PGY 1，必修課程
NSP GI Essential course

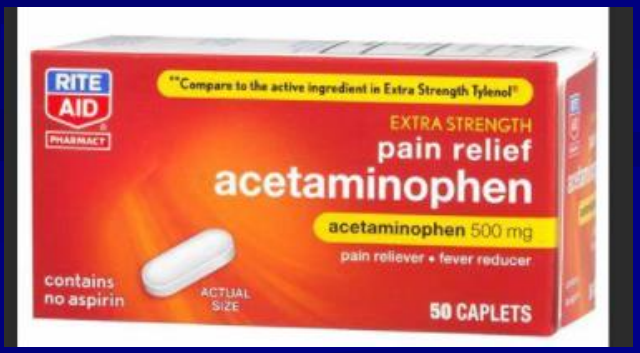
急性肝衰竭. Acute hepatic failure

Medical complications related to Acetaminophen

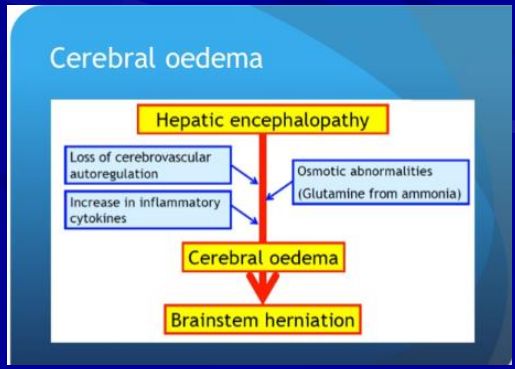
Management (Guidelines)

王正一

2025.09.26 .



ICU APPROACH TO FHF



Covid 19 疫情的影響
Self medication的”教育”太多了

- 有些藥看起來很安全→-其實不然
- 有些藥真的很有效-Panadol--止痛及退燒-
- 很便宜又容易買到
- 最麻煩的是只有少數醫師知道會有很嚴重的問題,大多數醫師也隨便應用。
- 發生問題還不知道是drug toxicity.當成一般肝病
- 因此案例報告不多.
-

Home › Health Tips › 5 shocking Dangers of Self Medication you must know

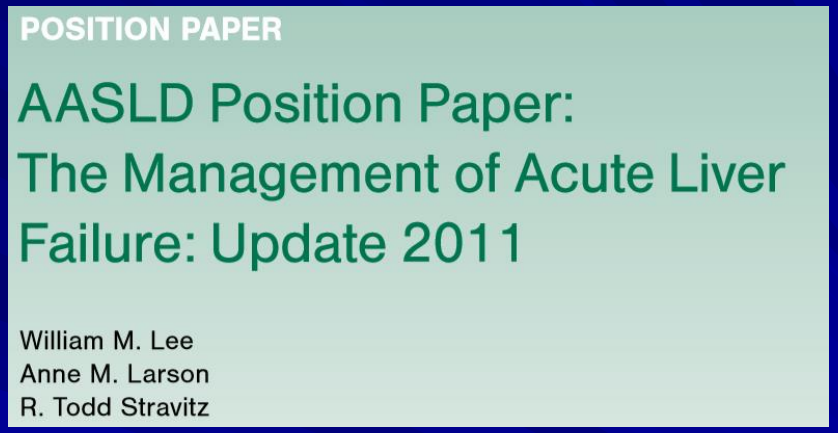
Health Tips

5 shocking Dangers of Self Medication you must know

by Dr. Brahmanand Nayak October 16, 2020 20 138

@@@Management of ALF guidelines

- Introduction to the Revised American Association for the Study of Liver Diseases Position Paper on Acute Liver Failure 2011
- William M. Lee,
- R. Todd Stravitz, and
- Anne M. Larson


POSITION PAPER

AASLD Position Paper:
The Management of Acute Liver Failure: Update 2011

William M. Lee
Anne M. Larson
R. Todd Stravitz

Table 1. Quality of Evidence on Which a Recommendation Is Based[3]

Grade	Definition
I	Randomized controlled trials
II-1	Controlled trials without randomization
II-2	Cohort or case-control analytic studies
II-3	Multiple time series, dramatic uncontrolled experiments
III	Opinions of respected authorities, descriptive epidemiology

@@@ EASL guidelines

EASL Clinical Practical Guidelines on the management of acute (fulminant) liver failure☆

European Association for the Study of the Liver*

J. Hepatology 2017 66:1947-1081

Grade of evidence	
I	Randomized, controlled trials
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Grade of recommendation	
1	Strong recommendation: Factors influencing the strength of the recommendation included the quality of the evidence, presumed patient-important outcomes, and cost
2	Weaker recommendation: Variability in preferences and values, or more uncertainty: more likely a weak recommendation is warranted Recommendation is made with less certainty: higher cost or resource consumption

1. Guyatt GH, et al. BMJ. 2008:336:924–6;
EASL CPG ALF. J Hepatol 2017;66:1047–81

EASL™ The Home of Hepatology

Anaesthesia Critical Care & Pain Medicine
Volume 39, Issue 1, February 2020, Pages 143-161

Guidelines

Management of liver failure in general intensive care unit ☆, ☆☆

C. Paugam-Burtz [1 2], E. Levesque [3 4], A. Louvet [5], D. Thabut [6], R. Amathieu [7 8], C. Bureau [9 10 11], C. Camus [12], G. Chanques [13], S. Faure [14], M. Ferrandière [15], C. Francoz [16 17], A. Galbois [18], T. Gustot [19 20], C. Ichai [21], P. Ichai [22 23 24], S. Jaber [25], T. Lescot [26], R. Moreau [27 28 29 30], S. Roullet [31 32], F. Saliba [33]... E. Weiss [37 38]

BMJ Best Practice

@@@ Acute liver failure

Acute liver failure (ALF) is a rare syndrome defined by a **rapid decline in hepatic function** characterised by jaundice, coagulopathy (INR >1.5), and hepatic encephalopathy in patients with no evidence of prior liver disease. The interval from the onset of jaundice to the development of encephalopathy occurs within 24 to 26 weeks and may further classify ALF into categories based on **hyperacute, acute, or subacute** presentations. Although clinical jaundice is considered a defining feature of ALF, it may not always be present, particularly in hyperacute presentations. The term **acute liver failure** is preferred over fulminant hepatic failure or acute hepatic necrosis, although these terms have been used historically to classify hepatic failure.

