Correct Answers for Posttest Questions

1. (C) is correct. All commercially available antipsychotic drugs reduce dopaminergic neurotransmission to various degrees which contribute to both the therapeutic effect as well as certain undesirable side effects. The effectiveness of dopamine receptor antagonists for the positive symptoms of psychosis is due to the blockade of dopaminergic receptors in the mesolimbic pathway. Blockade of dopamine receptors in the nigrostriatal pathway may result in extrapyramidal symptoms (EPS). Blockade of dopamine receptors in the tuberoinfundibular pathway may result in hyperprolactinemia. Deficits in dopamine transmission in the mesocortical pathway are thought to cause cognitive dysfunction and negative symptoms in schizophrenia and blockade may either fail to address adequately or even worsen negative symptoms and cognitive dysfunction.

2. (A) is correct. DA D_2 receptor antagonism causes tardive dyskinesia and extrapyramidal symptoms (EPS) such as drug induced parkinsonism, akathisia and acute dystonia. Central antagonism of H1 receptors may result in sedation and weight gain. Alpha adrenergic antagonism may result in orthostatic hypotension, and reflex tachycardia. Peripheral muscarinic cholinoceptor antagonism may result in blurred vision due to loss of accommodation, dry mouth, urinary retention and constipation. Beta antagonism may result in bradycardia due to beta-1 blockade, and bronchoconstriction due to beta-2 blockade.

3. (A) is correct. The patient is exhibiting parkinsonian symptoms, including bradykinesia, tremor, rigidity and a shuffling gait. These side effects are treated with anticholinergics, often benztropine. This drug is also a standard drug in the treatment of Parkinson's disease. Benzodiazepines and beta blockers can be used to treat akathisia, another of the extrapyramidal symptoms; however, they are not used for pseudoparkinsonism. L-DOPA is a dopamine analog that can cross the blood brain barrier; it is used in the treatment of Parkinson’s disease. It should be avoided in patients with schizophrenia, as it will exacerbate psychotic symptoms. Fluoxetine is a selective serotonin reuptake inhibitor (SSRI) and is a first-line treatment for depression; SSRIs are not used in the treatment of pseudoparkinsonism.

4. (C) is correct. The tendency of high-potency antipsychotics to cause extrapyramidal symptoms like dystonia is their main drawback. Low potency and high potency typical antipsychotic medications are equally effective. Low potency antipsychotics are associated with a higher incidence of autonomic side effects.

5. (D) is correct. This is a patient with a history of several failed trials of antipsychotic medications, and most likely has “treatment-resistant schizophrenia”. His complaints (fever, weakness, lethargy, sore throat), and physical examination findings (oral thrush) are suggestive of infection. Laboratory values are consistent with agranulocytosis (ANC less than $500/mm^3$). Clozapine is an atypical antipsychotic medication indicated for treatment-resistant schizophrenia; it is associated with a 1-2% incidence of agranulocytosis.

6. (C) is correct. Olanzapine is an atypical antipsychotic medication. The atypical antipsychotic drugs share the property of weak DA D_2 receptor antagonism and more potent 5-HT_{2A} receptor blockade. Haloperidol is a typical antipsychotic medication with high affinity to DA D_2 receptors. Olanzapine is less likely to cause EPS, and tardive dyskinesia. Olanzapine is effective in treating both positive and negative symptoms of schizophrenia while haloperidol is limited to its effectiveness in treating positive symptoms. Olanzapine can cause significant weight gain due to metabolic side effects and haloperidol is least likely to cause weight gain.

7. (D) is correct. Neuroleptic malignant syndrome is a very dangerous condition which occurs very rarely following the initiation of antipsychotic treatment. It resembles a very severe form of parkinsonism with pronounced autonomic side effects and high fever. Treatment involves immediate discontinuation of antipsychotic medication and supportive medical procedures (e.g. aggressive cooling measures and IV hydration). Pharmacologic treatments with dantrolene and/or bromocriptine (dopamine receptor agonist) are sometimes employed in the treatment of this condition.

8. (A) is correct. Chlorpromazine is a low potency typical antipsychotic medication with potent H1 histamine receptor blockade resulting in increased sedative effects. All other medications listed are less sedating.

9. (B) is correct. The patient is exhibiting symptoms of acute dystonia which commonly include muscle spasms of tongue, face, neck and trunk. The patient complains of her eyes rolling into her head (oculogyric crisis). Laryngospasm may occur rarely, but can be fatal. Time of onset of acute dystonia is usually within 1 to 5 days of initiating therapy with an antipsychotic medication and occurs due to abrupt decreases in nigrostriatal DA D_2 neurotransmission. These side effects are treated with anticholinergics, often benztropine or diphenhydramine. Anticholinergic medications are also used in the treatment of Parkinson's disease. Clonazepam is a benzodiazepine and propranolol is a nonselective β blocker with good CNS penetration which can be used to treat akathisia. However, they are not used for treatment of acute dystonia. L-DOPA is a dopamine analog that can cross the blood brain barrier; it is used in the treatment of Parkinson's disease. Selective serotonin reuptake inhibitors (SSRIs) are the first-line treatment for depression; they are not used in the treatment of acute dystonia.

10. (C) is correct. Olanzapine and clozapine both have significant risk for metabolic disturbances, including weight gain, hyperglycemia, and dyslipidemia which may lead to insulin resistance and development of type 2 diabetes. Because of this, patients on olanzapine and clozapine need to have labs drawn to regularly monitor their blood glucose and lipid levels. Cardiac arrhythmia is more likely with ziprasidone, though all antipsychotics carry the risk of QT interval prolongation. Cataract formation is most commonly associated with the use of quetiapine.