in knee osteoarthritis may worsen the degeneration of the joint cartilage?

Intraarticular steroid injections. This modality gives relief for a maximum of three months and also predisposes to joint infections, especially in diabetics.

Ideally all sexually active child-bearing age group women should use two simultaneous forms of contraception while taking this drug. Name the drug.

Isotretinoin. One must rule out pregnancy and instruct the use of dual contraceptives starting one month prior to initiating isotretinoin. The dual contraception should then be continued for one month after stoppage of isotretinoin.

Amongst first line agents for AKT which one is most likely to cause hepatotoxicity?

INH.

In an anaphylactic attack, the first drug to be administered without delay is adrenaline. What is the preferred mode of injection in the OPD?

Intramuscular. Subcutaneous injections are poorly absorbed when there is hypotension. Intravenous injections run the risk of ventricular tachyarrhythmias. The preferred site of injection is the mid outer thigh (vastus lateralis muscle).

IRON THERAPY - CIRCUMVENTING INTOLERANCE TO ORAL IRON

INTRODUCTION

At least 20% of patients report gastrointestinal distress with oral iron. Chief symptoms are abdominal pain, nausea, vomiting, or constipation.

If oral iron is not tolerated due to GI symptoms, we have several options. These two are the most popular -

OPTION 1

Choose a lower dose of elemental iron and administer with vitamin C.

For example, give 25 mg of oral iron every day or every alternate day with 500 mg of Vitamin C to maximize absorption.

OPTION 2

Give intravenous iron sucrose or ferric carboxymaltose. The latter is more expensive but preferred.

The dose required is calculated as follows -

Body weight (kg) x 2.3 x (15 - patient's haemoglobin) + 500 mg (for stores)

Typically, ferric carboxymaltose is given 15 mg/kg/dose (to a maximum 750gms per dose) on two occasions 7 days or more apart.

Dilute 500 mg in 100 ml NS. Higher dose requires 250 ml NS. Minimum administration time for 500 mg is 15 minutes.

Darkening of skin is a side effect that may last days to weeks.

ALL ANSWERS START WITH 'J' or 'K'

Most cases of 'BRONJ' occur in cancer patients receiving intravenous zoledronic acid. 'BRONJ' may also occur in persons receiving oral bisphosphonates for prolonged periods. What does J in BRONJ stand for?

Jaw. BRONJ stands for Bisphosphonate-Related Osteonecrosis of the Jaw.

If you have prescribed propylthiouracil to a pregnant patient with thyrotoxicosis, what clinical sign should you always look for on general examination?

Jaundice. Propylthiouracil is not used in non-pregnant hyperthyroid patients because of its severe hepatotoxicity. However, it is safer in the first trimester of pregnancy than methimazole or carbimazole.

Which adverse drug reaction does not allow the use of SGLT2 inhibitors in type 1 diabetics?

Ketoacidosis.

Alpha-blockers like tamsulosin can cause retrograde ejaculation. What regular exercises by the male patient taking tamsulosin may reduce this side-effect?

Kegel exercises also known as pelvic floor exercises.

Which vitamin contained in brands like Gemcal DS and Bon DK may interfere with action of warfarin increasing risk of thromboembolism?

K.

ALL ANSWERS START WITH 'L'

After Parkinson's disease, the second-most common cause of parkinsonism is drug-induced parkinsonism. These drugs include typical antipsychotics like haloperidol. Which component of brands like Razo-L, Veloz-L, Pepcia-L may cause parkinsonism on long term use?

Levosulpiride. This drug is commonly prescribed by physicians for GERD and often taken for long durations. Two other commonly used drugs that can cause drug-induced Parkinsonism are flunarizine (Sibelium) and cinnarizine (Stugeron).

N.B. Please see the note on Drug-Induced Parkinsonism further down on page 43.

Clavulanic Acid Dose should not exceed 375 mg/day in an adult. Thus, you cannot give more than three tablets per day of Augmentin 625 or cefixime CV 200. A higher dose for a very long duration can cause toxicity to which organ?

Liver (Cholestatic Jaundice).

If Aerocort Forte is used for long term, one of its components can paradoxically induce exacerbations of allergen-induced asthma. Which component?

Levosalbutamol.

Serotonin syndrome is characterized by altered sensorium, neuromuscular hyperactivity and autonomic dysfunction. It can occur due to serotonergic drugs like SSRIs and SNRIs. Which antibiotic when combined with these drugs can increase the incidence of serotonin syndrome?

Linezolid. Another important caution with linezolid is that it can cause bone marrow suppression especially if used for more than ten days.

If you were not sure about a drug's safety profile in breastfeeding mothers, which app would you download and refer to?

LactMed.

Which drug used in the treatment of pneumonia and sinusitis is unsafe in pregnancy but can be safely given to lactating mothers?