Guidelines 1

- 1.所有 acute liver failure 的病人都應入院且
- 經常密切監視狀況。最好是住入 **ICU.**
- 1. Patients with ALF should be hospitalized and
- monitored frequently, preferably in an ICU (III).

ICU
Coma Unit
Liver ICU

ICU Management & Practice, ICU Volume 15 - Issue 1 – 2015.

Are survival rates for acute liver failure (ALF) still improving? What can that be attributed to?
Yes, the outcome for ALF continues to improve, and this is seen both in those managed medically and in those who require transplantation. The reasons for this are multiple and depend largely on small incremental improvements, critical care management for the medically treated and surgical and anaesthesia management in addition to critical care for those proceeding to transplantation.
Acute liver failure has a relatively high mortality rate. Professor Julia Wendon is a liver intensive care specialist and Clinical Director of the Critical Care Division at King’ s College Hospital in London, UK.

Anaesthesia Critical Care & Pain Medicine
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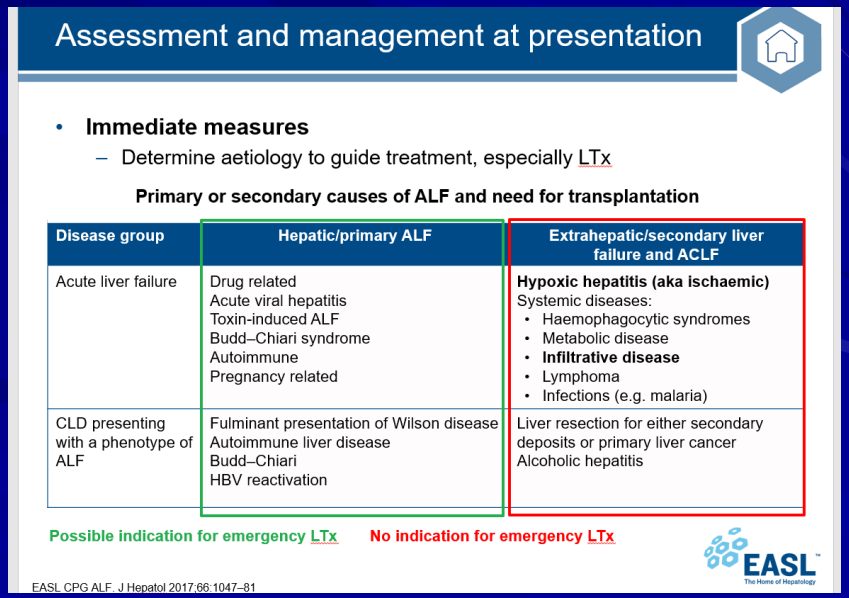
2. Contact with a **transplant center**
3. 找出precise etiology of ALF

- 2. Contact with a **transplant center** and plans to transfer appropriate patients with ALF should be initiated early in the evaluation process (III).
- 3. The precise etiology of ALF should be sought to guide further management decisions (III).



Assessment and management at presentation

- **Immediate measures**
  - Determine aetiology to guide treatment, especially LTx

Primary or secondary causes of ALF and need for transplantation

Disease group	Hepatic/primary ALF	Extrahepatic/secondary liver failure and ACLF
Acute liver failure	Drug related Acute viral hepatitis Toxin-induced ALF Budd–Chiari syndrome Autoimmune Pregnancy related	**Hypoxic hepatitis (aka ischaemic)** Systemic diseases: • Haemophagocytic syndromes • Metabolic disease • **Infiltrative disease** • Lymphoma • Infections (e.g. malaria)
CLD presenting with a phenotype of ALF	Fulminant presentation of Wilson disease Autoimmune liver disease Budd–Chiari HBV reactivation	Liver resection for either secondary deposits or primary liver cancer Alcoholic hepatitis

Possible indication for emergency LTx **No indication for emergency LTx**

EASL CPG ALF. J Hepatol 2017;66:1047–81

EASL The Home of Hepatology

2.Contact with a liver transplantation center

- 聯繫肝移植中心,作必要之準備

15. NYU Langone Hospitals (tie)

NYU Langone Health Manhattan Campus. Courtesy of NYU Langone Health

NYU Langone Transplant Institute

Single-Bedded Rooms

We are the only area hospital with single-occupancy rooms for all of our patients who receive transplants.

Shorter Recovery Times

Our heart, liver, and lung transplant recipients go home sooner after surgery than patients at any other New York state hospital.

