

Lab results

Collect Date :	01/01/08	01/01/08	01/01/08	01/01/08	01/01/08	01/01/08	01/01/08	01/01/08
Collect Time :	13:09	13:20	14:19	14:19	16:15			
Arrive Date :	01/01/08	01/01/08	01/01/08	01/01/08	01/01/08			
Arrive Time :	13:39	13:38	14:44	14:44	16:29			
Request No. :								
Urgency :								

Sodium	124 L	--	--	129 L	--			
Potassium	5.0 H	--	--	4.4	--			
Urea	7.7 H	--	--	7.0	--			
Creatinine	205 H	--	--	195 H	--			
Total Protein	49 L	--	--	36 L	--			
Albumin	25 L	--	--	14 L	--			
Globulin	24	--	--	22 L	--			
Total Bilirubin	1.63 H	--	--	1.01 H	--			
ALP	109	--	--	67	--			
ALT	6900 H	--	--	4050 H	--			
Calcium	--	--	--	1.60 L	--			
Phosphate	--	--	--	2.25 H	--			
Glucose, spot	--	2.6	7.7	--	13.2			

Lab results

Collect Date :	01/01/08	01/01/08
Collect Time :	14:19	14:22
Arrive Date :	01/01/08	01/01/08
Arrive Time :	15:26	15:26
Request No. :		
Urgency :		

Clinical Details:	Sepsis	
Paracetamol		T/F --
Salicylate		-- 0.96
Ethanol		T/F --
Collect Date :	01/01/08	
Collect Time :	14:19	
Arrive Date :	01/01/08	
Arrive Time :	15:26	
Request No. :		
Urgency :		

Paracetamol	<100	
Ethanol	4	
Collect Date :	02/01/08	
Collect Time :	00:01	
Request No. :		
Remark :	LIVER FAILURE	

Paracetamol	<30	
Salicylate	<0.3 L	
Ethanol	<3.0	

Lab results

Date Collected: 02/01/08 00:01

Clinical Details: LIVER FAILURE

pH 5
Ketones Negative
Glucose Negative

Toxicology screening (Urine):
None of the compounds on the following list are detected.

Toxicology screening (Gastric):
None of the compounds on the following list are detected.

- ## Patient 1
- Non-invasive BP unrecordable,
 - Arterial catheter SBP ~ 30mmHg on arrival
 - High dose inotropic support
 - Oozing from the puncture site / Coffee ground vomitus / Tarry stool
 - Blood & FFP transfusion
 - Hx from husband – ingestion of wild mushroom days ago in South Africa
 - Developed multi-organ failure
 - Certified death ~6 hr after QMH admission
 - Postmortum: result not a/v yet

- ## Patient 2
- M / 44, husband of the diseased
 - Attended QMH A&E at 23:14 on 1/1/2008
 - Picked 10+ pieces of white mushroom~5cm in diameter of each piece on hillside on 27-12-2007 in S. Africa
 - Made mushroom soup
 - Shared with 4 other people at 5pm
 - All had GI symptoms half day after ingestion at 6am on 28-12-2007

- ## Patient 2
- Admitted into a local hospital between 28/12/2007 and 30/12/2007
 - Treated as mushroom poisoning with iv medications
 - Results of mushroom analysis unknown
 - 2 friends – staying in S. Africa hospital
 - 1 friend – returned to China, seriously ill
 - Travelled with wife to HK on 31/12/2007
 - Wife developed confusion and dizziness on aeroplane on 1/1/07, admitted to PMH ICU and transferred to QMH ICU, died on 2/1/2008 for acute liver failure

Patient 2

- V & D since 28/12/2007, ~3 times a day
- Mild epigastric discomfort
- GI symptoms subsided on 1/1/2008 morning
- Attended QMH A&E on 1/1/2008 23:00
- P/E: afebrile, vital signs stable
alert
mild jaundice+
- ECG: NSR
- Blood tests: AST 150, ALT 2116, Bili 23, INR 1.0
Cr 120,
- ABG: pH 7.39, pO2 18, pCO2 3.6, HCO3- 16, BE -7
- ICU consulted, refused take over
- Patient was admitted to EMW for further management.

