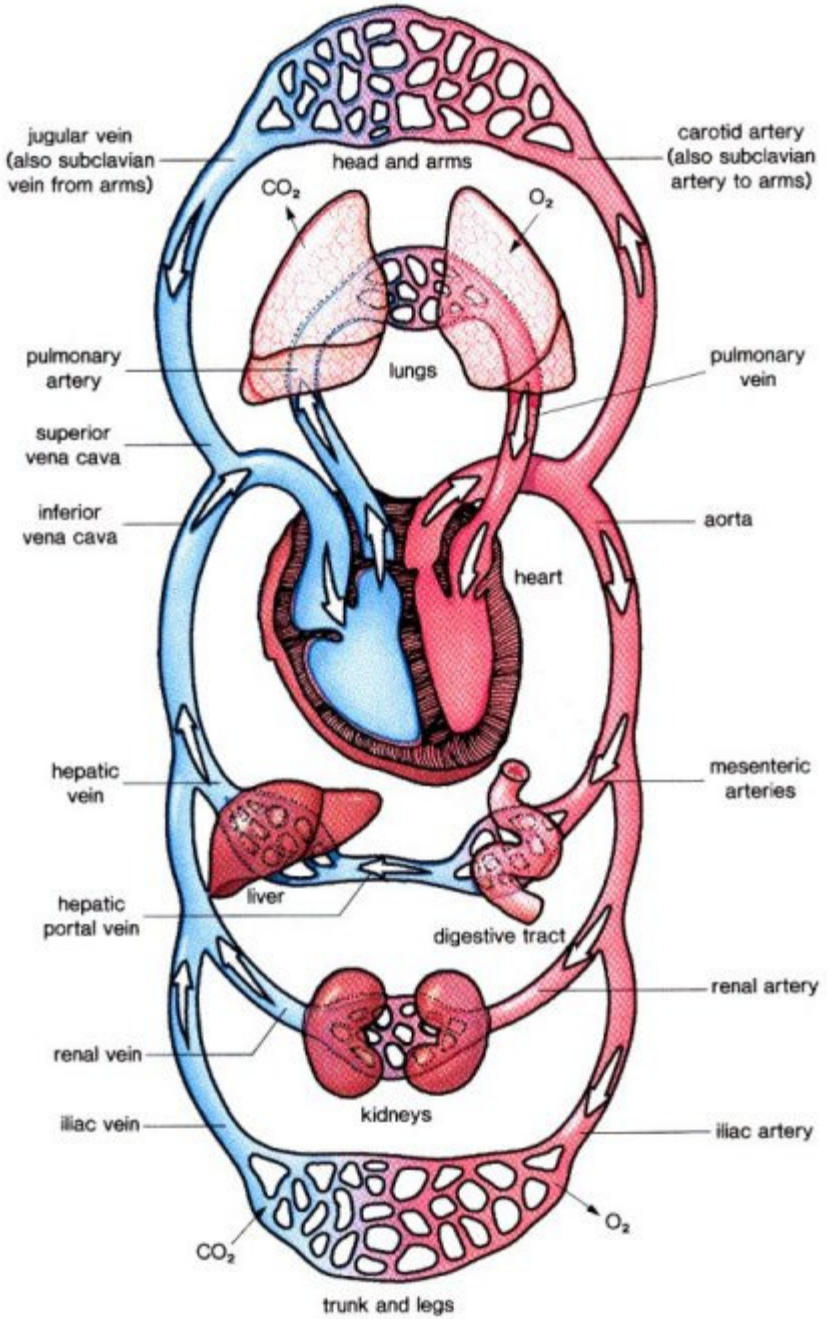
How the body deals with drugs
& how drugs effect the nervous system

Routes to the brain..