3. 找出precise etiology of ALF

Differential diagnosis based on clinical features

Aetiology	Clinical features
Paracetamol	Very high levels of aminotransferases and low level of bilirubin. Rapidly progressive disease, acidosis and renal impairment. Low phosphate may be seen as a good prognostic marker but replacement is required
Non-paracetamol	Subacute clinical course can mimic cirrhosis, clinically and radiographically
Acute Budd–Chiari syndrome	Abdominal pain, ascites and hepatomegaly; loss of hepatic venous signal and reverse flow in portal vein on ultrasound
Wilson disease	Young patient with Coombs (DAT)-negative haemolytic anaemia with a high bilirubin to ALP ratio; Kayser–Fleischer ring; low serum uric acid level; markedly increased urinary copper
Mushroom poisoning	Severe gastrointestinal symptoms after ingestion; development of early AKI
Autoimmune	Usually subacute presentation – may have positive autoantibodies, elevated globulin and characteristic lymphocyte pattern when compared to viral and seronegative aetiologies
Malignant infiltration	History of cancer, massive hepatomegaly; elevated ALP or other tumour markers
Acute ischaemic injury	Marked elevation of aminotransferases, increased lactic dehydrogenase and creatinine, which normalize soon after stabilization of haemodynamic instability. Patients with severe congestive heart disease or respiratory disease

Possible indication for emergency LTx **No indication for emergency LTx**

Malignant infiltration of the liver *and* ***acute ischaemic injury*** *are not indications for LTx (EASL)*

4. 如果是acetaminophen overdose

- 4. For patients with known or suspected **acetaminophen overdose** within 4 hours of presentation**, give activated charcoal just prior to starting NAC dosing (I).**

- **Drug-induced liver injury** is the most frequent cause of severe ALI and ALF
  - Especially paracetamol overdose

Recommendations	Grade of evidence	Grade of recommendation
At admission, a **toxicology screen and determination of paracetamol level are necessary in every patient,** although levels will frequently be negative. If the patient already has coagulopathy and increased serum aminotransferases, **N-acetyl cysteine therapy should be given**	II-2	1
Prognosis is worse in patients with staggered ingestion of paracetamol. These cases are more likely to develop multiple organ failure when compared to those with a single ingestion point	II-3	1
ALF caused by non-paracetamol drug-induced hepatotoxicity is a diagnosis of exclusion	III	2

EASL

5.盡快使用NAC, IV

- 5. . Begin NAC promptly in all patients where the quantity of acetaminophen ingested, serum drug level or rising aminotransferases indicate impending or evolving liver injury (II-1).
- NAC: **N-ACETYL CYSTEINE**
  - **OTHER NAME(S):** Acetyl Cysteine, Acétyl Cystéine, Acetylcysteine,
  - Acétylcystéine, Chlorhydrate de Cystéine, Cysteine, Cystéine, Cysteine Hydrochloride..
  - N-acetyl cysteine is used to counteract acetaminophen (Tylenol) and carbon monoxide poisoning

6.只要有懷疑acetaminophen引起,即可使用NAC

- 6. NAC may be used in cases of acute liver failure in which acetaminophen ingestion is possible or when knowledge of circumstances surrounding admission is inadequate but aminotransferases suggest acetaminophen poisoning (III).

7.mushroom poisoning即使用Penicillin and NAC,並準備移植

- 7. In ALF patients with known or suspected mushroom poisoning, consider administration of penicillin G and N-acetylcysteine (III)
- 8. Patients with acute liver failure secondary to mushroom poisoning should be listed for **transplantation,** as this procedure is often the only lifesaving option (III).

8.儘快完成檢驗 Initial lab. Analysis in ALF

Table 2. Initial Laboratory Analysis

Prothrombin time/INR
Chemistries
sodium, potassium, chloride, bicarbonate, calcium, magnesium, phosphate glucose
AST, ALT, alkaline phosphatase, GGT, total bilirubin, albumin creatinine, blood urea nitrogen
Arterial blood gas
Arterial lactate
Complete blood count
Blood type and screen
Acetaminophen level
Toxicology screen
Viral hepatitis serologies
anti-HAV IgM, HBsAg, anti-HBc IgM, anti-HEV§, anti-HCV, HCV RNA*, HSV1 IgM, VZV
Ceruloplasmin level#
Pregnancy test (females)
Ammonia (arterial if possible)
Autoimmune Markers
ANA, ASMA, Immunoglobulin levels
HIV-1, HIV-2‡
Amylase and lipase

CBC
LFT:
Prothrombin time
Acetaminophen level
Viral markers
- *Anti –HAV IgM*
- *Anti HBV, Ig M*
- *Anti HCV and HCV RNA*
- *HSV1 IgM*
- *VZV*

Ceruloplasmin level
Pregnancy test
Blood Ammonia

9.必知曉之前醫師之處方以及病人自行服用之藥品(名稱,含中草藥)

- 9. Obtain details (including onset of ingestion, amount and timing of last dose) concerning all prescription and **non-prescription drugs**, herbs and dietary supplements taken over the past year (III).--**Medication history**
- 10. Determine ingredients of non-prescription medications whenever possible (III).
- 11. In the setting of acute liver failure due to possible drug hepatotoxicity, discontinue all but essential medications (III)
- 12. N-acetylcysteine may be beneficial for acute liver failure due to drug-induced liver injury (I).

10.如確知有肝炎(A,B,C,E),即給予有效之治療

- 13. Viral hepatitis A- (and E-) related acute liver failure must be treated with supportive care as no virus-specific treatment has proven to be effective (III).

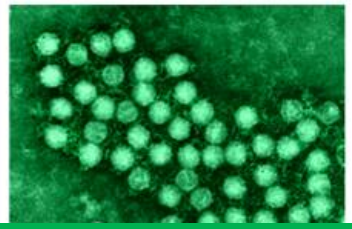
Hepatitis A

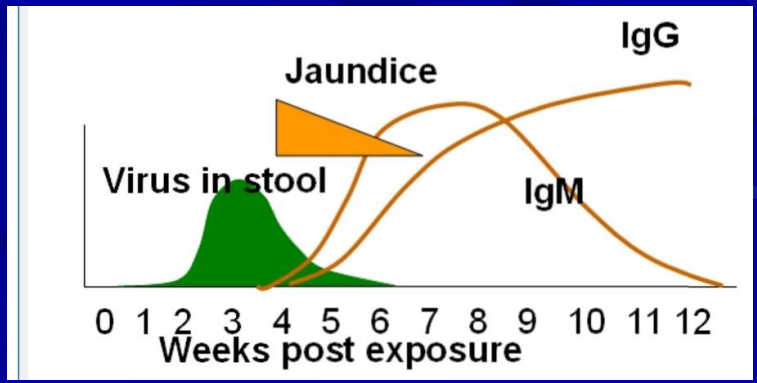
IgM anti HAV

Hepatitis A

Virology

Order: *Picornavirales*
Family: *Picornaviridae*
Genus: *Hepatovirus*
Species: *Hepatitis A virus*
Structure: small; 27 nm in diameter, non-enveloped spherical particle
Genome: +ssRNA (positive sense, single stranded RNA)





