

GI Bleed & Acute Liver Problems

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SCENARIO 1

Scenario 1

- 82 year old lady
- 3 weeks on stroke rehab ward
- CKD3, angina
- HAP 2 days



Scenario 1

- Call at 2pm tachycardia, epigastric pains
- ECG fine
- Coffee ground vomit



Scenario 1

- Call at 6pm
- Further coffee ground vomit
- Hb 100, urea 12, creat 130

- 2days ago, Hb 105, urea 8, creat 110



- Call at 3am
- Collapse on commode
- Black stool
- Bp 80/50, p110, sats 90%
- Hb75, urea 21, creat 140



Scenario 1

- What are you going to do?

- NICE Guideline CG141, Aug 2016
 - Acute upper GI bleeding in over 16s, management
- Management of acute upper gastrointestinal bleeding
 - *BMJ* 2019;364:l536

- Resuscitation of patient
 - Blood transfusion
- Risk stratification
- Endoscopy

Blatchford Score

		Assigned score
Blood urea, mmol/L	6.5 -7.9	2
	8.0-9.9	3
	10.0-24.9	4
	≥ 25	6
Hemoglobin for men, g/dL	12 -12.9	1
	10-11.9	3
	< 10	6
Hemoglobin for women, g/dL	10-11.9	1
	< 10	6
Systolic blood pressure, mmHg	100-109	1
	90-99	2
	< 90	3
Other markers	Pulse ≥ 100	1
	Melena	1
	Syncope	2
	Hepatic disease	2
	Cardiac failure	2

Rockall Score

	Score			
Variable	0	1	2	3
Age	<60	60-79	≥80	
Shock	'No shock', systolic BP ≥100 pulse <100	'Tachycardia', systolic BP ≥100 pulse ≥100	'Hypotension', systolic BP <100	
Comorbidity	No major comorbidity		Cardiac failure, ischemic heart disease, any major comorbidity	Renal failure, liver failure, disseminated malignancy
Diagnosis	Mallory-Weiss tear, no lesion identified and no SRH	All other diagnoses	Malignancy of upper GI tract	
Major SRH	None or dark spot only		Blood in upper GI tract, adherent clot, visible or spurting vessel	

- Endoscopy
 - DU with bleeding vessel
- Omeprazole 80mg iv bolus and 8mg/hr infusion 72hrs
 - Twice daily iv 40mg
- When to restart Asprin/Clopidogrel?



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SCENARIO 2

- 24 year old man
- Overdose 100 paracetamol 6hours previously,

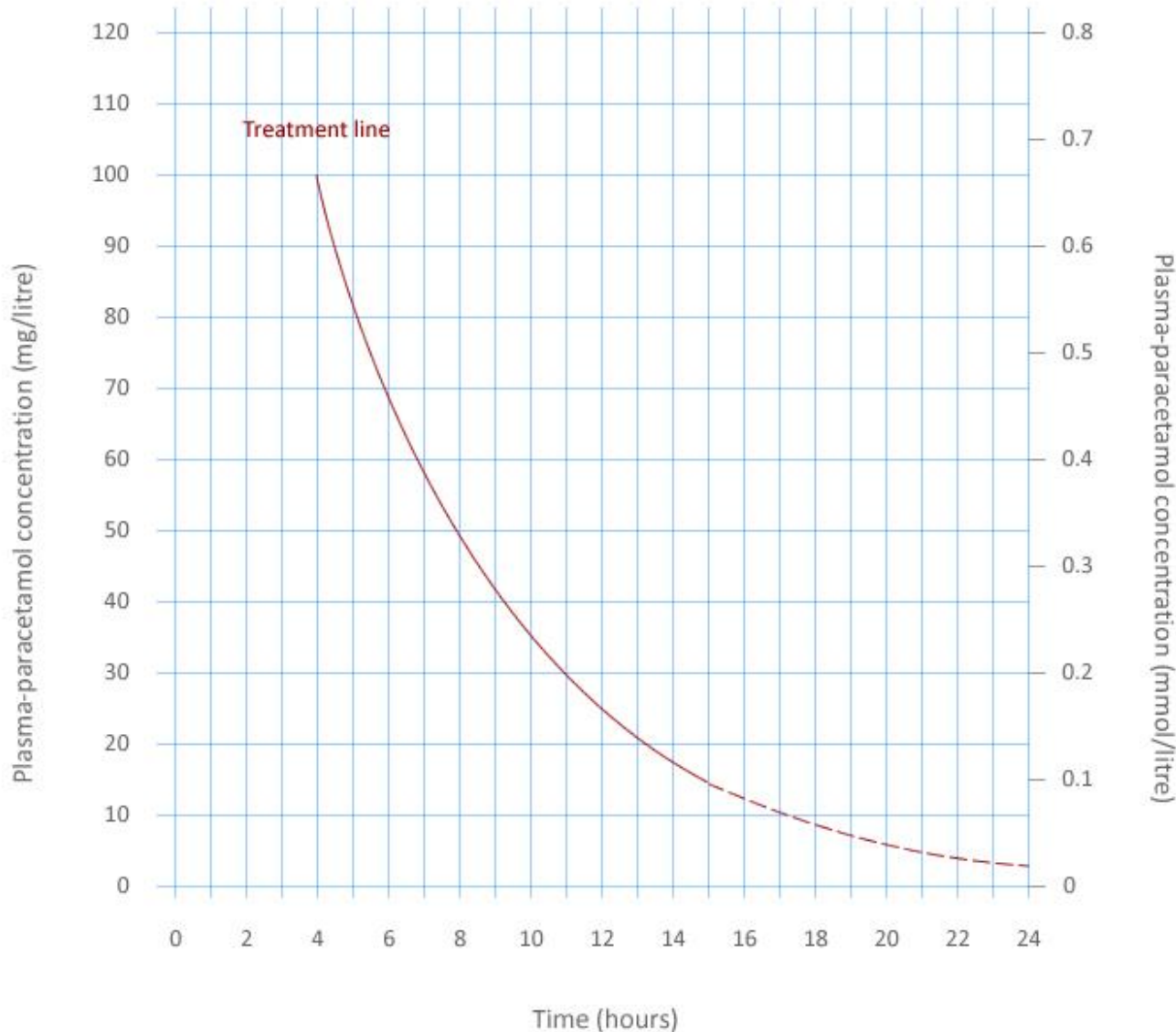
- Na 135, K 3.8, Urea 12, Creat 190
- Bili 8, ALT 2747, AlkPhos 150, Albumin 43
- PT 22