Lab results

Collect Date :	01/01/08	02/01/08	02/01/08	02/01/08	Ref. Range	Units
Collect Time :	23:47	09:17	14:32	21:21		
Request No. :	1					
Remark :	mushroom toxicity.					
Mask Type :	Room Air					
Flow Rate :	0.0					
% inspired O2 :	18					
pH :	7.39					
pO2 :	18.0 H					
pCO2 :	3.6 L					
HCO3- :	16 L					
Base excess :	-7 L					
CBC						
WBC	7.00					10.01
RBC	4.90					4.70
HGB	16.1					15.5
HCT	0.433					0.421
MCV	88.3					89.6
MCH	32.9					33.0
MCHC	37.3 H					36.8 H
RDW	11.7					12.0
PLT	209					205
WBC DIFFERENTIAL						
DC Type		MACHINE		MACHINE		
#Neutrophil	4.03					6.56
#Lymphocyte	1.30					1.43
#Monocyte	0.87 H					1.10 H
#Eosinophil	0.50					0.70 H
#Basophil	0.06					0.04
Film Review		N		N		
Coagulation						
PT	12.2	12.5	12.5	12.1	11.3 - 13.5	seconds
INR(*)	1.0	1.1	1.1	1.0		
APTT	26.8	25.8 L	26.9	27.1	25.9 - 33.7	seconds

Lab results

Collect Date :	01/01/08	01/01/08	02/01/08	02/01/08	02/01/08	Ref. Range	Units
Collect Time :	23:47	23:49	09:17	14:32	21:21		
Request No. :							
Remark :	mushroom toxicity	mushroom toxicity. Please contact	mushroom toxicity	mushroom toxicity. mushroom poisoning	mushroom toxicity		
Comment	Below	Below	Below	Below	Below		
Na	132 L	--	137	136	137	136 - 148	mmol/L
K	3.4 L	--	3.7	3.1 L	3.2 L	3.6 - 5.0	mmol/L
Chloride	104	--	104	104	107	100 - 109	mmol/L
Urea	11.8 H	--	9.5 H	8.5 H	7.5	3.6 - 7.8	mmol/L
Creatinine	120 H	--	123 H	116 H	103	67 - 109	umol/L
R Glucose	6.2	--	--	--	--	2hr pp < 7.8	mmol/L
Calcium	2.16	--	--	--	--	2.11 - 2.55	mmol/L
Adjusted Calcium	2.22	--	--	--	--	2.11 - 2.55	mmol/L
Phosphate	1.13	--	--	--	--	0.88 - 1.45	mmol/L
Total Protein	74	--	71	68	65 L	68 - 84	g/L
Albumin	39	--	40	38 L	36 L	39 - 50	g/L
Globulin	35	--	31	30	29	24 - 37	g/L
Ammonia	--	28	--	--	--	< 33	umol/L
Total Bilirubin	23	--	25 H	33 H	12	4 - 23	umol/L
ALP	71	--	68	66	67	42 - 110	U/L
ALT	2116 H	--	1815 H	1612 H	1377 H	8 - 58	U/L
AST	150 H	--	120 H	105 H	114 H	15 - 38	U/L
GGT	151 H	--	--	--	164 H	11 - 62	U/L
LDH	215	--	--	--	--	118 - 221	U/L
CK	146	--	--	--	--	65 - 355	U/L
Amylase	71	--	--	--	--	25 - 124	U/L

Lab results

Clinical Details: DER LFT ?AMATOXIN POSIONING

Date Collected: 02/01/08 13:00

pH 5
Ketones Positive
Glucose Negative
Toxicology screening (Urine):
Metoclopramide metabolites.