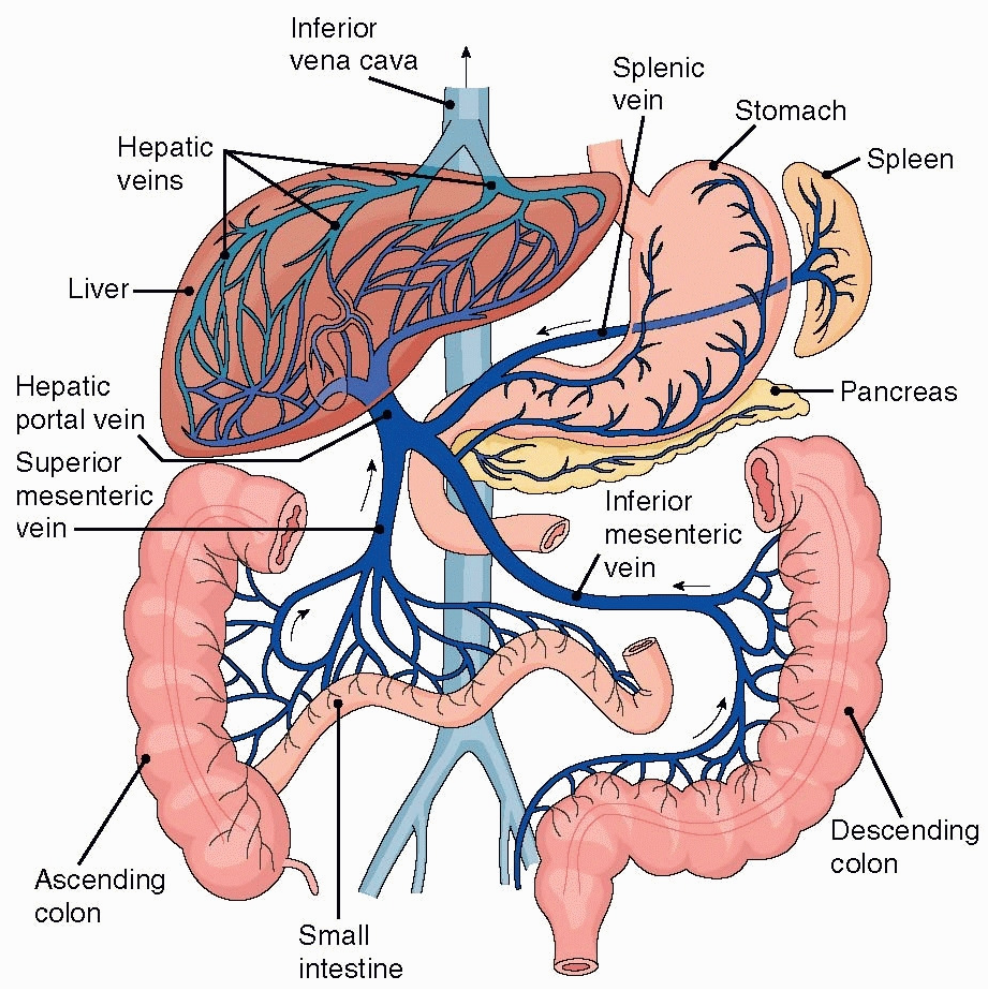
Circulatory system

Digestive system

Respiratory system


jugular vein
(also subclavian
vein from arms)
head and arms
carotid artery
(also subclavian
artery to arms)
CO_2
O_2
pulmonary
artery
lungs
pulmonary
vein
superior
vena cava
inferior
vena cava
aorta
heart
hepatic
vein
mesenteric
arteries
liver
hepatic
portal vein
digestive tract
renal artery
renal vein
kidneys
iliac vein
iliac artery
O_2
CO_2
trunk and legs

Hepatic Portal System



Getting drugs to the brain

- Oral (swallowing)
  - Drug absorbed from the intestines into the blood stream, transported to the liver. How effectively it is absorbed depends on how easily it can pass from the intestine to the blood stream.
  - Once in the liver the drug will be metabolised. Drugs can be substantially broken down by the liver so relatively little may end up getting to the brain.

Getting drugs to the brain

- Sublingual (dissolving under the tongue)
  - Drug absorbed from the lining of the mouth into the bloodstream, the blood supply from here does not travel directly to the liver so the drug will not be substantially metabolised by the liver.

Getting drugs to the brain

- Intravenous (injecting into a vein)
  - Drug is delivered directly into the bloodstream
  - Since this avoids the GI tract there are no problems with absorption or solubility,
  - this route bypasses the liver so relatively little metabolism of the drug takes place
  - A large amount of the drug is available to the brain, the effect tends to be more intense

Getting drugs to the brain

- Intramuscular injection & subcutaneous injection
  - The drug is absorbed from the tissues into the blood stream, much slower effect than intravenous injection.
  - This route bypasses the liver so relatively little metabolism of the drug takes place.