Levofloxacin.

The first-choice drug to treat pregnancy-induced hypertension used to be methyldopa. Since it causes significant fatigue and is slow in achieving BP control, another drug has replaced methyldopa. Name it.

Labetalol. Amusingly, one of the brand names of labetalol is Alphadopa L.

Which DMARD should be stopped by a female with rheumatoid arthritis two years before conceiving to prevent teratogenicity?

Leflunomide. The other side-effects of leflunomide are diarrhoea, hair loss, and weight loss.

N.B. A male taking methotrexate should stop it three months prior to planning a baby. HCQ and sulfasalazine are the two DMARDs safe in pregnancy.

Name the only angiotensin-receptor blocker that has drug interactions via the CYP enzymes.

Losartan. It is metabolized primarily by CYP2C9 and CYP3A4. Losartan is also the only ARB that is uricosuric.

ALL ANSWERS START WITH 'M'

Which ADR occurs in nearly every patient of infectious mononucleosis if given amoxicillin?

Maculopapular Rash.

Which is the first choice OAD in pregnancy that is safe in all trimesters?

Metformin. Glibenclamide is considered the safest amongst sulfonylureas. Of the three basal insulins glargine (Lantus), detemir (Levemir), and degludec (Tresiba), detemir is considered the safest.

A pregnant female in second trimester is travelling from Mumbai to Kenya. What is the correct malaria-prophylaxis drug for her?

Mefloquine. Mefloquine is contraindicated in persons with epilepsy or psychotic disorders.

Regular use of Gelusil or Digene should be avoided in pregnancy near term. Why?

Magnesium contained in both can prevent onset of labour.

Name the drug that is teratogenic and is therefore used as an abortifacient by gynaecologists.

Methotrexate.

Name the pneumonia-causing organism that can trigger Stevens Johnson syndrome especially in children.

Mycoplasma pneumoniae.

Trazodone and bupropion are atypical antidepressants and are weight-neutral. Which atypical antidepressant causes weight gain?

Mirtazapine.

MEDICINE SICK DAY RULES

This is a useful patient handout created by British health authorities.

When you are unwell with any of the following -

1. Vomiting or diarrhoea (unless only minor)
2. Fevers, sweats and shaking

Then **STOP** taking the medicines listed below.

Restart when you are well (after 24-48 hours of eating and drinking normally)

MEDICINES TO STOP ON SICK DAYS -

- **ACE inhibitors** - medicine names ending in ‘pril’
e.g. lisinopril, perindopril, ramipril
- **ARBs** - medicine names ending in ‘sartan’
e.g. losartan, candesartan, valsartan
- **NSAIDs** - anti-inflammatory pain killers
e.g. ibuprofen, diclofenac, naproxen
- **Diuretics** - sometimes called ‘water pills’
e.g. furosemide, spironolactone, indapamide, hydrochlorothiazide
- **Metformin** - a medicine for diabetes

ALL ANSWERS START WITH 'N'

What is the commonest ADR of the urinary antibiotic fosfomycin?

Nausea. Though fosfomycin has been recommended as a treatment for uncomplicated cystitis in women, many authorities feel that we should spare the antibiotic for use in multidrug resistant UTI.

If a person is on warfarin and you need to treat for amoebic colitis, giving nitroimidazoles like metronidazole may cause increased levels of the anticoagulants. What drug is then an alternative?

Nitazoxanide. Nitazoxanide dose is 500mg bds x 3 days. It is also used in giardiasis and as an antihelminthic. Even in alcoholics, nitazoxanide may need to replace metronidazole.

Which tricyclic antidepressant is least likely to cause anticholinergic side-effects and should be preferred if TCAs have to be given in the elderly?

Nortriptyline.

An asymptomatic patient on long-standing oral steroids comes with a CBC showing a WBC count of 15000. Should you start antibiotics?

No. Steroids can raise WBC count even in the absence of infection.

Which complication is commoner in persons consuming calcium supplements and less common in persons consuming high dietary calcium?

Nephrolithiasis. The mechanism of lower incidence with higher dietary calcium intake is related to the resultant reduced absorption of oxalates.

Which drug used by some to prevent contrast-induced nephropathy is unpleasant to take because of its unpleasant odour?

N-acetylcysteine.