Patient 2

- Treatment
 - Soft diet
 - MDAC with sorbitol
 - IV NAC
- Discharged at 10:25 on 3/1/2008
- FU arranged on 8/1/2008 but defaulted

Mushroom Poisoning

Mushroom toxins

- 4 categories of mushroom toxins according to their physiological effects
 1. Protoplasmic poisons
 2. Neurotoxins
 3. Gastrointestinal irritants
 4. Disulfiram-like toxins

Protoplasmic poisons

- Poisons that result in generalised destruction of cells, followed by organ failure
 - Amatoxins
 - Hydrazines
 - Orellanine

Amatoxin

- Toxin produced by several mushroom species
- Including:
 - Death Cap or Destroying Angel (*Amanita phalloides*, *A. virosa*),
 - Fool's Mushroom (*A. verna*) and several of their relatives,
 - Autumn Skullcap (*Galerina autumnalis*) and some of its relatives.

Amatoxins

Amanita phalloides (Death cap)

Smelling sickly sweet to foetid, this common mushroom grows in forests, under oaks, pines, and poplars.

In South Africa, it's found extensively in the Cape Province, Gauteng and Kwa Zulu Natal, especially after good rains

Amatoxins

- Heat-stable, insoluble in water, not destroyed by drying.
- At least 5 subtypes of amatoxins exist: alpha and beta amatoxins are the most significant subtype
- Not hydrolysed by enzymes, thus readily absorbable

Toxicokinetics

- Concentrate in liver and kidney cells
- Fragmentation of the nucleoli as early as 30 min after administration
- Changes in the cytoplasm as early as 48 hours after poisoning and rapidly leading to necrosis
- Parenchymal cells of liver and kidney are targeted by low molecular amatoxins
- Sinusoidal cells targeted by macromolecular protein conjugates



Toxicokinetics

- Amatoxins primarily inhibit RNA polymerase II
- Cells with the highest rate of multiplication, such as the intestinal mucosa, are injured first
- Liver and kidney are next
- Renal excretion
- Amatoxins were present in serum only during the first 24 to 48 hours and at very low concentration
- Highest amatoxin concentration in urine occurs during 24-48 hours, amatoxin could be detected up to 72 to 96 hours post-ingestion



Clinical features

1st Phase:

- long latent period (range 6-24 hours, average 6-15 hours)
- Including abdominal pain, persistent vomiting and watery diarrhea.

2nd Phase:

- Occurs during the next 24-28 hours
- GI symptoms appear to recover of a short time
- Renal and Hepatic function deteriorate



3rd Phase:

- 3-5 days following ingestion
- Hepatic and renal failure, shock, multi-organ failure
- Death occurs within 6-16 days (Mean 8 days)
- Autopsy will usually reveal fatty degeneration and necrosis of the liver and kidney



Amatoxin-type mushroom testing

- Meixner test
- also known as the Wieland Test
- Uses concentrated hydrochloric acid and newspaper to test for the deadly poisonous amatoxins
- This test can detect amatoxin concentrations as low as 0.2 mg/mL
- If amatoxins are present, a blue color will develop within 2 minutes
- False +ve results can be present at high temperature or exposure to sunlight or toxins like psilocybin, bufotenine, and certain terpenes
- Always perform the test with positive and negative controls
- Limited reliability



Management of Amatoxin mushroom poisoning

- Supportive treatment
ABC, correct fluid and electrolyte disturbance, correct clotting deficiency, renal and hepatic supportive therapy
- Monitoring
- Decrease exposure to toxin
- Enhanced elimination of toxin



Monitoring

- Serum level of amatoxin do not correlate with severity of poisoning
- Elevated AST, ALT, LDH, bilirubin are the 1st and best indicator of liver damage
- Glucose, fibrinogen and PT are the best indicator of hepatocellular failure
- PT is a reliable prognosis factor, patients with PT less than 10% have a high fatality rate
- Maximum hepatic transaminase levels and minimum PT level were reached during the 3rd days after ingestion.

