

March 2010  
QUESTION 13

Describe the physiological basis of the effects seen in the serotonin syndrome (80% marks). List the classes of drugs that may cause the serotonin syndrome (20% marks).

### Serotonin

is produced from the decarboxylation of L-tryptophan  
stored in vesicles and released from presynaptic neurons  
metabolised in the presynaptic neurons by monoamine oxidases  
7 receptors are known, 5HT<sub>1-7</sub>, all are GPCR except 5HT<sub>3</sub> which is an ligand gated ion channel  
receptors are in both CNS and PNS, especially in the midline raphe nuclei (brainstem to medulla)  
CNS receptors regulate  
    wakefulness, mood, thermoregulation, emesis, sexual behaviour, nociception and motor tone  
PNS receptors regulate  
    GIT motility and vascular tone

### Serotonin syndrome

is a predictable consequence of excess serotonergic antagonism  
produces a spectrum of clinical findings  
    mental status changes  
    autonomic hyperactivity  
    neuromuscular abnormalities  
clinical manifestations range from mild to lethal  
it is caused by administration of medications (usually in combination) which  
    decrease serotonin reuptake (SSRIs)  
    metabolism (MAOI)  
    sensitise 5HT receptors (amphetamines)  
    affect the hepatic metabolism of drugs which act on 5HT pathways (ritonavir)  
all receptors appear implicated but 5HT<sub>2A</sub> is the principle target

### Drugs involved

SSRIs (fluoxetine)  
SNRIs (venlafaxine)  
Tricyclic antidepressants (amitriptyline)  
MAOI (phenelzine)  
Anticonvulsants (valproate)  
Antiemetics (ondansetron, metoclopramide)  
Antimigraine (sumatriptan)  
Analgesics (fentanyl, tramadol)  
Antibiotics (linezolid, ritonavir)  
Drugs of abuse (MDMA, LSD)  
St Johns Wort