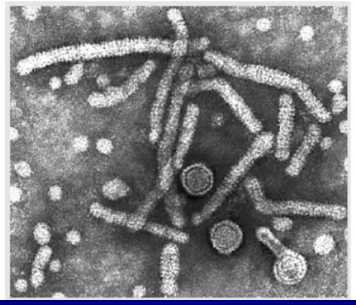
11.如確定B肝病毒,立即使用抗B肝病毒之藥物(Nucleostide)

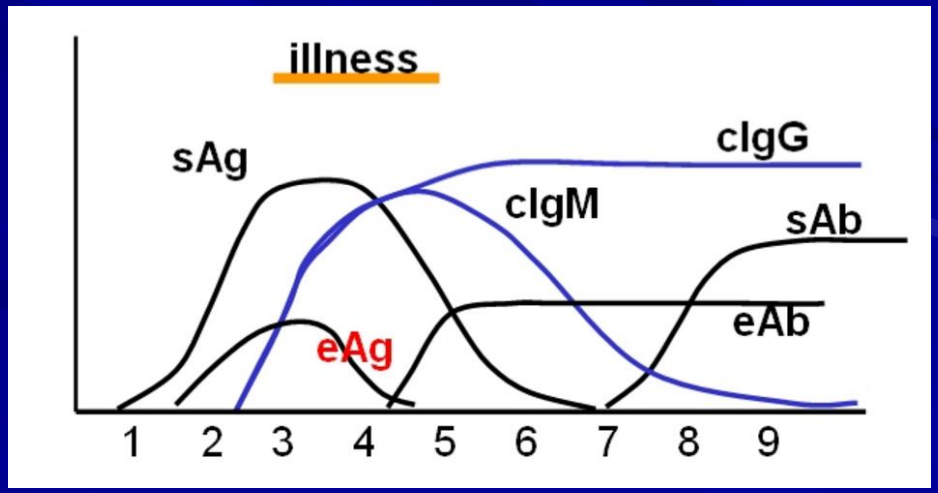
- 14. Nucleos(t)ide analogues should be considered for hepatitis B-associated acute liver failure and for prevention of post-transplant recurrence.(III)

Hepatitis B

Virology

Order: none
Family: *Hepadnaviridae*
Genus: *Orthohepadnavirus*
Species: *Hepatitis B virus*
Subtypes: A-H
Structure: 42 nm in diameter, enveloped spherical particle [also called the Dane particle]
Genome: circular DNA, incompletely double stranded; 3.2 kilobases in size
Excess surface antigen is produced, forming spheres and cylinders 22nm in diameter





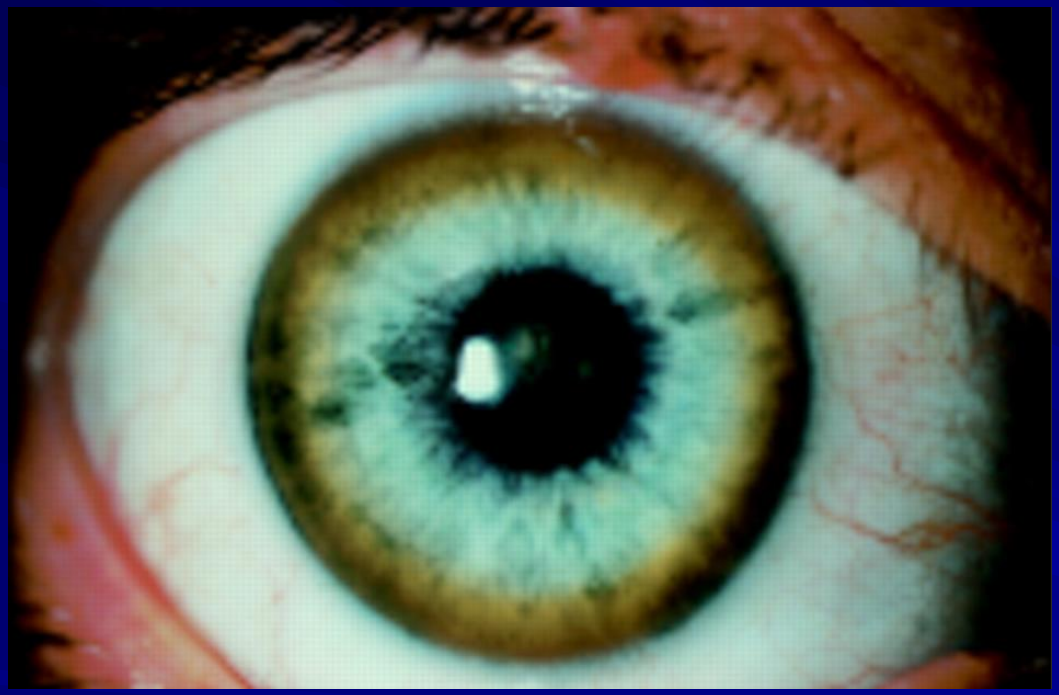
12. 作必要之檢驗(ceruloplasmin and Cu)以排除Wilson disease

- 16. To exclude Wilson disease one should obtain ceruloplasmin, serum and urinary copper levels, slit lamp examination for Kayser-Fleischer rings, hepatic copper levels when liver biopsy is feasible, and total bilirubin/alkaline phosphatase ratio (III).

