DEADLINE WEDNESDAY 5 JULY 2017

Paracetamol induced hepatotoxicity.
Mahadevan SB, McKiernan PJ, Davies P, Kelly DA. *Arch Dis Child* 2006; **91** (7): 598-603.
Assessment No: 010317

01	Although large doses of paracetamol may lead to severe hepatic necrosis, it does not necessarily lead to fatal hepatic failure.
02	Orthotopic liver transplantation (OLT) is a therapeutic option for liver failure following paracetamol overdose.
03	Due to age-associated differences in the drug metabolism and detoxification of paracetamol metabolites, infants and young children may be more susceptible to paracetamol toxicity after acute ingestion than adults.
04	Evidence suggests that although younger children may tolerate doses higher than 150mg/kg, they may develop toxicity after repeated therapeutic or supratherapeutic doses of paracetamol.
05	In this study, significant hepatotoxicity was defined as serum alanine or aspartate transaminase (ALT or AST) level less than 1,000IU/L.
06	There were 61 children included in this study, who were then divided into two groups.
07	All patients in this study received N-acetylcysteine.
08	The data collected from this study included age, sex, reported dose of paracetamol ingested, time from reported ingestion to presentation at the hospital but not grade of encephalopathy.
09	Three children in group I and two in group II, all under seven years old, received multiple cumulative overdoses accidentally or intentionally.
10	All children in group I recovered with conservative management, while children in group II developed rapidly progressing encephalopathy ≥ grade III and were listed for liver transplantation.
11	Survival was 100% in children with grade ≤II (group II) compared to 18% in those with grade ≥III encephalopathy (group I).
12	The main cause of death in group II children with grade ≥III encephalopathy was acute liver failure.
13	Haemofiltration for progressive renal impairment was necessary in one patient in group I and five in group II, and only one in each group survived.
14	In this study, hepatic encephalopathy ≥grade III was the best single predictor of poor prognosis as only 18% of children survived despite liver transplantation.
15	Paracetamol overdose leading to toxic liver damage and encephalopathy occurs more frequently in children than in adults, and is fatal.
16	Most patients were adolescent males who took an accidental paracetamol overdose following an impulsive act.
17	This study noted that delayed presentation (24 vs. 44 hours) to hospital after overdose was a risk factor for severe renal failure.
18	Jaundice was an evident clinical feature in this study.
19	Although children less than seven years old may be less susceptible to acute paracetamol poisoning, 6/51 patients less than seven years old developed hepatotoxicity following multiple dosing.
20	In this study, one of the main factors for poor outcome was delay in establishing treatment.

Pathology at the tipping point.
cancerresearchuk.org/sites/default/files/testing_times_to_come_nov_16_cruk.pdf
(Executive Summary only, up to page 12). Assessment No: 010917

01	It is becoming ever cheaper to deliver pathology services.
02	This document addresses pathology in England only.
03	Due to a burden of clinical work, pathologists carry out less in the way of research and educational activities.
04	It is felt that more electronic and IT use would improve efficiency.
05	It is unnecessary to include pathology staff in NHS England workforce planning as there are plenty of professionals involved already.
06	Cancer Research UK receives a small amount of government funding.
07	The level of molecular testing requested annually appears to have plateaued.
08	It would be high risk to try and retain consultants who are approaching retirement.
09	Biomedical and clinical scientists should be used in advanced and extended roles.
10	Avoiding duplicate and inappropriate testing may reduce pressure.
11	There are good national data available across all areas of pathology.
12	Over the last 40 years, cancer survival rates have doubled.
13	In 2013 there were 352,000 new cases of cancer in the UK.
14	All member countries of the UK have standardised waiting time targets.
15	Histopathology consultant numbers are currently inadequate.
16	There are now more medical laboratory support staff to qualified staff as a ratio than figures six years earlier.
17	Unless action is taken, pathology turnaround times will increase beyond acceptable limits.
18	Molecular testing should be standardised.
19	There should be investment to support research programmes.
20	Pathology is included in the curriculum of all medical schools.

REFLECTIVE LEARNING QUESTIONS

01	What do you understand by acute and staggered paracetamol overdose? Do you have any guidelines for paracetamol estimation in your laboratory? If yes, then what are the guidelines? If no, then do you think there should be any?
02	How is paracetamol absorbed in the body at therapeutic and overdose levels? Describe the role of activated charcoal in gut contamination.

01	What impact do you consider that this report should have on government statements on funding for pathology staff, education and infrastructure, given the incidence of cancer across the UK and the world?
02	Cancer Research UK (CRUK) is a charity rather than an arm of the NHS. What sort of legitimacy do you consider that this report has, based on the status of CRUK as the commissioner?