NSAIDs - SOME TAKE HOME MESSAGES RELATED TO THEIR ADRs

- NSAIDs are some of the most abused drugs in medicine. The abuse is more by physicians than by patients.
- All NSAIDs are equally nephrotoxic. Ketorolac, however, has been singled out in that its use for more than five days is prohibited to avoid nephrotoxicity.
- In persons with AIA - Aspirin-Induced Asthma - most other NSAIDs will aggravate asthma too. However, the selective COX-II inhibitor etoricoxib and the partially selective COX-II inhibitors etodolac and nimesulide may be safer to use in AIA.
- Etoricoxib is the least toxic NSAID as far as the gastrointestinal tract is concerned but is the most toxic NSAID with respect to the cardiovascular system.
- In patients who need NSAIDs but have significant upper GI symptoms with non-specific NSAIDs, should be given etodolac. The GI safety of etodolac is comparable to etoricoxib and the cardiovascular risk is lesser.
- Naproxen has the reputation of being the lesser evil amongst NSAIDs with respect to the cardiovascular system.
- The oxicam group of NSAIDs - piroxicam and meloxicam - cause Stevens Johnson syndrome more commonly than other NSAIDs. These drugs should have no place in our armamentarium.
- Injectable diclofenac is a useful weapon in several acute pains. Do prefer the aqueous preparation whenever possible.
- Nimesulide has been withdrawn from many countries because of the risk of hepatotoxicity. Its use should be reserved in patients of AIA who require NSAIDs.

OUR RESOLUTIONS RELATED TO NSAIDs

1. We resolve to reduce the overall use of NSAIDs in our practice.
2. We try very hard not to prescribe NSAIDs for more than five days at a time.
3. We never ever give a combination of two NSAIDs at one go. Neither do we combine corticosteroids with NSAIDs as far as possible.
4. If a patient is already on aspirin, we give a PPI with the NSAID prescription.
5. We closely monitor the prescriptions meted out by orthopaedicians, dentists etc.
6. We try, wherever possible, to use substitutes to oral NSAIDs including paracetamol, tramadol, NSAID gels/sprays, and placebos.
7. We resolve to educate patients about rational NSAID use.
8. We ask the patient whether the pain is bothersome enough for taking medications.

ALL ANSWERS START WITH 'O'

Overenthusiastic treatment of hypothyroidism can cause TSH to fall below 0.3 mIU/L. This can cause atrial fibrillation and weight loss. Which skeletal ADR can this also cause?

Osteoporosis.

Name one irreversible side-effect of aminoglycosides.

Ototoxicity especially vestibular. Nephrotoxicity due to aminoglycosides is usually reversible and is typically non-oliguric.

If an asthmatic on long term inhaled steroid presents with dysphagia, what ADR of inhalational therapy should be suspected?

Oesophageal Candidiasis.

To prevent first-dose hypotension due to alpha-blockers, start with the lowest possible dose. What is the lowest available dose of prazosin and terazosin?

One mg.

Name a rare but devastating side-effect of dental surgery in patients on long term bisphosphonates.

Osteonecrosis of the jaw.

Which type of pharmacological contraception is avoided in the first thirty days after delivery in view of increased risk of DVT?

Oestrogen-progesterone combination contraceptive pills.

In which orthopaedic disorder is duloxetine approved for use despite its side-effects of somnolence and dizziness?

Osteoarthritis of the knee. Duloxetine should be considered for pain-relief when maximum doses of paracetamol are ineffective and NSAIDs cannot be used for long periods.

Which anti-obesity drug may reduce the absorption of fat-soluble vitamins A, D, E, and K?

Orlistat.

ALL ANSWERS START WITH 'P'

If a patient is on a particular group of GI drugs and requires calcium, calcium citrate should be used and not calcium carbonate. Which group of drugs are we talking about?

PPI. Long term PPI use can increase risk of fractures due to reduced GI absorption of calcium in the diet. For example, there is a 40% reduction in calcium absorption after 14 days of omeprazole. Calcium citrate brands like CCM should be preferred over calcium carbonate brands like Shelcal in patients on PPIs.

Amongst the first line AKT drugs - H, R, Z, E - which one may cause both hepatotoxicity and hyperuricemia?

Pyrazinamide. Arthralgias due to hyperuricemia caused by pyrazinamide do not respond to colchicine. One must differentiate this pain from Poncet's disease which is a reactive arthritis of tuberculosis.

N.B. Allopurinol inhibits xanthine oxidase which metabolize pyrazinamide. Giving allopurinol to treat hyperuricemia due to pyrazinamide may backfire as pyrazinamide serum levels will rise.

Which vitamin prevents peripheral neuropathy caused by INH and reduces the efficacy of levodopa.

Pyridoxine or Vitamin B6. We should make it a habit to check the supplements consumed by a patient of parkinsonism and eliminate pyridoxine. N.B. Prolonged high doses of pyridoxine can themselves cause peripheral neuropathy.

A sewage worker comes to you in August with odynophagia - pain in the lower sternum while swallowing. He says he has taken some medication once a week for the last eight weeks. Which complication has he developed?