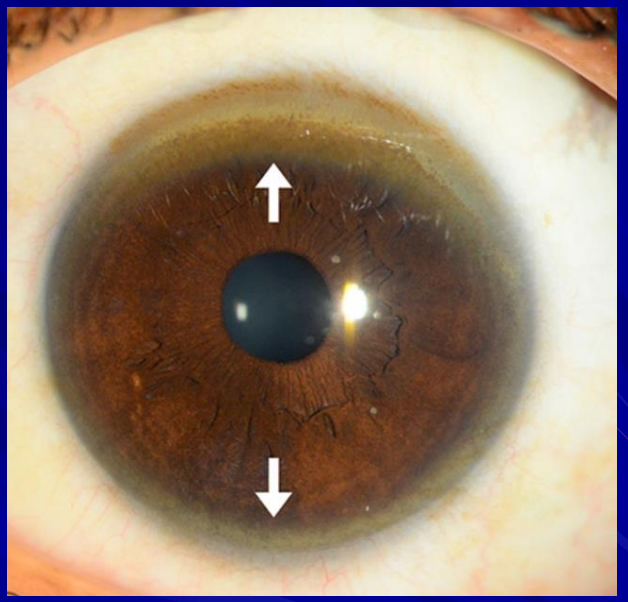
檢驗項目(中文/英文)	Ceruloplasmin /藍胞漿素；轉銅素測定
適用檢體別	血清
採檢容器	黃頭管 3ml（SST）
檢體採集量	6 mL。
檢體保存方式	2-8℃保存8天，-20℃保存一年，避免多次解凍。
採檢注意事項	不須空腹。
可送檢時間	24 小時
報告完成時間	10 天
操作組別/分機	臨床血清組 (委外代檢項目) / 4305 委外代檢單位：台北聯合醫事檢驗所
檢驗操作方法/儀器	Magnetic Particle Immunoassay
參考值(單位)	17-31 ng/mL
參考資料：	聯合醫事檢驗所 聯合檢驗目錄2014

9.檢驗方法	免疫散射法(Immunonephelometry assay)
10.生物參考區間	16.0-28.8 mg/dL (95 percentile central interval)
11.適應症	定量血清中ceruloplasmin濃度，協助Wilson's Disease, Menke's syndrome及肝臟疾病之診斷。
12.臨床意義	藍胞漿素合成於肝臟為血液中之主要運銅蛋白，其次具有氧化?的活性；患有原發性膽道硬化、原發性膽道閉鎖及其他嚴重肝炎時，血液中之濃度會降低，其降低的原因來自於肝臟的總代謝量有所限制，而不是藍胞漿素的合成量不足。在某些先天異常如威爾森氏症(Wilson, s Disease)；Menke's syndrome(遺傳性銅代謝疾病)其濃度亦會降低。當藍胞漿素增加表示它是在急性反應期，通常所有發炎的疾病都會測得濃度上升；此外，在網狀內皮細胞瘤、膽道阻塞、雌激素治療、懷孕等情況中，藍胞漿素也會增加。

Kayser-Fleischer rings, 50. Looking for K-F ring



Dense Kayser-Fleischer ring in asymptomatic Wilson's disease (hepatolenticular degeneration)
Charlotte Anne Sullivan1, A Chopdar2, G A Shun-Shin3**BJ of Ophthalmology**



Anterior segment optical coherence tomography to look for Kayser-Fleischer
rings
Mittanamalli S Sridhar1, Roberto Pineda2
BMJ

13. 如是Wilson disease請即考慮肝移植Transplantation for Wilson disease

- 17. Patients in whom Wilson disease is the likely cause of acute liver failure must be promptly considered for liver **transplantation** (III).

14, 如果是autoimmune hepatitis, 請作肝切片並給予corticosteroid

- 18. Liver biopsy is recommended when **autoimmune hepatitis** is suspected as the cause of acute liver failure, and autoantibodies are negative (III).
- 19. Patients with coagulopathy and mild hepatic encephalopathy due to **autoimmune hepatitis** may be considered for corticosteroid treatment (prednisone, 40-60 mg/day) (III).

15. 如果是孕期發生急性脂肪肝即HELLP syndrome應儘快生產,如果恢復慢,應施行肝移植

- 21. For acute fatty liver of pregnancy or the **HELLP syndrome**, expeditious(迅速) delivery of the infant is recommended. Transplantation may need to be considered if hepatic failure does not resolve quickly following delivery (III).

16, 如因心衰竭發生之ischemic liver injury應儘速控制心衰竭

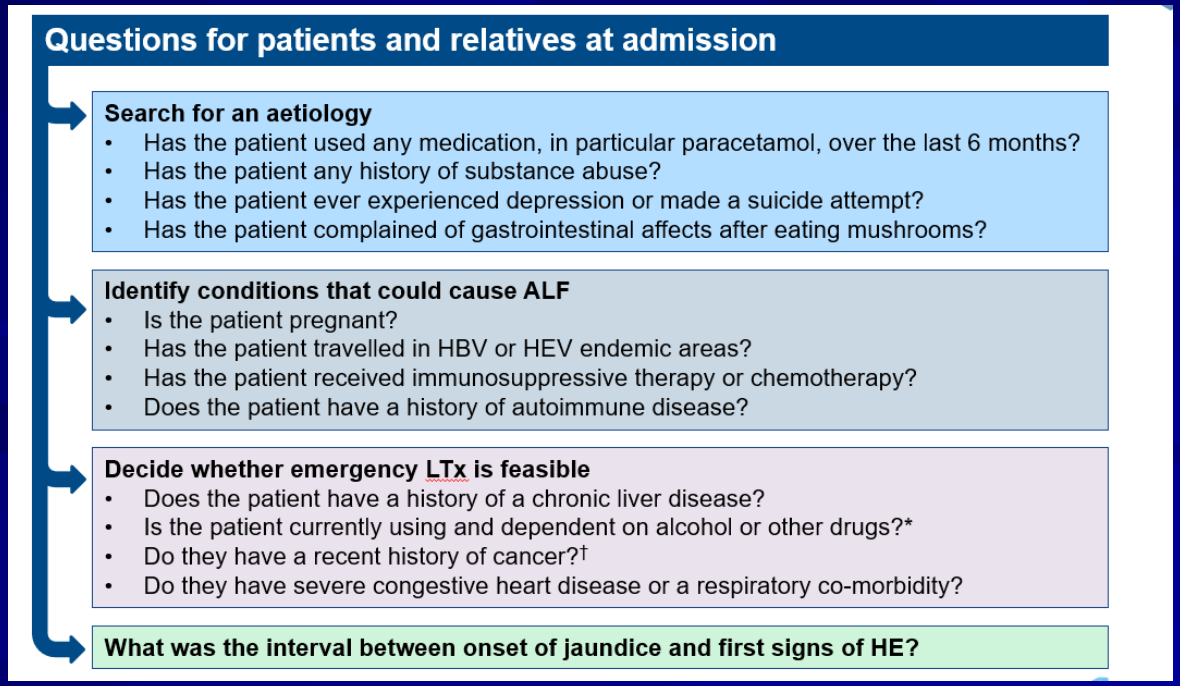
- 22. In ALF patients with evidence of **ischemic injury**, cardiovascular support is the treatment of choice (III).

