**Question 2**

The NSAID with the least gastro-intestinal upset is

A Ibuprofen

B Aspirin

C Indomethacin

D Naproxen

Explanation A

Ibuprofen in doses of 2.4g a day are anti-inflammatory. Doses less than this are analgesic and not anti-inflammatory.

Indomethacin at normal doses cause the usual GIT side effects including pancreatitis.

Naproxen’s incidence of GIT bleeding is double that of ibuprofen

Ketoprofen is not superior to other NSAIDS in clinical effectiveness. GIT complications are common

Aspirin causes about double the gastric ulcers as compared to ibuprofen at normal doses

**Question 4**

Peak blood concentration of acetaminophen following oral route is achieved in?

A 30-60min

B 10-15min

C 10-30min

D 20-40min

Explanation A

Peak blood concentration of acetaminophen following oral route is usually achieved in 30-60min. IVI route takes 15min, however the analgesic effect does not last as long via the IVI route

**Question 5**

Which pathway produces the toxic metabolite in paracetamol overdose?

A Conjugation with glutathione

B Sulfation

C N-hydroxylation

D Glucoronidation

Explanation C

N-hydroxylation forms the NAPQI toxic metabolite, which leads to liver failure

Normally acetaminophen is metabolized via glucuronidation (40% to 67%), sulfation (20–40%), and N-hydroxylation/rearrangement/GSH conjugation (less than 15%). With excessive dosing of acetaminophen, the glucuronide and sulfate conjugation pathways become saturated, and increasing amounts of acetaminophen then undergoes N-hydroxylation (CYP-mediated) to form NAPQI, which is a toxic metabolite.

**Question 6**

Regarding aspirin, which of the following statements is correct?

A Alkalinising the urine will decrease excretion

B It is a reversible inhibitor of cyclo-oxygenase

C It has a pKa of 6.5

D In moderate doses it increases respiratory rate

Explanation D

Aspirin has a pKa of 3.5. It is an irreversible inhibitor of cyclo-oxygenase and, at moderate doses, causes an increased respiratory rate. In higher doses a respiratory alkalosis occurs followed by a metabolic acidosis. Alkalinising the urine will increase excretion of aspirin. Aspirin effects last the life of platelets which is 8-10 days. Aspirin demonstrates capacity limited clearance at low doses. I.e. saturable elimination at low doses

**Question 13**

Regarding allopurinol, which of the following statements is correct?

A It has no side effects

B It is metabolised by xanthine oxidase

C It has a low oral bioavailability

D It is useful in acute gout

Explanation B

Allopurinol is not useful in acute attacks but rather the period between attacks of gout. It can cause a gouty arthritis when initially started.

You need to take colchicine and NSAIDS concurrently. It has a bioavailability of 80%, its half life 1-2 hrs and is metabolized by xanthine oxidase but the resulting compound, alloxanthine, retains the capacity to inhibit xanthine oxidase and has a long enough duration of action so that allopurinol can be given once a day. Side effects include GIT intolerance, depression of bone marrow, hepatic toxicity and renal disease.

By inhibiting xanthine oxidase, those purine ribonucleotides not incorporated into nucleic acids are NOT oxidised to uric acid.

**Question 14**

Regarding paracetamol toxicity which of the following statements is correct?

A N-acetylation produces the toxic metabolite

B Toxic metabolite is due to sulphanation

C Toxicity is related to glutothione consumption

D Enhanced with cimetidine

Explanation C

Acetaminophen is conjugated to harmless glucuronide and sulfate metabolites when taken at normal doses. If abnormal doses are taken the metabolic pathways are overwhelmed and a P450-dependant system converts some of the drug to NAPQI, a reactive intermediate. NAPQI is conjugated with glutathione to a third harmless product if the stores of glutathione are adequate. If the stores are exhausted, the NAPQI combines with essential hepatic cell proteins causing hepatic cell death. Administration of other sulhydryl donors e.g. acetylcysteine may be life saving. Enzyme inducers may increase acetaminophen toxicity because they increase phase I metabolism more than phase II thus resulting in increased production of NAPQI

Note: the toxic pathway is N-hydroxylation, not N-acetylation.

**Question 15**

Regarding paracetamol, which of the following statements is correct?

A It is hydrophillic

B It doesn't cause hyperuricaemia

C It is only given orally

D It is highly protein bound

Explanation B

Paracetamol can be given orally, IVI and rectally. It is slightly protein bound. Half-life is 2-3hrs and is relatively unaffected by renal function

**Question 17**

Regarding ibuprofen, select the correct answer.

A It is not effective in closing the patent ductus arteriosis in the preterm infant

B It is a non selective COX inhibitor

C It causes more gastric side effects than aspirin

D It has a low bioavailability

Explanation B

Ibuprofen is more than 99% protein bound, is rapidly cleared and has a terminal half-life of 1-2hrs. It is a reversible inhibitor of COX1 and COX 2. GIT irritation and bleeding do occur, but with less frequency than aspirin. Its bioavailability is 50-73%. It may cause closure of the patent ductus arteriosis

**Question 23**

Regarding ibuprofen, which of the following statements is correct?

A Eating the drug with food significantly lowers its bioavailability

B It is a strong organic acid

C It has a half life 2 hours

D Urinary excretion of unchanged drug is 20%

Explanation C

Ibuprofen, like most NSAIDS is absorbed well orally and food does not substantially change its bioavailability. All but one are weak organic acids- nabumetone. Ibuprofen has a half life of 2hrs and is urinary excretion of unchanged drug is <1%. Interestingly, Ibuprofen in doses <600mg QID has analgesic and no anti-inflammatory properties.