- What are you going to do?

- Fluid resuscitation
- N-acetylcysteine
- Monitoring bloods
- Mental Health Team review

- When to refer to a Liver Unit

Scenario 2



- Do not use nomogram if
 - Staggered overdose
 - OD taken over an hour duration



- **First infusion**
- 150mg/Kg Nacetylcysteine injection to 200 mL of infusion fluid and infuse over **1 hour**.
- **Second infusion**
- 50mg/Kg Nacetylcysteine injection to 500 mL of infusion fluid and infuse over the next **4 hours**.
- **Third infusion**
- 100mg/Kg Nacetylcysteine injection to 1 litre of infusion fluid and infuse over the next **16 hours**

Scenario 2

Adult acetylcysteine prescription (each ampoule = 200mg/mL acetylcysteine)					Please circle appropriate weight and volume.	
Regimen	First Infusion		Second Infusion		Third Infusion	
Infusion fluid	200 mLs 5% glucose or sodium chloride 0.9%		500 mLs 5% glucose or sodium chloride 0.9%		1000 mLs 5% glucose or sodium chloride 0.9%	
Duration of infusion	1 hour		4 hours		16 hours	
Drug dose	150 mg/kg acetylcysteine		50 mg/kg acetylcysteine		100 mg/kg acetylcysteine	
Patient Weight ¹	Ampoule volume ²	Infusion Rate	Ampoule volume ²	Infusion Rate	Ampoule volume ²	Infusion Rate
kg	mL	mL/h	mL	mL/h	mL	mL/h
40-49	34	234	12	128	23	64
50-59	42	242	14	129	28	64
60-69	49	249	17	129	33	65
70-79	57	257	19	130	38	65
80-89	64	264	22	131	43	65
90-99	72	272	24	131	48	66
100-109	79	279	27	132	53	66
≥110	83	283	28	132	55	66

- **Phases of POD**
- Phase I – 0-24h
 - Anorexia, nausea and vomiting, malaise
 - LFT derangement at 12h
- Phase II – 18-72h
 - RUQ pain
 - LFT derangement
- Phase III – 72-96h
 - Centrilobar necrosis
 - Liver failure
- Phase IV – 4d-3wk
 - Recovery, transplant or death
 - No chronic state

Scenario 2 Management of *coagulopathy*

- PT <25seconds
 - Ensure well hydrated
 - 24 hours Parvolex
 - Ignore the transaminase rise
 - Monitor PT 8hrly until clearly plateaus and starts to fall



Scenario 2 Management of *coagulopathy*

- PT <30 seconds
 - Ensure generous hydration
 - Continue Parvolex until PT less than 25 seconds
 - Ignore transaminase rise

Scenario 2 Management of coagulopathy

- Single PT 30 – 50 seconds
 - Aggressive fluid resuscitation to correct hypovolaemia; use 0.9% Saline
 - Then 250ml/hr once intravascularly replete
 - Urinary catheter and hourly urine monitoring
 - Broad spectrum antibacterial and antifungal
 - 5 days and review
 - Cef + Met + Fluconazole 200mg
 - Prolonged Parvolex 150mg/kg/day continuous infusion until PT <25seconds
 - Acid suppression – PPI
 - REVIEW OTHER RESULTS



Scenario 2 Management

- Poor prognosis if
- HIGH LACTATE
 - >3.5
- ACIDOSIS
 - if persisting despite adequate fluid resuscitation
- HIGH CREATININE
- HIGH PHOSPHATE – severe liver cell necrosis

- Referral to Liver Unit

Day 2	Day 3	Day 4
Arterial pH <7.30	Arterial pH <7.30	INR >6 or PT >100 s
INR >3.0 or PT >50 s	INR >4.5 or PT >75 s	Progressive rise in PT to any level
Oliguria	Oliguria	Oliguria
Creatinine >200 $\mu\text{mol/l}$	Creatinine >200 $\mu\text{mol/l}$	Creatinine >300 $\mu\text{mol/l}$
Hypoglycaemia	Encephalopathy	Encephalopathy
	Severe thrombocytopenia	Severe thrombocytopenia