17.如果有肝靜脈栓塞應作肝移植,但先思考其原因,是否有惡性腫瘤.

- 23. **Hepatic vein thrombosis** with acute hepatic failure is an indication for liver transplantation, provided underlying malignancy is excluded (II-3).

18.如果原因不明,除仔細問病史找出原因外,可考慮肝切片

- **Recommendation 25**. If the etiological diagnosis remains elusive (捉摸不定)after extensive initial evaluation, **liver biopsy** may be appropriate to attempt to identify a specific etiology that might influence treatment strategy (II)



好好問病史,找出原因,何時開始肝昏迷

19,肝昏迷之初期即應使用lactulose oral or enema並檢查 Blood ammonia

- 26. In early stages of encephalopathy, **lactulose** may be used either orally or rectally to effect a bowel purge, but should not be administered to the point of diarrhea, and may interfere with the surgical field by increasing bowel distention during liver transplantation (III).

20,肝昏迷嚴重(grade 3-4)應考慮插管

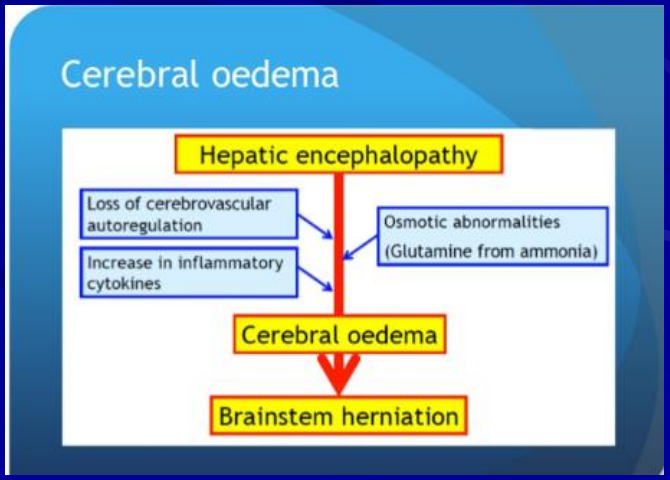
- 27. Patients who progress to high-grade hepatic encephalopathy (grade III or IV) should undergo **endotracheal intubation** (III).

21, 如昏迷嚴重,應量測腦壓且持續監視,即作ICP monitoring, 如不作ICP monitoring, 每小時作一次神經學之評估亦可.

- 29. **Intracranial pressure monitoring** is recommended in ALF patients with high grade hepatic encephalopathy, in centers with expertise in ICP monitoring, in patients awaiting and undergoing liver transplantation (III).
- 30. In the absence of ICP monitoring, **frequent (hourly) neurological evaluation** is recommended to identify early evidence of intracranial hypertension (III).

22來作ICP monitoring者要常檢查注意腦壓太高,會導致uncal herniation

- ***32.In the absence of ICP monitoring, frequent evaluation for signs of intracranial hypertension are needed to identify early evidence of uncal herniation (III).***



23,如果腦壓升高,應使用mannitol.

- 31. In the event of intracranial hypertension, a **mannitol bolus** (0.5-1.0 gm/kg body weight) is recommended as first-line therapy; however, the prophylactic administration of mannitol is not recommended (II-2).
- 33. ***In the event of intracranial hypertension, mannitol should be given and hyperventilation may be considered in order to temporarily reduce the ICP, but prophylactic use of these interventions is not helpful and therefore not recommended (I).***

24.如血小板減少,prothrombin time延長應考慮補充,特別是有出血之顧慮,如要施行invasive procedures 前一定要補足

- 37.***Replacement therapy for thrombocytopenia and/or prolonged prothrombin time is recommended only in the setting of hemorrhage or prior to invasive procedures (III).***

25, 為減少因stress引發胃酸相關性之胃腸道出血(acid-related gi bleeding),應使用PPI預防

- 38. ***Patients with ALF in the ICU should receive prophylaxis with H2 blocking agents or PPIs (or sucralfate as a second-line agent) for acid-related gastrointestinal bleeding associated with stress (I, III).***

26.靜脈輸液以維持足夠之血管內之容積(intravascular volume)

- 39.***Careful attention must be paid to fluid resuscitation and maintenance of adequate intravascular volume in patients with acute liver failure (III).***

27.如需洗腎,要採持續 (Continuous mode)使用,而非間斷(intermittent mode)使用。

- 40. ***If dialysis support is needed for acute renal failure, it is recommended that a continuous mode rather than an intermittent mode be used (I).***

28.如血壓或循環不穩,應考慮肺動脈插管(pulmonary artery catheterization)作輸液之補充

- ***41. Pulmonary artery catheterization should be considered in a hemodynamically unstable patient to ensure that appropriate volume replacement has occurred (III).***

29.如血壓偏低,輸液之後仍在60 mm Hg以下、應使用vasopressor agents.如levophed, dopamines,而不使用vasopressin.