Pill Oesophagitis. This occurred due to doxycycline given to prevent leptospirosis. The other drugs that can cause pill oesophagitis include iron, aspirin, other NSAIDs, oral bisphosphonates, and potassium chloride.

If Dr. Faroukh Udwalla has prescribed Bosentan or Ambrisentan to your patient, you should remind the patient to do LFT every month. What are these drugs given for?

Pulmonary Hypertension. These drugs are endothelial receptor antagonists.

Long term oral steroids are often used in IPF. Periodic eye check-up should be advised for which two ocular complications?

Posterior Subcapsular Cataract and Elevated IOP (Glaucoma)

Name a beta-blocker that is useful to prevent situational anxiety but whose long-term use may cause depression.

Propranolol.

Which one of these antidepressants causes most sexual dysfunction – bupropion, mirtazapine, or paroxetine?

Paroxetine.

Long term use of domperidone may increase blood levels of which hormone?

Prolactin. This may result in galactorrhoea and amenorrhoea.

Which haematological ADR may be caused by testosterone replacement therapy?

Polycythaemia.

Besides metformin and all DPP4 inhibitors, hypoglycaemia is rare with which one more OAD when that drug is used alone?

Pioglitazone.

Sinarex, Febrex Plus, Solvin Cold, Sinus 77, Crocin Cold and Flu, all contain a drug that is pregnancy category D and can cause gastroschisis, a birth defect in which the intestines extend outside of the body through a hole. What content of these brands causes gastroschisis?

Phenylephrine. Decongestants pseudoephedrine and phenylephrine should be avoided in the first trimester. Dextromethorphan and codeine are both considered safe in all trimesters.

A patient with a baseline serum triglyceride of 500 mg/dL should not be given a thiazide diuretic for fear of which complication?

Pancreatitis. In patients with high triglyceride levels, one must also avoid oestrogens, tamoxifen, steroids, isotretinoin, and atypical antipsychotics.

The risk of falls in the elderly increases with the use of five or more prescription drugs. What is the term used when multiple drugs are prescribed?

Polypharmacy.

Albendazole is contra-indicated in pregnancy. Which anti-helminthic is considered safe for infestations like roundworm and hookworm?

Pyrantel Pamoate.

Iron deficiency, B12 deficiency, increased fracture risk, intestinal infections including *C. difficile*, along with acute and chronic kidney disease are all ADRs of long-term use of which group of drugs used to treat gastrointestinal complaints?

Proton-Pump Inhibitors.

The dose of which drug should not exceed 2g/day in persons taking warfarin, in cirrhotics and in alcoholics?

Paracetamol.

Which drug, often used for symptom relief in diabetic neuropathy in a starting dose of 75mg/day may cause severe dizziness, and somnolence, after the very first dose?

Pregabalin. Gabapentin, which is used in the same indications as pregabalin, may cause less intolerance because of slower absorption and because smaller starting doses are available. In general, 75mg pregabalin is equivalent to 450mg gabapentin.

DRUG INDUCED PARKINSONISM

Drug-induced Parkinsonism (DIP) is the second-most-common cause of Parkinsonism in the elderly after Parkinson Disease (PD).

Common offending drugs include -

A. TYPICAL ANTIPSYCHOTICS AND ANTIHISTAMINES

1. Chlorpromazine (Largactil)
2. Prochlorperazine (Stemetil)
3. Promethazine (Phenergan)
4. Trifluoperazine (Trazine)
5. Haloperidol (Serenace)

B. ATYPICAL ANTIPSYCHOTICS

1. Risperidone (Risdone)
2. Olanzapine (Oleanz)
3. Quetiapine (Qutipin) is the least likely of the three to cause DIP

C. PROKINETICS

1. Metoclopramide (Perinorm)
2. Levosulpiride (Lesuride)

D. CALCIUM-CHANNEL BLOCKERS

1. Flunarizine (Sibelium)
2. Cinnarizine (Stugeron)

ALL ANSWERS START WITH 'Q'

In a patient of enteric fever, you will never combine ciprofloxacin with azithromycin for fear of which ADR?

QTc Prolongation.

Aminoglycosides can aggravate myasthenia gravis. Name an antibiotic drug group that has both oral and parenteral formulations and can aggravate myasthenia gravis.

Quinolones. Doxycycline, macrolides, and chloroquine are also known to aggravate symptoms of myasthenia gravis.

Since ACTs are not used in the first trimester what is the drug of choice in falciparum malaria in the first trimester of pregnancy?

Quinine. Quinine is avoided in the third trimester as it causes hypoglycaemia.

A cluster of symptoms including tinnitus, hearing loss, nausea, vomiting called 'cinchonism' is a side effect of which drug?

Quinine.

Which second-generation antipsychotic has the least hyperglycaemia, the most sedation and the least extra-pyramidal reaction amongst all drugs in the group?