Getting drugs to the brain

- smoking
  - Drug is absorbed directly into the blood stream via the lungs.
  - This route bypasses the liver so relatively little metabolism of the drug takes place.

Getting drugs to the brain

- snorting
  - Similar to sublingual, the drug is absorbed from the lining of the nose into the blood stream
  - This route bypasses the liver so relatively little metabolism of the drug takes place.

Getting drugs to the brain

- rectal
  - Drug is absorbed into the blood stream via the rectum.
  - This route bypasses the liver so relatively little metabolism of the drug takes place.

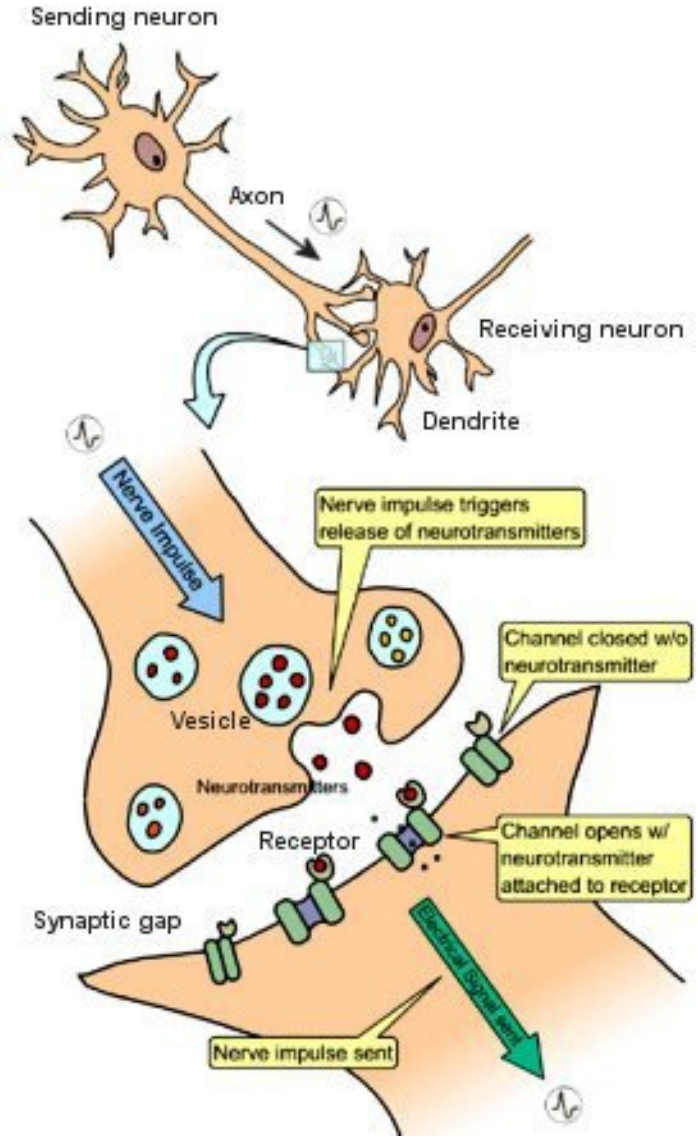
How fast are the different routes of administration?

Method	**Speed of onset**
• Inhale	• 3-5 secs.
• Inject	• 30-60 secs.
• Sniff / snort	• Up to 3 mins.
• Swallow	• 20-60 mins.

Generally speaking, the quicker the drug reaches the CNS, the shorter the duration of the drugs effect.

Injecting drugs increases the potency of the dose

Neurotransmitters and neurones



How drugs interact with the nervous system

- Drugs can activate neurotransmitters (agonists)
- Drugs can block the receptor (antagonists)
- Drugs can block the re-uptake of neurotransmitters (re-uptake inhibiters)

Examples of agonists, antagonists & re-uptake inhibitors

- Heroin activates the opiate receptor
- Naltrexone blocks the opiate receptor
- SSRI’s blocks the re-uptake of a neurostransmitter (serotonin)

GABA

- Gamma aminobutyric acid
  - A neurotransmitter that has a calming effect on the central nervous system.
  - Many anaesthetics act on the gaba system
  - As do alcohol and benzodiazepines

GABA in action

GABA, Alcohol, Anxiety and Coma

- If drugs such as alcohol or benzodiazepines are consumed regularly the nervous system will begin to produce less GABA
- If the alcohol or benzodiazepines are suddenly stopped...
  - symptoms of CNS excitement will begin because there is little GABA to calm everything down