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SCENARIO 3

Scenario 3

- 32 year old lady, housewife, 9year old daughter and 5 year old son
- Drinks 1 ½ bottles wine most days
- Admission with 4 weeks progressive abdominal distension, anorexia, jaundice and vomiting
- Stopped drinking 3 weeks ago
- No PMH, not on any medication

- O/E agitated, confused,
 - Spider naevi, bruises on arms and back
 - Ascites, jaundiced
- Na 120, K 2.5, urea 5.4, creat 210
- Mg 0.5,
- Bili 238, ALT 46, AlkPhos 438, GGT 160, Albumin 22
- PT 28
- Hb 94, MCV 105, WCC 15, platelets 64

- What are you going to do?
 - Why is she confused?
 - First 24hours?

National Confidential Enquiry into Patient Outcome and Death



Measuring the Units

A review of patients who died with alcohol-related liver disease

- Response to the NCEPOD report: development of a care bundle for patients admitted with decompensated cirrhosis—the first 24 h
 - *Frontline Gastroenterology* 2016;**7**:16-23.
McPherson S, Dyson J, Austin A, *et al*
- NICE CG100 Alcohol use disorders
- NICE NG150 Cirrhosis management
- NICE CG141 Upper GI bleed
- NICE CG32 Nutrition support for adults
- STOPAH and various reviews

- Confusion causes
 - Delirium Tremens (within first week of stopping drinking)
 - Wernicke Korsakoff
 - Delirium from sepsis
 - Encephalopathy
 - Electrolyte disturbance, hypoglycaemia
 - GI bleed
 - Sepsis
 - Cerebral bleed

Patient details



Decompensated Cirrhosis Care Bundle - First 24 Hours

Decompensated cirrhosis is a medical emergency with a high mortality. Effective early interventions can save lives and reduce hospital stay. This checklist should be completed for all patients admitted with decompensated cirrhosis within the first 6 hours of admission.

1. Investigations			
a) NEWS <input type="checkbox"/>	FBC <input type="checkbox"/>	U/E <input type="checkbox"/>	LFT <input type="checkbox"/>
b) Blood cultures <input type="checkbox"/>	Urine Dip/MSU <input type="checkbox"/>	Coag <input type="checkbox"/>	Gluc <input type="checkbox"/>
Perform ascitic tap in all patients with ascites using green needle irrespective of clotting parameters and send for ascitic PMN/WCC, culture and fluid albumin		Ca/PO ₄ /Mg <input type="checkbox"/>	CRP <input type="checkbox"/>
Done		Y	N/A
d) Record recent daily alcohol intake	 Units	
2. Alcohol - if the patient has a history of current excess alcohol consumption (>8 units/day Males or >6 units/day Females) N/A <input type="checkbox"/>			
a) Give IV Pabrinex (2 pairs of vials three times daily)		Y	N
b) Commence CIWA score if evidence of alcohol withdrawal		Y	N
3. Infections - if sepsis or infection is suspected N/A <input type="checkbox"/>			
a) What was the suspected source?.....			
b) Treat with antibiotics in accordance with Trust protocol Y N			
c) If the ascitic neutrophils >0.25 x 10 ⁹ /L (>250/mm ³)(i.e. SBP) then give: Y N			
i) Treat with antibiotics as per trust protocol Y N NA			
ii) IV albumin (20% Human Albumin solution) 1.5g/kg (20g of albumin in 100ml of 20% Human Albumin Solution) Y N NA			
4. Acute kidney injury and/or hyponatraemia (Na <125 mmol/L) N/A <input type="checkbox"/>			
AKI defined by modified RIFLE criteria			
1: Increase in serum creatinine ≥ 26µmol/L within 48hrs or			
2: ≥50% rise in serum creatinine over the last 7 days or			
3: Urine output (UO) <0.5mls/kg/hr for more than 6 hrs based on dry weight or			
4: Clinically dehydrated			
a) Suspend all diuretics and nephrotoxic drugs		Y	N NA
b) Fluid resuscitate with 5% Human Albumin Solution or 0.9% Sodium Chloride (250ml boluses with regular reassessment: 1-2L will correct most losses)		Y	N
c) Initiate fluid balance chart/daily weights		Y	N
d) Aim for MAP>80mmHg to achieve UO>0.5ml/kg/hr based on dry weight		Y	N
e) At 6 hrs, if target not achieved or EWS worsening then consider escalation to higher level of care		Y	N NA
5. GI bleeding – if the patient has evidence of GI bleeding and varices are suspected N/A <input type="checkbox"/>			
a) Fluid resuscitate according to BP, pulse and venous pressure (aim MAP >65 mmHg)		Y	N
b) Prescribe IV terlipressin 2mg four times daily (caution if known ischaemic heart disease or peripheral vascular disease; perform ECG in >65yrs)		Y	N NA
c) Prescribe prophylactic antibiotics as per Trust protocol (cefuroxime unless contraindicated)		Y	N
d) If prothrombin time (PT) prolonged give IV vitamin K 10mg stat		Y	N NA
e) If PT> 20 seconds (or INR >2.0) – give FFP (2-4 units)		Y	N NA
f) If platelets <50 – give IV platelets		Y	N NA
g) Transfuse blood if Hb <7.0g/L or massive bleeding (aim for Hb >8g/L)		Y	N NA
h) Early endoscopy after resuscitation (ideally within 12 hours)		Y	N