Quetiapine.

ALL ANSWERS START WITH 'R'

Patients receiving which antibiotic are warned against using soft contact lenses as they may get permanently stained?

Rifampicin.

What is the name given to chronic rhinitis caused by prolonged use of xylometazoline or oxymetazoline nasal spray?

Rhinitis Medicamentosa.

Neomycin use in hepatic encephalopathy caused nephrotoxicity and ototoxicity. Which antibiotic has replaced neomycin?

Rifaximin.

A child with viral infection and fever is given aspirin. She develops encephalopathy. What syndrome should we think of?

Reye Syndrome.

Abrupt cessation of clonidine in a hypertensive person can cause what acute complication?

Rebound HT.

N.B. Abrupt cessation of beta-blockers can precipitate acute coronary syndrome in patients with coronary artery disease.

In which disease is methotrexate given in an oral dose if the dose is 15mg or less per week and in a subcutaneous injectable form if the dose is more than 15mg?

Rheumatoid Arthritis. A higher dose of methotrexate is preferably given as an injectable because of greater absorption and better GI tolerability.

ALL ANSWERS START WITH 'S'

PC enema or Proctoclysis enema is a popular brand. It should not be used in patients with high creatinine because of its chief constituent. Which constituent? **Sodium Phosphate.** Sodium phosphate in proctoclysis may cause hyperphosphatemia in patients of CKD. This can in turn have cardiovascular complications. Bulk laxatives should not be used in patients with suspected obstructions or diverticulitis.

What grave ADR occurs with allopurinol but not with febuxostat?

Stevens Johnson Syndrome. Despite this fact, allopurinol should be the first choice as a xanthine-oxidase inhibitor because of the cardiovascular toxicity of febuxostat.

Verizet D contains 5 mg levocetirizine and 120 mg pseudoephedrine. What are the diametrically opposite side effects of these two components?

Somnolence and Insomnia respectively.

Which psychiatric drug group can paradoxically both cause anxiety and relieve anxiety?

SSRI. Anxiety can worsen in the first few weeks off SSRI therapy. Clonazepam is often concurrently administered in this initial phase.

What is the desirable side-effect of antidepressants trazodone and mirtazapine which is not present in SSRIs?

Sedation.

Which side-effect is reduced temporarily by giving drug holidays on weekends to patients on SSRIs?

Sexual dysfunction.

Which drug retards progression of CKD but can worsen HT and CCF? **Sodium Bicarbonate.** It is the only drug proven to retard progression of CKD. It can also reduce muscle wasting and bone loss in these patients.

Solifenacin and tolterodine are both used to treat overactive bladder. Which one of the two causes less CNS side effects like dizziness?

Solifenacin. Another important difference is that solifenacin is inactivated by CYP3A4 while tolterodine is chiefly inactivated by CYP2D6.

Which drug group reduces mortality in diabetics but increases incidence of new diabetes in hitherto non-diabetics?

Statins. The link between statin use may be stronger than previously believed. The risk is more in patients who are overweight.

Pioglitazone can worsen existing heart failure. Which gliptin can do the same?

Saxagliptin. Both saxagliptin and alogliptin can cause heart failure particularly in patients with existing renal and heart disease.

Which one of these causes greatest weight gain at equivalent doses - glargine (Lantus), biphasic Insulin (say Mixtard) in two doses, or short acting insulin (say Actrapid) in multiple doses?

Short Acting Insulin.

The migraine drug brand 'Headset' should not be given to patients with coronary artery disease due to which component of headset?

Sumatriptan. Triptans are contraindicated in persons with atherosclerotic disease as they are vasoconstrictors.

Effect of maternal drugs on breastfeeding infants decreases significantly after what age?

Six months. By the age of six months the liver matures enough to metabolise drugs. The increasing body weight also means that the dose from breast milk becomes relatively small.

The MMR vaccine multidose vial must be used within four hours of reconstitution. What ADR can occur if it is used later?

Staphylococcal Infection.

STATIN-ASSOCIATED MUSCLE SYMPTOMS (SAMS)

- Muscle symptoms caused by statins usually begin within weeks after starting statins. These in turn return to normal over days to weeks after drug discontinuation.
- The principal symptoms are myalgias and muscle weakness.
- These can occur in as many as 10% of patients receiving statins.
- Severe myonecrosis and clinical rhabdomyolysis are much rarer. When they do occur, they can lead to acute tubular necrosis.
- Myalgias can occur without an elevation in serum creatine kinase (CK/CPK).
- Fluvastatin and pravastatin cause much less muscle toxicity than other statins.
- It is preferable to avoid use of simvastatin and atorvastatin in patients who are receiving or are likely to receive drugs that are strong inhibitors of CYP3A4. In such patients, rosuvastatin or pitavastatin are preferred.
- Uncontrolled hypothyroidism makes a person more susceptible to SAMS.
- The incidence of SAMS may be reduced by giving vitamin D in adequate quantities to all patients receiving statins.
- Co-enzyme Q10 is of no value in preventing SAMS.
- Concomitant use of fenofibrate increase the risk of SAMS.
- Alternate day therapy is an option in patients who have myalgias even with small doses of statins. Another option in these patients is to add ezetimibe to be able to reduce the dose of statins.
- One must educate all patients on statins to report muscle pain.