Other prognostic factors

- Minimal PT
- PSS assessment 60 hours after ingestion
(PSS: poison severity score
PSS1:mild intoxication, transaminase<1000IU/L
PSS2:moderate intoxication, transaminase 1000-2000IU/L
PSS3:severe intoxication, transaminase>2000IU/L)
- Evolution of PT and hepatic transaminase

Severity classification

- Grade 1: GI upset only, no liver or kidney failure→ symptomatic Tx only
- Grade 2: all signs of intoxication, with a mild to moderate rise in transaminases(>500 unit/L)→ symptomatic Tx only
- Grade 3: transaminase > 500units/L, prolong PT → to transport to unit with LTx
- Grade 4: steep rise in transaminase, steep decline in clotting function, steep rise in bilirubin, renal impairment→ poor prognosis

GI decontamination

- GL: if within 1 hr of ingestion
- AC
- MDAC:
Amatoxins appear to undergo enterohepatic circulation and repeat dose activated charcoal may interrupt this cycle and reduce toxicity, however, not shown to affect outcome

Penicillin G

- Use based on animal studies in mice, rats, and dogs
- Protective against lethal doses of amatoxin by reducing or inhibiting the liver uptake of amatoxin
- Most frequently utilized chemotherapy
- True efficacy is difficult to assess as it is often given as a part of a multi-drug therapy
- Early treatment with high dose penicillin G should be considered
- However, efficacy has not been proven in controlled clinical trial
- Up to 1 megaU/kg/d IV continuous infusion

Silibinin

- **Silibinin** is the major active constituent of **silymarin**, and extraction from blessed milk thistle
- hepatoprotective (antihepatotoxic) properties and antioxidant properties
- competitively antagonize toxin binding to liver cell membrane receptors in mushroom poisoning and other hepatotoxic exposure
- Administration of silibinin up to 48 h after mushroom ingestion appears to be an effective measure to prevent severe liver damage in *Amanita phalloides* poisoning
- IV 20-50 mg/kg/d

Other treatments:

- NAC:
-to start early
-doses used were suggested by acetaminophen poisoning
-no evidence of any specific benefit
- Cimetidine:
-act as a cytochrome P450 inhibitor
-animal study only
- Dexamethasone
-inhibitors for human hepatic uptake transporter for amatoxins
-Maybe useful for the treatment of amatoxin poisoning

Enhanced Elimination

- Because amatoxins are cleared rapidly from the plasma by the kidneys, extracorporeal elimination techniques may not clear significant amounts of toxin
- Different techniques of extracorporeal elimination given after 25 to 48 hours are generally not thought of as useful or indicated

Enhanced Elimination

- Diuresis: significant amounts of amatoxin are eliminated in urine, maintenance of a normal or slightly high urine output especially during the first 48 hours
- HP: maybe helpful to remove amatoxins in early stages
- HD: if renal failure occurs

MARS

- Molecular Absorbent Regeneration System
- for removing protein bound substances in patients with liver failure and hepatic encephalopathy
- to stabilize the condition of a patient until spontaneous liver regeneration occurs or as a bridge to liver transplant

Liver transplant-

King's college non-paracetamol criteria:

- EITHER PT > 100 sec (INR >7)
- OR at least 3 of the followings:
 - PT >50sec (INR >3.5)
 - bilirubin >300umol/L
 - age < 10 or age > 40
 - an interval between jaundice and encephalopathy >7 days

2. Hydrazines

- Gyromitrin, a protoplasmic poison
- Monomethylhydrazine, a volatile hydrazine derivative
- Found in certain species of False Morel (*Gyromitra esculenta* & *G. gigas*)

2. Hydrazines

- Clinical features resemble Amanita poisoning, but less severe
- Latent period of 6-10 hours
- Followed by sudden onset of abdominal discomfort, vomiting, diarrhoea, severe headache
- Primarily affect the liver
- Haemolysis and CNS disturbance are rare
- Mortality rate 2-4%
- Treatment: supportive
- Pyridoxine may be given for CNS symptoms