- 42.*Systemic vasopressor support* ***with agents such as epinephrine, norepinephrine, or dopamine but not vasopressin should be used if fluid replacement fails to maintain MAP of 50-60 mm Hg (III, II-1).***

30. 代謝物之平衡(Metabolic homeostasis)包括血糖及電解質(P,K,Mg),要定期檢測.隨時校正.

- 43. ***Metabolic homeostasis must be carefully maintained in patients with acute liver failure. Overall nutritional status as well as glucose, phosphate, potassium and magnesium levels should be monitored frequently, with expeditious correction of derangements (I***

31.如預後指數偏高(prognostic indicators),有生命之危險者,應及早作肝之移植

- ***44. Urgent hepatic transplantation is indicated in acute liver failure where prognostic indicators suggest a high likelihood of death (II-3).***

32.目前已在使用之人工肝臟系統,效果可疑,除參予臨床試驗,不建議應用。將來是否作為急性肝衰竭之治療選項有待証明

- 45.***Currently available liver support systems are not recommended outside of clinical trials; their future in the management of acute liver failure remains unclear (I, II-1).***

Multicenter Study > J Hepatol. 2025 Apr;82(4):615-621. doi: 10.1016/j.jhep.2024.09.034. Epub 2024 Oct 1.

Plasma exchange does not improve overall survival in patients with acute liver failure in a real-world cohort

Laura Burke [1], William Bernal [2], Tasneem Pirani [2], Banwari Agarwal [3], Rajiv Jalan [4], Jennifer Ryan [5], Mansoor Nawaz Bangash [6], Phillip El-Dalil [7], Nick Murphy [7], Mhairi Donnelly [8], Janice Davidson [8], Ken Simpson [8], Hannah Giles [9], Phyo Set Mone [10], Steven Masson [11], Andrew Davenport [12], Ian Rowe [1], Joanna Moore [13]

Affiliations – collapse

Affiliations

1 Leeds Liver Unit, Leeds NHS Teaching Hospitals Trust, Leeds, UK; Leeds Institute for Medical Research, University of Leeds, Leeds, UK.

PEX 在現實世界中治療 ALF 的應用及其療效。

包括 2013 年 6 月至 2021 年 12 月期間入住英國所有七家三級肝臟移植中心的連續 ALF 患者。評估了 PEX 治療後臨床變量的變化，同時將接受 PEX 治療的患者的總生存率和出院前的無移植生存率與接受標準藥物治療的患者進行了比較

我們納入了378位急性肝衰竭（ALF）患者（中位數[IQR]年齡36歲（28-48歲），64% [n = 242]為女性），其中120例接受了PEX治療。

1.PEX治療後，大多數臨床指標均顯著改善，包括去甲腎上腺素的中位數劑量（從0.35 μg/kg/min [0.19-0.70 μg/kg/min]降至0.16 μg/kg/min [0.08-0.49]，p = 0.001）。

2.PEX治療組與標準藥物治療組在總存活率（分別為51.4% vs. 62.6%，p = 0.12）及非移植存活率（42.6% vs. 53.1%，p = 0.24）均無顯著差異。

33.目前使用之預後積分系統(prognostic scoring systems)無法確實預測後果或作為肝移植之確定依據,臨床醫師仍要密切觀察病人之變化,決定採取肝移植之選項

- 46.***Currently available prognostic scoring systems do not adequately predict outcome and determine candidacy for liver transplantation. Reliance entirely upon these guidelines is thus not recommended. (II-2, II-3, III).***
- ***Most important thing is to closely observe patient condition.***密切觀察

34.如果腦壓高,無法控制時,可使用短效型barbiturates

- ***47.Short-acting barbiturates may be considered for refractory intracranial hypertension (III).***

35,肝昏迷病人腦壓過高,絕對不可使用corticosteroids

- ***48. Corticosteroids should not be used to control elevated ICP in patients with acute liver failure (I).***