STEVENS JOHNSON SYNDROME - A BRIEF NOTE

If a person has had SJS with any drug, you must avoid all the following as far as possible -

ANTIBIOTICS - Sulfonamides, Penicillins, Cephalosporins, Quinolones, Tetracyclines, Rifampicin, Imidazoles

N.B. Other sulfa compounds can also cause SJS. One example is sulfasalazine used in autoimmune disorders like inflammatory bowel disease.

NSAIDs - Aspirin, Etoricoxib, Piroxicam, Meloxicam, Diclofenac, Ibuprofen, Nimesulide, Naproxen etc.

ANTICONVULSANTS - Barbiturates, Phenytoin, Primidone, Carbamazepine, Oxcarbazepine, Lamotrigine

MISCELLANEOUS - Allopurinol, Nevirapine (part of ART), Tamoxifen, Promethazine, Dicyclomine

SAFE DRUGS IN PERSONS WITH HISTORY OF SJS

While remembering that almost any medicine can cause SJS, including paracetamol, if you need to use antibiotics, newer macrolides are the first option. Febuxostat seems safe and so does levetiracetam. Amongst injectable antibiotics, aminoglycosides are the safest.

N.B. The risk of SJS seems to be limited to the first eight weeks of treatment.

ALL ANSWERS START WITH 'T'

Which ADR of quinolones occurs more commonly in athletes?

Tendon rupture especially of the Achilles tendon.

What complication risk increases if erythropoietin use in chronic kidney disease causes the haemoglobin to rise above 11 g/dL?

Thrombotic events including stroke.

DPP4 inhibitors can cause pancreatitis. Incidence of which organ cancer increases due to DPP4i use?

Thyroid. The incidence of medullary thyroid carcinoma increases. DPP4 inhibitors should be avoided in patients with family history of this cancer.

A patient is being treated by a neurologist for migraine. He comes to you with a severe ureteric colic. He has forgotten both the drug name and the neurologist's name. What drug was prescribed for migraine?

Topiramate. A peculiar ADR of topiramate is word-finding difficulty. Other side-effects include paraesthesias and nephrolithiasis.

A 65-year-old male returns home on Monday after an anniversary holiday to Maldives. He presents on the same day with unstable angina. What drug should he not have taken in the last 48 hours for you to safely give him nitroglycerin?

Tadalafil.

Name an antimuscarinic agent used to treat overactive bladder whose side-effects can be gauged by anticholinergic symptoms like dry mouth and a significant post-void residue on ultrasound.

Tolterodine.

TERMINOLOGIES OF NEUROLOGIC ADRs EXPLAINED

AKATHISIA -

This is the most common form of extrapyramidal syndrome typically occurring due to antipsychotics. It usually presents as motor restlessness with a compelling urge to move and an inability to sit still.

DYSTONIA -

These are sustained involuntary muscle contractions of antagonistic muscle groups in the same body part, leading to abnormal posturing or jerky, twisting, intermittent spasms. Antipsychotics & antiemetics are commonest causes. Symptoms such as torticollis, retrocollis, oculogyric crisis, and opisthotonus are examples of dystonia.

TARDIVE DYSKINESIA -

These consist of characteristic involuntary movements that occur after chronic use of antipsychotic medications (tardive means late). Some examples are Sucking, smacking of lips, choreoathetoid movements of the tongue, facial grimacing, lateral jaw movements.

DISCONTINUATION SYNDROME -

Abrupt discontinuation of an antidepressant medication taken for at least six weeks may result in symptoms like flu, insomnia, nausea, imbalance, sensory disturbances, and hyperarousal. This is called Antidepressant Discontinuation Syndrome

AUGMENTATION -

This is defined as a paradoxical worsening of symptoms of restless leg syndrome (RLS) due to the dopaminergic drug given for RLS. Levodopa causes the greatest augmentation and hence is not used in RLS.

SEROTONIN SYNDROME -

This is a potentially life-threatening ADR resulting from excess serotonergic activity, characterized by mental, autonomic, and neuromuscular changes due to SSRI dosage increase without titration, self-poisoning, and adjuvant therapy with another SSRI or serotonergic drug like tramadol or triptans.