Initials:
Time:

Initials:
Time:

Initials:
Time:

Initials:
Time:

Initials:
Time:

Continues overleaf..→

Please place in medical notes

1. Encephalopathy		N/A <input type="checkbox"/>	
a)	Look for precipitant (GI bleed, constipation, dehydration, sepsis etc.)	Y	N
b)	Encephalopathy – lactulose 20-30ml QDS or phosphate enema (aiming for 2 soft stools/day)	Y	N
c)	If in clinical doubt in a confused patient request CT head to exclude subdural haematoma	Y	N/A
2. Other			
a)	Venous thromboembolism prophylaxis – prescribe prophylactic LMWH (patients with liver disease are at a high risk of thromboembolism even with a prolonged prothrombin time; withhold if patient is actively bleeding or platelets <50)	Y	N NA
b)	GI/Liver review at earliest opportunity (ideally within 24 hrs)		<input type="checkbox"/>

Initials:
Time:

Initials:
Time:

Name.....Grade.....Date.....Time.....

Decompensated Cirrhosis Care Bundle - First 24 Hours

The recent NCEPOD report 2013 on alcohol related liver disease highlighted that the management of some patients admitted with decompensated cirrhosis in the UK was suboptimal. Admission with decompensated cirrhosis is a common medical presentation and carries a high mortality (10-20% in hospital mortality). Early intervention with evidence-based treatments for patients with the complications of cirrhosis can save lives. This checklist aims to provide a guide to help ensure that the necessary early investigations are completed in a timely manner and appropriate treatments are given at the earliest opportunity.

- Decompensated cirrhosis is defined as a patient with cirrhosis who presents with an acute deterioration in liver function that can manifest with the following symptoms:
 - Jaundice
 - Increasing ascites
 - Hepatic encephalopathy
 - Renal impairment
 - GI bleeding
 - Signs of sepsis/hypovolaemia
- Frequently there is a precipitant that leads to the decompensation of cirrhosis. Common causes are:
 - GI bleeding (variceal and non-variceal)
 - Infection/sepsis (spontaneous bacterial peritonitis, urine, chest, cholangitis etc)
 - Alcoholic hepatitis
 - Acute portal vein thrombosis
 - Development of hepatocellular carcinoma
 - Drugs (Alcohol, opiates, NSAIDs etc)
 - Ischaemic liver injury (sepsis or hypotension)
 - Dehydration
 - Constipation

When assessing patients who present with decompensated cirrhosis please look for the precipitating causes and treat accordingly. The checklist shown overleaf gives a guide on the necessary investigations and early management of these patients admitted with decompensated cirrhosis and should be completed on all patients who present with this condition. The checklist is designed to optimize a patient's management in the first 24 hours when specialist liver/gastro input might not be available. Please arrange for a review of the patient by the gastro/liver team at the earliest opportunity. Escalation of care to higher level should be considered in patients not responding to treatment when reviewed after 6 hours, particularly in those with first presentation and those with good underlying performance status prior to the recent illness.

- Full assessment
 - Full liver screen, ultrasound, culture everything
- Stop Nephrotoxics
- Fluid resuscitation
- Ascitic drain if tense ascites
- Early OGD for bleeding