Ways that drugs can interact

- Some drugs cause **liver enzymes** to 'speed up' → lower levels of other drugs in the body

- Rifampicin, smoking nicotine/cannabis/tobacco, St Johns Wort

- **Disulfiram and Amitriptyline** –
  - Disulfiram inhibits metabolism of leading to increased plasma concentrations.
  - Can also lead to an increased reaction when alcohol is used

Cont…

- **Methadone + Rifampicin** → methadone is eliminated more quickly

- **Smoking cannabis resin in a cigarette(nicotine) + Clozapine** → when stopped smoking effect of Clozapine enhanced and led to increased sedation

ANTIDEPRESSANTS

•Anti depressant medication (particularly SSRI's) often targets the serotonin pathway to increase the level of serotonin in the brain

SEROTONIN

Serotonin pathways regulate:

- Body temperature
- Cognitive function
- Regulate emotions (including panic and anxiety)
- Regulate appetite and satiety
- Sleep-wake cycle
- Sexual functioning

Excess serotonin may lead to:

- Increased body temperature
- Increased heart rate
- Anxiety / panic
- Confusion → coma → death
- Sweating
- Shivering
- Nausea
- Twitching → hyperreflexia → seizures

Cont…

- **Ecstasy** acts on the serotonin system as well as dopamine pathways
- Patients on high dose **SSRI's** can often feel sweaty
- More than one anti depressant - with caution – risk of **serotonin syndrome**

Serotonin syndrome

Source Medline: http://www.nlm.nih.gov/medlineplus/ency/article/007272.htm

- Serotonin syndrome is a potentially life threatening drug reaction that causes the body to have too much serotonin, a chemical produced by nerve cells.

Noradrenergic Pathways

‘fight or flight’

- **Stimulant** drugs mimic the effect of adrenaline
- Increased BP
- Increased HR
- Blood diverted to skeletal muscles
- Peripheral blood vessels narrow to move blood to muscles

Stimulants

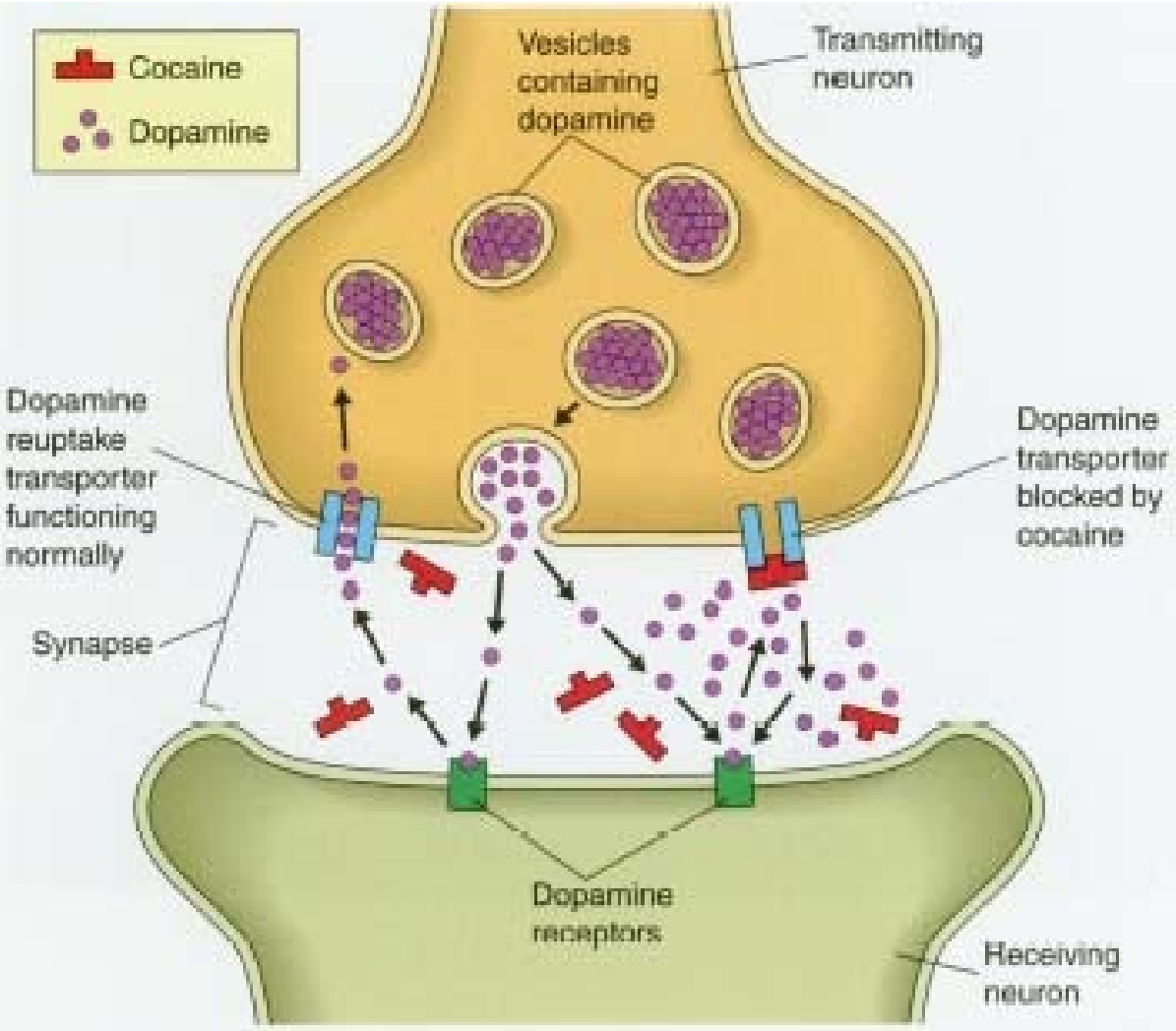
- Arrhythmia with anaesthetics
- Cerebral/cardiac – cocaine with older antidepresssants
- Hyperthermia/dehydration – ecstasy
- Reduce efficacy of antipsychotics and antidepressants
- Hypertension with MAOI's and beta blockers
- Hepatotoxic/cardiotoxic with Carbamazepine
- Bleeding risk with warfarin