NEUROLEPTIC MALIGNANT SYNDROME -

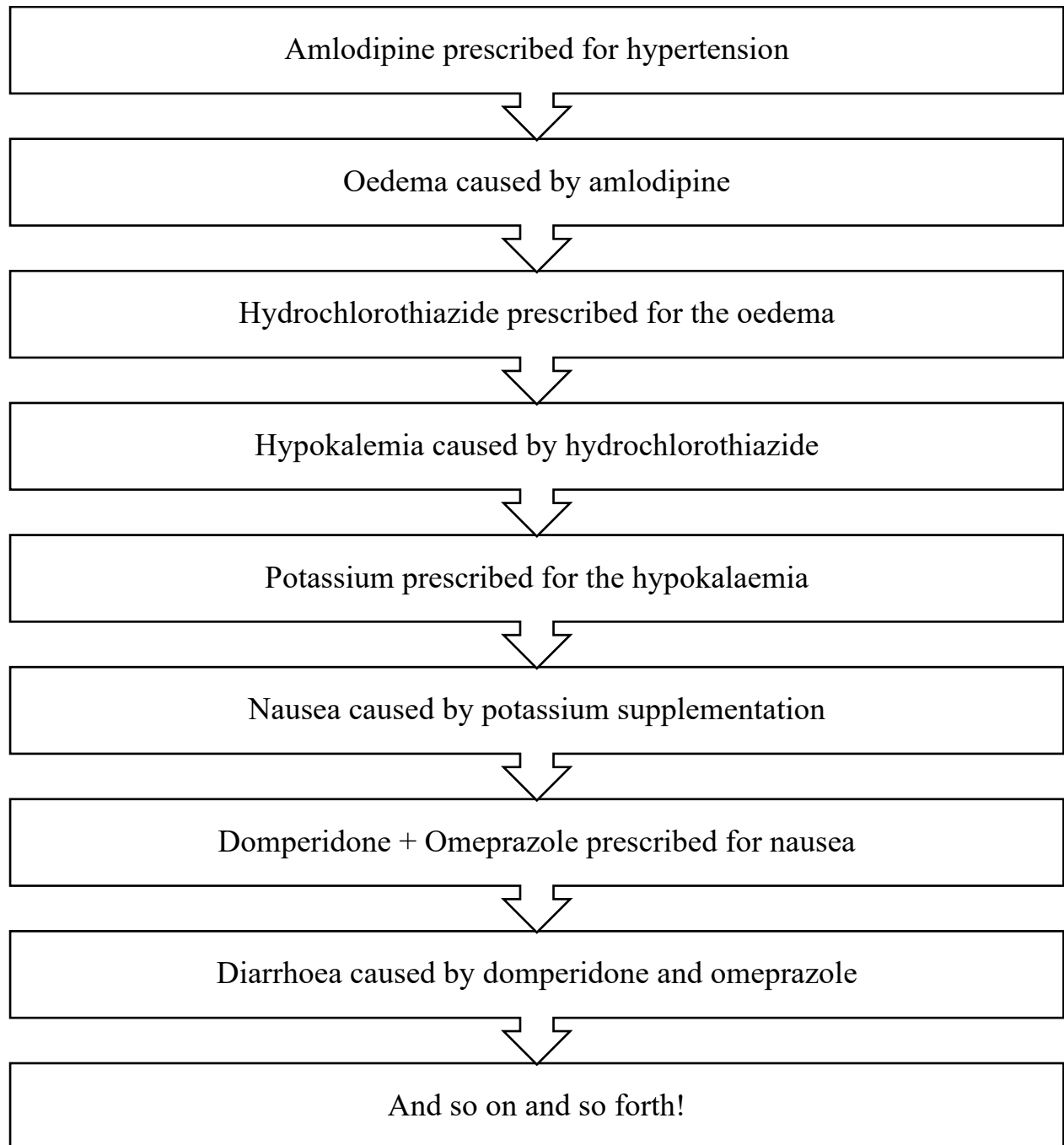
This is a life-threatening neurologic emergency associated with the use of neuroleptic agents like haloperidol. It is characterized by a distinctive clinical syndrome of mental status change, rigidity, fever, and autonomic instability.

PARKINSONIAN SYNDROME -

Drug-Induced Parkinsonism (DIP) consists of mask-like facies, resting tremor, cogwheel rigidity, shuffling gait, and bradykinesia. See page 43 for a list of drugs that can cause DIP.

THE CASCADE PHENOMENON

Cascade Iatrogenesis or The Cascade Phenomenon is defined as a series of adverse events following an initial medical intervention, each adverse event prompting the addition of a new drug. It occurs most commonly in the geriatric population. An example follows -



ALL ANSWERS START WITH 'U' OR 'V'

A patient with cardiovascular disease is on low dose aspirin and hydrochlorothiazide. He presents with acute monoarticular pain and swelling in the right elbow. What blood test will you ask for?