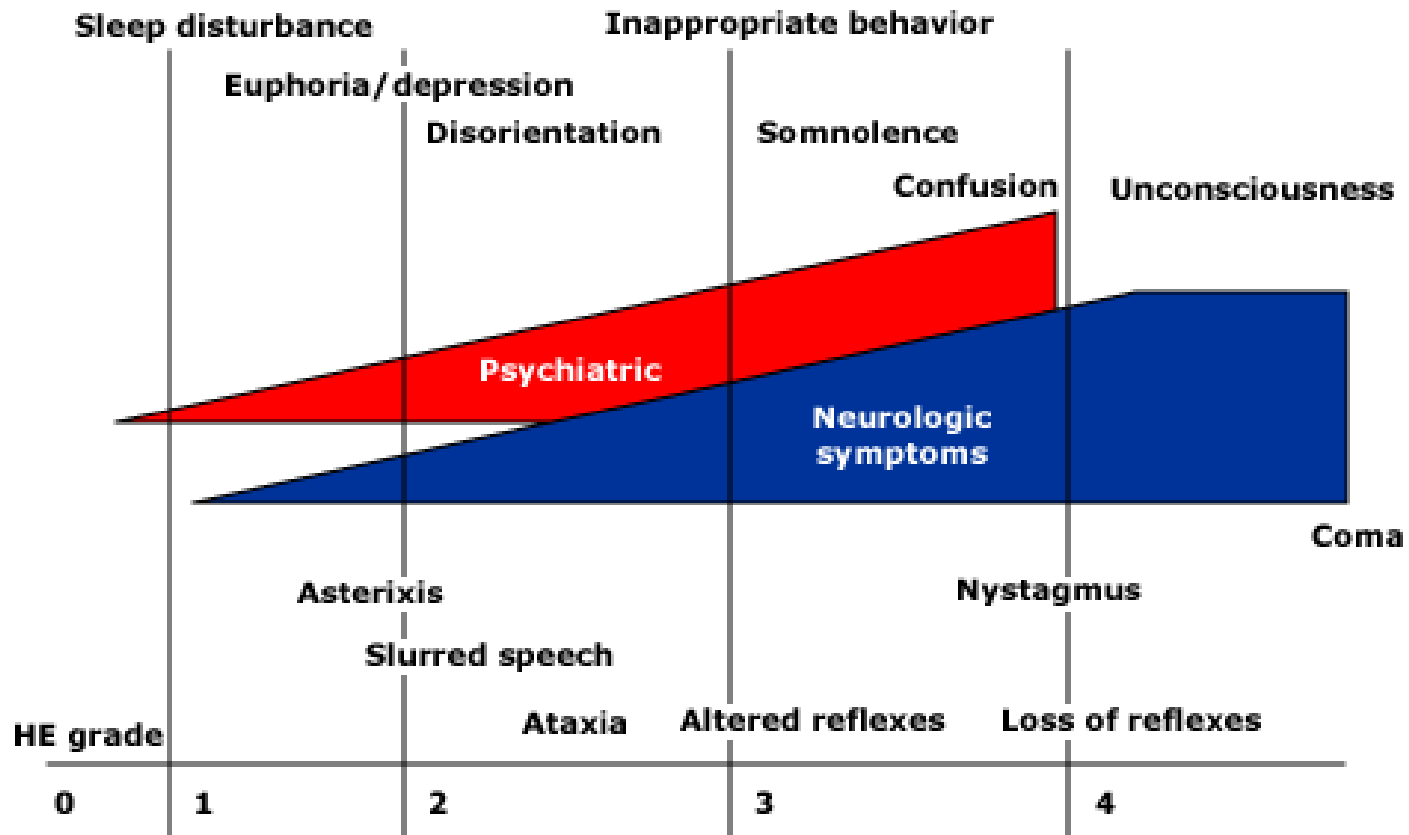


- Agitation NOT due to alcohol withdrawal
 - Alcohol withdrawal symptoms can start 8 hours from last drink
 - Peak at 48 to 72 hours
 - Generally recovered by 3 to 7 days from last drink
 - DTs more severe form and can start 3 days after last drink
 - ~5% of alcohol withdrawal patients get DTs
- **Giving chlordiazepoxide in this scenario can induce encephalopathy**