Dopamine and Antipsychotics

- **Dopaminergic** pathways

  Linked to ‘movement and madness’
- **Nigrostriatal dopamine pathway** – smooth movements – Parkinsons
- **Mesolimbic dopamine pathway** – pleasure sensations, behaviours (pleasure-reward), euphoric effect
- **Excess dopamine** – hallucinations, delusions (often of a paranoid type) schizophrenia-like illness
- **Stimulant** street drugs act on this system.

Cocaine and Dopamine



Amphetamine/Cocaine/Crystal Meth Effects

Awake, excited, aroused and exhilarated

Energy – prolonged activity

Increased HR

Increased BP

Narrowing of blood vessels

Amphetamine/Cocaine/Crystal Meth Excess

- Strain on heart
- Increased BP – stroke
- Panic/anxiety
- Aggression
- Irritable
- Psychosis
- Overheating – increased body temp.
- Increased risk of heart attack x24
- Increase libido
- Convulsions
- Low mood

Cont…

ALCOHOL

- Changes in HR and BP → CVS toxicity
- Combined use with cocaine → cocaethylene
- May diminish positive impact of antipsychotic medication
- **MAOI's –** should not give to anyone using stimulants as risk of serotonin ↑ as well as dopamine, adrenaline and noradrenaline.

Cont…

ANTIPSYCHOTICS

- Flupenthixol - may reduce cocaine craving
- Haloperidol – may moderate stimulant effects
- Clozapine increases cocaine levels but reduces the cocaine high
- Buprenorphine – no notable interaction
- Cannabis – enhanced cardio toxicity (↑HR)
- Carbamazepine – may enhance cardiac effects of CBZ
- Lithium – little effect on cocaine
- Methadone – cocaine may accelerate methadone elimination

Cont…

- **Seizures** – threshold lowered with antipsychotics and alcohol
- **Methadone** and antipsychotics → ECG

Lithium

- Used in mania
- Regular bloods due to serious potential side effects – tremor, thirst, urinary frequency, dry mouth, kidney problems, weight gain, diarrhoea, abdominal discomfort, loss of appetite, loss of coordination, skin and hair changes, white cell count, hypothyroidism, tiredness, tension restlessness, concentration/memory, confusion, headache and sexual functioning
- **Alcohol** affects lithium levels