Uric Acid. Low dose aspirin can cause recurrent exacerbations in known cases of gout. Such patients may require long term allopurinol if aspirin cannot be substituted. Further, symptomatic hyperuricemia is a relative contraindication for giving thiazides.

Which side-effect of antimuscarinics used to treat overactive bladder is commoner in males with BPH and females with urethral strictures?

Urinary retention.

The atypical antidepressant trazodone can cause postural hypotension. Name the antidepressant belonging to the SNRI group that can cause hypertension.

Venlafaxine.

Which antiepileptic drug can cause alopecia, weight gain, tremor and hyperammonaemic encephalopathy?

Valproate.

A person is given three injections one week apart by a physician. He comes to you with ureteric colic. What injections might have been given that have caused urolithiasis?

Vitamin D. It is important not to give multiple intramuscular doses of vitamin D as this can cause hypercalcemia. If a patient comes with blood reports of vitamin D levels greater than 75 ng/ml, one must immediately ask for a serum calcium level.

VITAMIN DEFICIENCIES CAUSED BY DRUGS

B12 DEFICIENCY -

Proton-Pump Inhibitors

Metformin

FOLATE DEFICIENCY -

Anticonvulsants - phenytoin, barbiturates, and primidone.

Sulfasalazine

Alcohol - which is also associated with deficiencies of B1 and B5.

Methotrexate - inhibitor of dihydrofolate reductase

Trimethoprim - inhibitor of dihydrofolate reductase

VITAMIN D DEFICIENCY -

Rifampicin and INH

Phenytoin

Corticosteroids

B6 DEFICIENCY -

INH

ALL ANSWERS START WITH 'W'

What is the ADR caused by injecting 50% dextrose solution in hypoglycaemics without replacing thiamine simultaneously?

Wernicke's Encephalopathy. This happens typically in chronic alcoholics or severely malnourished persons. All persons receiving concentrated dextrose must be given a simultaneous intravenous dose of 100 mg thiamine. An example brand name is injection Optineuron.

A person with chronic atrial fibrillation is given a combination of ciprofloxacin and metronidazole. He starts bleeding on day 5 of therapy. What drug has the person been already taking?

Warfarin. Metronidazole inhibits CYP2C9 and thus can increase blood levels of warfarin. Ciprofloxacin inhibits CYP1A2 and thus can increase blood levels of warfarin. Importantly, itraconazole and ketoconazole inhibit CYP3A4 and thus can increase blood levels warfarin.

Which ADR is common to second-generation antipsychotics like olanzapine and drugs like mirtazapine, paroxetine, insulin, pioglitazone, and flunarizine?

Weight gain.

Which, sometimes welcome, side-effect is common to liraglutide, empagliflozin, metformin, thyroxine, and topiramate?

Weight loss.

DRUGS TO AVOID IN PATIENTS ON WARFARIN

1. High dose paracetamol. Avoid more than 2gm/day.
2. Macrolides especially clarithromycin and erythromycin.
3. Metronidazole and other nitroimidazoles.
4. Ciprofloxacin.
5. Cotrimoxazole.
6. Itraconazole and ketoconazole.
7. Fluconazole > 200 mg/d.
8. Fluoxetine, Paroxetine, Bupropion.

N.B. Please refer to our book on **The Day-To-Day Clinical Relevance of The Cytochrome P450 Enzyme Systems** for more information on drug interactions with warfarin.

ALL ANSWERS START WITH 'X', 'Y', or 'Z'

With respect to risk in pregnancy, what is the letter assigned to the category that includes teratogenic drugs?

X.

ACE inhibitors, ARBs, warfarin, isotretinoin, valproic acid, all belong to which pregnancy drug category?

X. Statins also belong to this category.

While sildenafil can cause blue vision, what can digoxin cause?

Xanthopsia or Yellow Vision.

For which medicine used in insomnia is the maximum dose 10 mg in men but 5 mg in women as women are more prone to adverse effects.

Zolpidem. Incidentally, zolpidem can cause sleep-walking, sleep-driving and sleep-eating as side-effects.

Which one of the 'Z drugs' used in insomnia may cause dysgeusia or altered taste as a side-effect?

Zopiclone. The three 'Z drugs' are zolpidem, zopiclone (and eszopiclone), and zaleplon. Do note that all sleeping tablets are associated with an increased risk of falls and fractures in the elderly and an overall increase risk of death.

The commonest side effect of this once a year IV injectable given for osteoporosis is a flu-like syndrome with fever and bodyache. Name the injectable.

Zoledronic Acid. The fever typically occurs with the first dose of zoledronic acid only. The patient may be premedicated with 1000mg of paracetamol.