3. Orellanine

- Found in Sorrel Webcap mushroom (*Cortinarius orellanus*) and some of its relatives
- Red brown cap with fibrillose surface
- Rusty yellow gills, yellow brown stem



3. Orellanine

- Toxins activated in liver, accumulates in kidney
- Extremely long latent period of 3 to 14 days
- Polydipsia and polyuria are the first symptoms
- Followed by nausea, headache, muscular pains, chills spasms and LOC
- Renal tubular necrosis & renal failure in severe case
- Death occurs several weeks after acute poisoning
- Mortality rate ~ 15%
- Recovery may require several months
- Treatment: supportive



Neurotoxins

- Compounds that cause neurological symptoms
 1. Muscarine
 2. Ibotenic acid/muscimol
 3. Psilocybin



1. Muscarine

- In *Inocybe* or *Clitocybe* species (*I. geophylla*, *C. dealbata*)



1. Muscarine

- Cholinergic symptoms
- Onset: 15-30 mins, duration: 2 hrs
- Profuse sweating, salivation, lacrimation common
- Abdominal pain, vomiting, diarrhoea, SOB
- No CNS symptoms
- Deaths, due to cardiac or respiratory failure, are rare
- Treatment: activated charcoal, supportive
- Atropine for moderate or severe symptoms



2. Ibotenic acid/Muscimol

- Fly Agaric (*Amanita muscaria*) & Panthercap (*Amanita pantherina*) produce both toxins

2. Ibotenic acid/Muscimol

- Both toxins produce same effects
- Muscimol is 5 times more potent than ibotenic acid
- Onset: within 1-2 hrs, duration: few hrs
- CNS depression: drowsiness, dizziness, deep sleep
- Followed by CNS excitement: hyperactivity, excitability, tremor, illusions and delirium
- Drowsiness may alternate with excitement
- Prognosis is good and fatality is rare in adults
- Children in large ingestion: convulsion and coma
- Treatment: supportive

3. Psilocybin

- In genera *Psilocybe* (*Psilocybe cubensis*), *Panaeolus*, *Copelandia*, *Conocybe*, etc.

3. Psilocybin

- Syndrome similar to alcohol intoxication
- CNS symptoms: euphoria, hallucination
- Sympathomimetic effects
- distinguished from ibotenic acid poisoning by the absence of drowsiness or coma
- Intentionally eaten for their psychotropic effects in religious ceremonies of certain American tribes
- Onset: 10-30 mins, duration: 2 hrs
- Rarely fatal in adults
- May cause fever, convulsion, coma and death in small children if large dose is taken

3. Psilocybin

- Treatment
 1. Activated charcoal
 2. Rest in quiet and safe environment
 3. Avoidance of external stimuli
 4. IV benzodiazepines in necessary

Gastrointestinal irritants

- Numerous mushrooms contains toxins that causes nausea, vomiting, diarrhoea and abdominal cramps
- Chemistry of toxin virtually unknown
- Symptoms similar to the protoplasmic poisons
- Chief diagnostic difference: rapid onset
- Symptoms may last for several days
- Major concerns: dehydration & electrolyte imbalance
- Fatalities are rare except in debilitated and extreme of age
- Treatment: supportive

Coprine

- Inky Cap Mushroom (*Coprinus atramentarius*)
- Generally considered edible



Coprine

- Converted to cyclopropanone hydrate in human body
- An inhibitor of aldehyde dehydrogenase, interferes with the breakdown of alcohol
- Produces disulfiram-like effect
- Symptomatic only if alcohol is consumed within 72 hrs after consumption of the mushroom
- Onset: 30 mins after drinking alcohol
- Duration: 2-3 hrs
- Headache, nausea, vomiting, flushing
- Palpitation, diaphoresis, anxiety



Thank you!