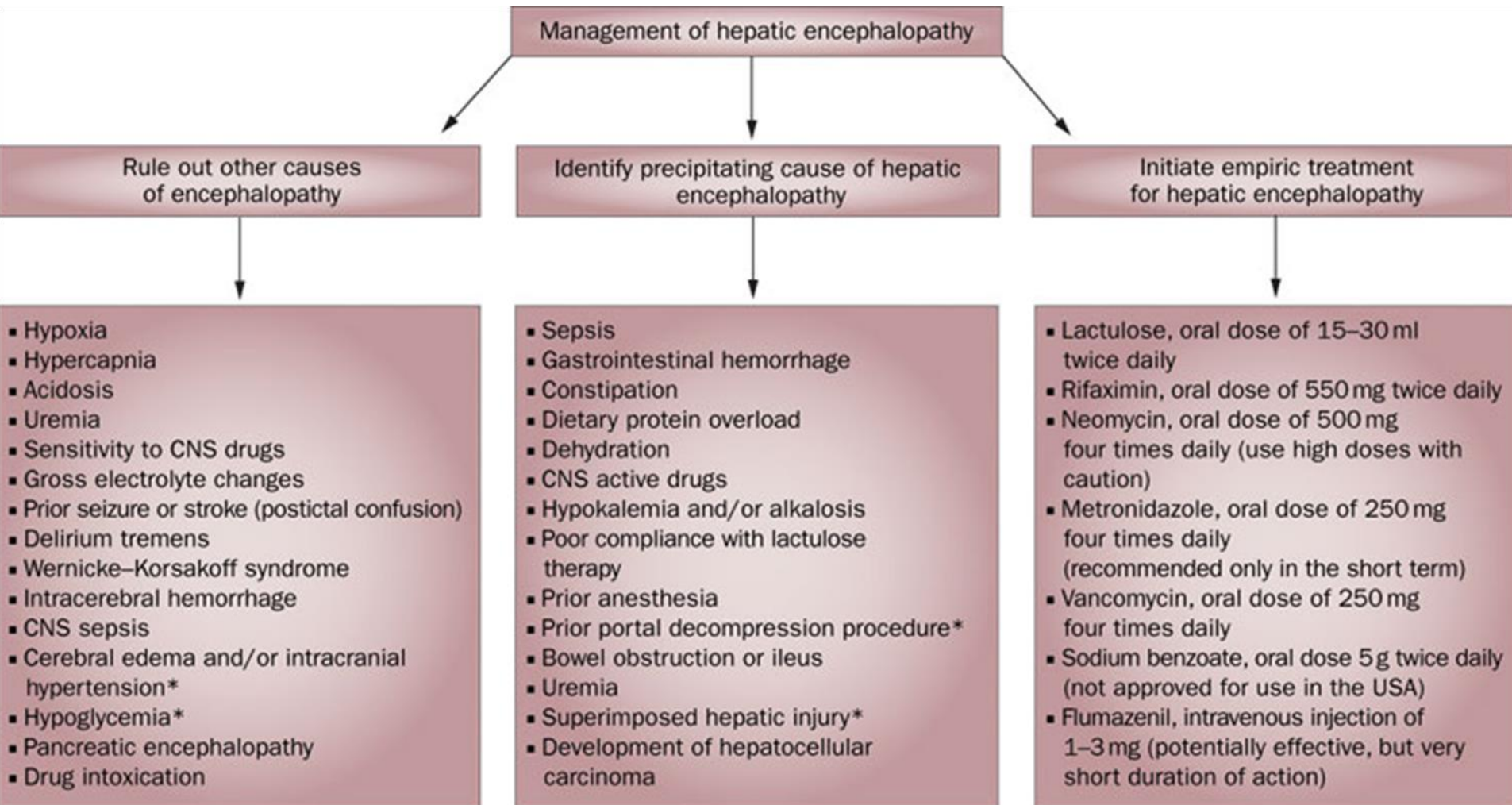


- Encephalopathy
- Spectrum of neuro-psychiatric abnormalities seen in patients with liver dysfunction,
 - after exclusion of other known brain disease
- HE is divided into two primary components:
 - overt HE (OHE) and
 - minimal HE (MHE)
- OHE can be diagnosed clinically through a constellation of signs and symptoms,
- MHE requires specialized testing

Evolution of hepatic encephalopathy



Scenario 3



- GI bleed causes in this scenario:
 - Varices
 - Portal hypertensive gastropathy
 - Oesophagitis
 - Peptic ulcer
- If numerous spider naevi, higher risk for oesophageal varices

- GI bleed
 - Fluid resuscitation
 - Terlipressin 2mg 6hrly until haemostasis
 - Broad spectrum antibiotics for 5 days
 - Bacterial translocation leads to bacteraemia and inflammatory response
 - Increases portal pressure and increases risk of rebleed
 - OGD as soon as resuscitated

- Renal dysfunction in patients with liver disease
 - 40 to 80% cases
 - Acute tubular necrosis (41.7%)
 - Pre-renal failure (38%)
 - Hepatorenal syndrome (20%)
 - Post-renal failure (0.3%)



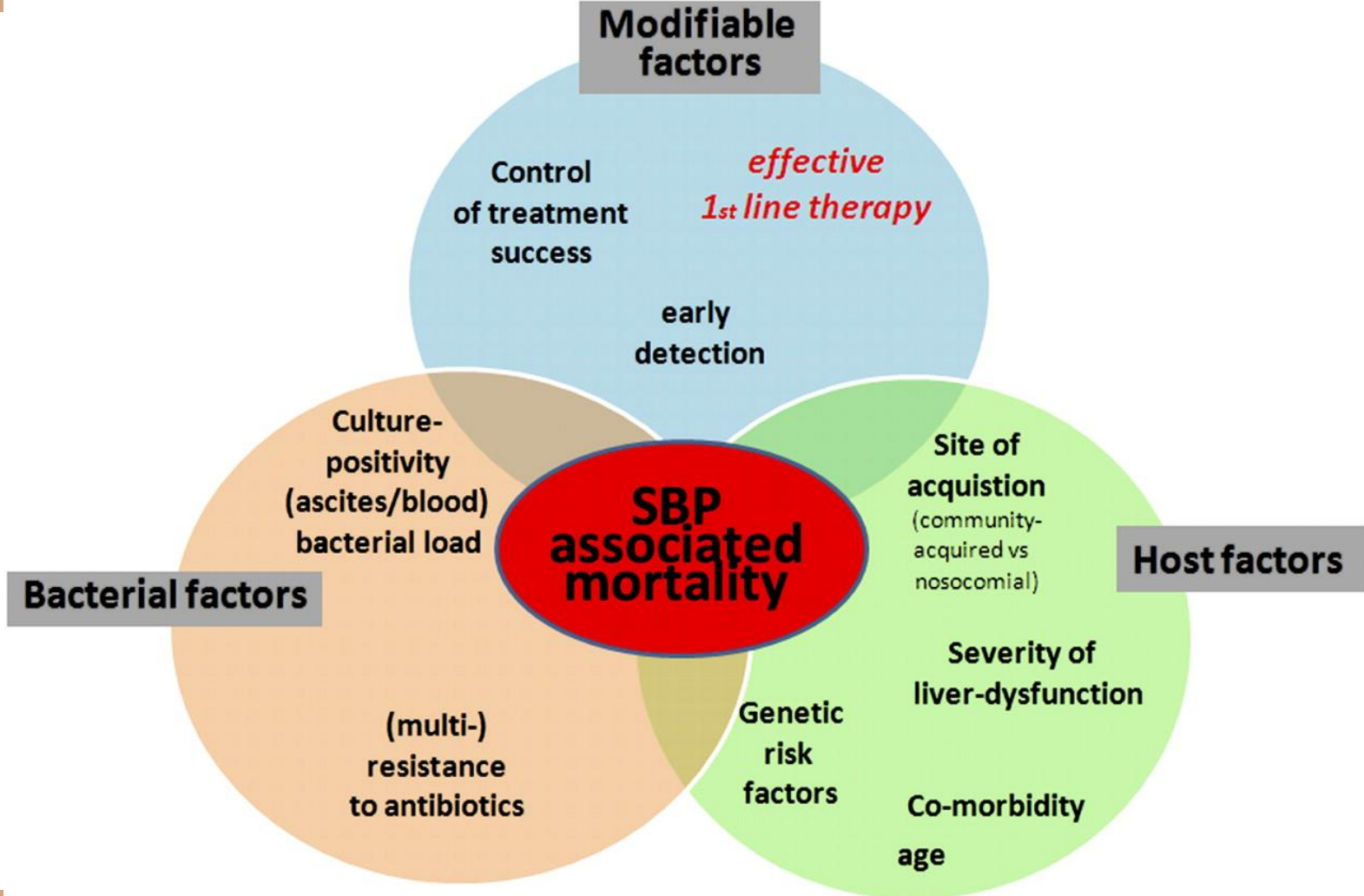
- **Hepatorenal syndrome**

- Cirrhosis with ascites
- Serum creatinine $>133 \mu\text{mol/L}$
- No improvement of serum creatinine to $<133 \mu\text{mol/L}$ after at least 2 days with diuretic withdrawal and volume expansion with albumin (1 g/kg up to a maximum of 100 g/day)
- Absence of shock
- No current treatment with nephrotoxic drugs
- Absence of parenchymal kidney disease as indicated by proteinuria ($>500 \text{ mg/day}$) or microhaematuria (>50 red blood cells per high-power field) and/or a normal renal ultrasonography

- Hepatorenal syndrome treatment
- Albumin and vasoconstriction
 - Albumin priming dose 1G/Kg followed by 20G to 40G/day
 - Terlipressin start at 0.5mg to 1mg every 4 to 6 hours
 - If no reduction of creatinine by 30% in 3 days then double the dose
 - Maximum 12mg/day
 - If respond to therapy continue until creatinine normal or baseline
 - Repeat treatment if relapse on discontinuing

- Spontaneous Bacterial Peritonitis
- Asymptomatic
- local symptoms and/or signs of peritonitis:
 - abdominal pain, abdominal tenderness, vomiting, diarrhoea, ileus;
- signs of systemic inflammation:
 - hyper or hypothermia, chills, altered white blood cell count, tachycardia, and/or tachypnoea;
- Causes:
 - worsening of liver function;
 - hepatic encephalopathy;
 - shock;
 - renal failure;
 - gastrointestinal bleeding

Scenario 3





- Spontaneous Bacterial Peritonitis
- Ascitic WCC >500, PMN >250
- Despite bedside inoculation, most culture negative
- Positive in ~40%
 - Gram Negative Bacteria
 - *E.coli*
 - Usually community acquired
 - Gram Positive Cocci
 - *Streptococci and Enterococci*
 - Usually nosocomial

- Spontaneous Bacterial Peritonitis Management
- Broad spectrum antibiotics
- Albumin 1.5g/Kg day 1 and 1g/Kg day3
 - Reduces mortality from 30% to 10%
 - Compared to antibiotic alone
 - By decreasing risk HRS type1 from 30% to 10%
- Failure to reduce ascitic WCC by 25% after 48hours treatment
 - Antibiotic resistance
 - Secondary bacterial peritonitis



- **Alcohol Hepatitis**
- Can arise weeks after stopping drinking
 - Increasing severity in first few weeks of abstinence
- May persist for months after cessation of alcohol
- If mild may not need hospital treatment



- **Acute Alcohol Hepatitis**
- ~35% alcoholics
- Mild inflammation to severely ill
- Features
 - Fever
 - Hepatomegaly
 - Jaundice
 - Anorexia
 - Coagulopathy
 - Encephalopathy
 - Leucocytosis
 - Renal failure



- Scoring systems in AAH
- Maddrey's Discriminant Function, 1977.
 - $4.6 \times [\text{patient's prothrombin time (seconds)} - \text{control prothrombin time (seconds)}] + \text{bilirubin (mg/dL)}$
 - >32 increased 28day mortality at $>50\%$
- Glasgow Alcohol Hepatitis Score
- MELD
- Lille score

- Glasgow Alcohol Hepatitis Score**

	Score given		
	1	2	3
Age	<50	≥50	–
WCC (10 ⁹ /l)	<15	≥15	–
Urea (mmol/l)	<5	≥5	–
PT ratio	<1.5	1.5–2.0	>2.0
Bilirubin (μmol/l)	<125	125–250	>250

Scenario 3

	Day 28 survival (%)	Day 84 survival (%)
Day 1 score		
GAHS < 9	87	79
GAHS ≥ 9	46	40
Day 6-9 score		
GAHS < 9	93	86
GAHS ≥ 9	47	37



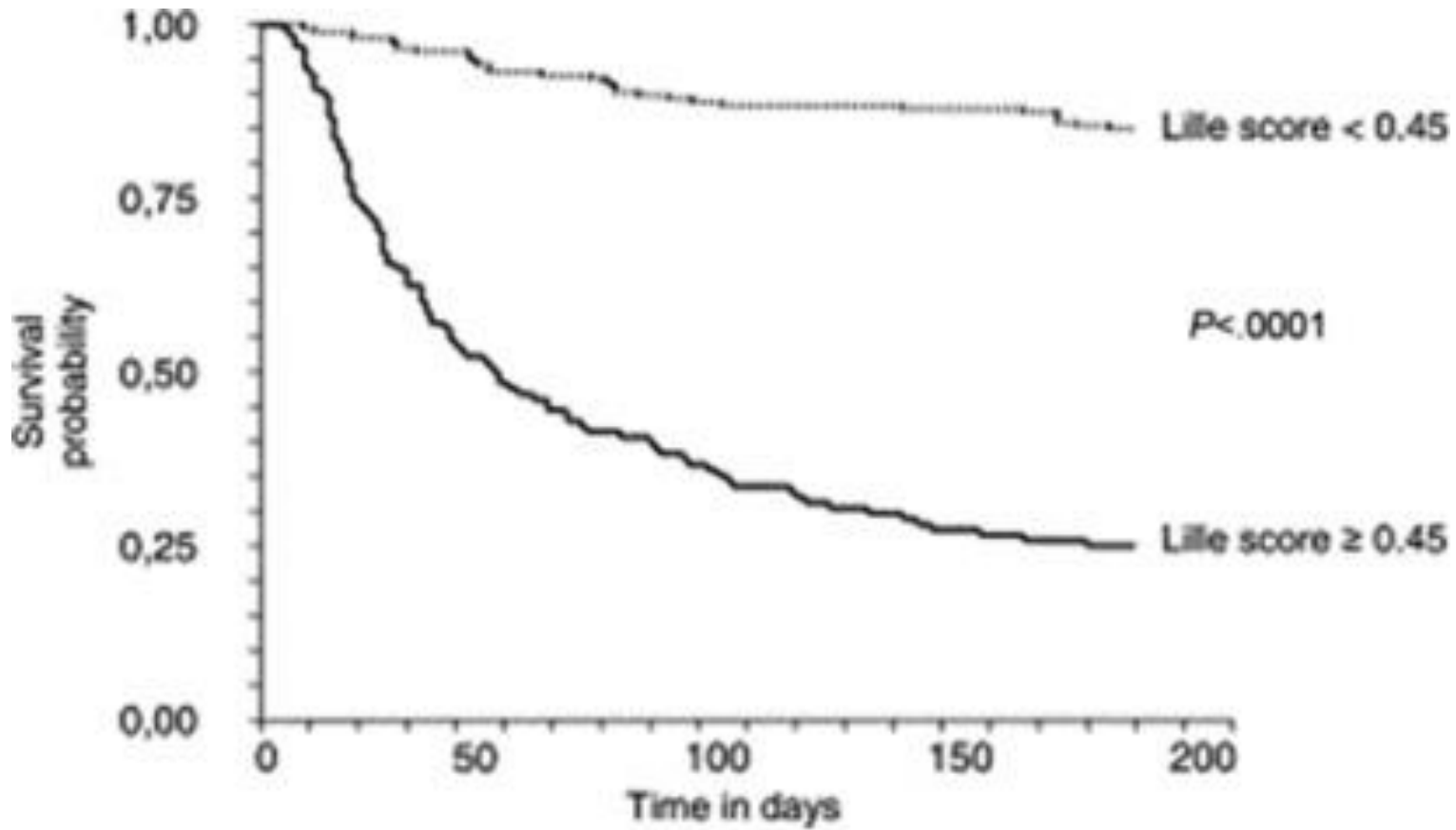
- **Treatment of Acute Alcohol Hepatitis**
 - Nutrition
 - 1-1.5G protein/kg body weight/day
 - 30-40 kcal/kg body weight/day
 - Steroids
 - 40mg Prednisolone
 - Not if active GI haemorrhage, Sepsis, Pancreatitis, renal failure

- **Treatment of Acute Alcohol Hepatitis**
 - Pentoxifylline 400mg tds
 - Non-selective phosphodiesterase inhibitor
 - Reduces inflammatory response
 - N-acetylcysteine
 - **Reduces mortality in combination with steroids to 8% cf 24% steroids**

- Assessment of response to treatment of AAH
- Lille score
 - $(\text{Exp}[-R]/[1 + \text{Exp}(-R)])$, where $R = 3.19 - 0.101 \times \text{age (y)} + 0.147 \times \text{albumin (g/L)} + 0.0165 \times \text{change in bilirubin (total bilirubin at Day 0 } \mu\text{mol/L} - \text{total bilirubin at Day 7 in } \mu\text{mol/L)} - 0.206 \times \text{renal insufficiency (0 or 1)} - 0.0065 \times \text{total bilirubin at Day 0 } (\mu\text{mol/L)} - 0.0096 \times \text{prothrombin time (seconds)}$
Renal insufficiency is rated as 1 if creatinine level at Day 0 is ≥ 1.3 mg/dL, and as 0 if creatinine level is < 1.3 mg/dL



Scenario 3



Scenario 3

	Day 28 survival (%)	Day 84 survival (%)
Day 1 score		
GAHS < 9	87	79
GAHS ≥ 9	46	40
Day 6-9 score		
GAHS < 9	93	86
GAHS ≥ 9	47	37

- If Day 7 score shows poor response to treatment of AAH
 - Assess suitability for referral to Liver Unit
 - Assess withdrawal of treatment and End of Life Care
 - Continue further 7 days and reassess

- Difficult case to manage
- Comprehensive assessment required
 - Pathophysiology complex and fluctuating
 - Acute Alcohol Hepatitis
 - Decompensated chronic liver disease
 - Acute on Chronic Liver Disease



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ANY QUESTIONS?