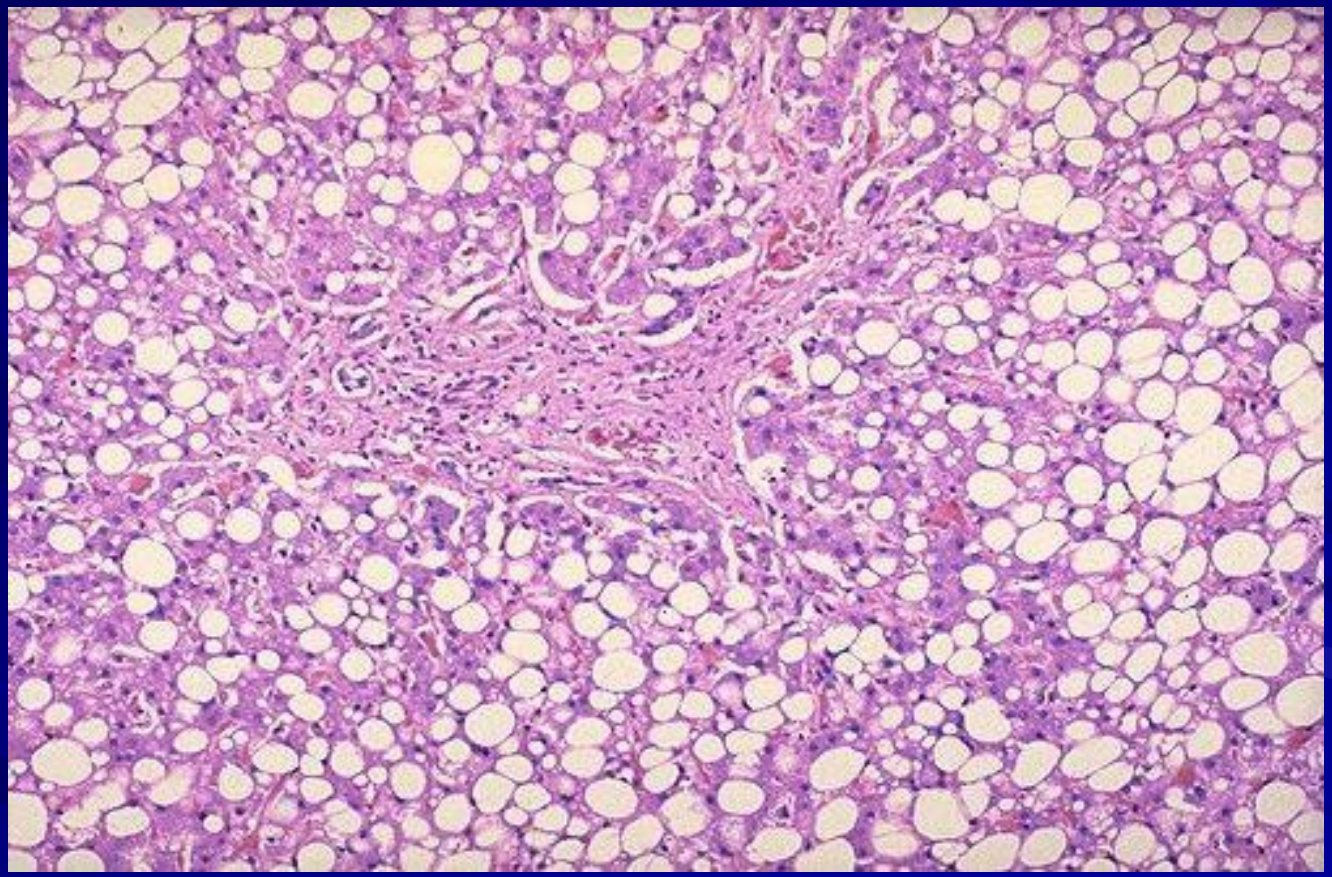
36, 肝衰竭病人,容易出現腦水腫者(包括血液**ammonia**高〉**150,**深度肝昏迷,急性腎衰竭及使用**vasopressors)**可用高張性鹽水**(hypertonic saline),**維持鈉值到**145-155 .**

- 49. In ALF patients at highest risk for **cerebral edema** (serum ammonia > 150 IM, grade 3/4 hepatic encephalopathy, acute renal failure, requiring vasopressors to maintain MAP), the prophylactic induction of hypernatremia with hypertonic saline to a sodium level of 145-155 mEq/L is recommended (I).

Monitoring of ICP

- **ICP : 20 mm Hg 以下**
- **Cerebral perfusion pressure : 50 mm Hg or more**
- **Cerebral perfusion pressure**
- **= Arterial pressure –ICP**
- 1.Bed elevation 有助於減輕 ICP.
- 2. Mannitol 0.5-1.0 gm/Kg BW IV and iv
- drip (Plasma Osm. 310-325)
- 3. 不可使用 dexamethasone.
- 4. induction of hypothermia.
- 5. prophylactic phenytoin 15 mg/kg slowly iv drip for
- seizures.
- 6. Indomethacin 25 mg iv for one min.

37.肝切片結果要及早判斷是否
Acute Fatty Liver of Pregnancy



38.檢測ABCE肝炎標幟. Check serology markers for Hepatitis A,B,C and E

Interpretation of HBV Serology

HBsAg anti-HBc anti-HBs	Negative Negative Negative		Susceptible
HBsAg anti-HBc anti-HBs	Negative Positive Positive		Immune due to natural infection
HBsAg anti-HBc anti-HBs	Negative Negative Positive		Immune due to HBV vaccination
HBsAg anti-HBc IgM anti-HBc anti-HBs	Positive Positive Positive Negative	@@	Acutely infected
HBsAg anti-HBc IgM anti-HBc anti-HBs	Positive Positive Negative Negative		Chronically infected
HBsAg anti-HBc anti-HBs	Negative Positive Negative		Interpretation unclear; 4 possibilities: 1. Resolved infection (most common) 2. False-positive anti-HBc, thus susceptible 3. "Low level" chronic infection 4. Resolving acute infection

From CDC.

39.肝衰竭之預防策略要多加注意:Preventive key points-1 (要點)

Preventive key points

(1)A型肝炎之預防

→去 hepatitis A 流行地區用vaccination

(2)B型肝炎感染者.

→不使用steroid

→及早使用 抗B肝之藥物(Lamivudine ,entecavir)

(3)**藥物**

- 不隨便用藥，不overdose, (包括常用之acetaminophen)
- 不用過期藥物

39.肝衰竭之預防策略要多加注意:Preventive key points-2 (要點)

Preventive key points-2

(4)有消化道出血,即灌腸，減少血液之再吸收，以免NH3↑

(5)維持大便暢通。(Lactulose 之應用)

(6)不可抽大量之腹水(ascites),至多以2000 ml為限,之後小心water-electrolyte之平衡、

(7)利尿劑diuretics 之病人也要小心(water electrolyte 之平衡) 特別是血鉀

(8)不可使用類固醇超過一個月(應及早停用)

@@40. 肝病病人最好不用 Acetaminophen

- **Can Paracetamol (Acetaminophen) be administered to Patients with Liver Impairment?** Hayward Klet al (Pharmacy Department, Princess Alexandra Hospital)
- Fulminant hepatic failure has been a well-documented consequence of paracetamol overdose since its introduction, while short- and long-term use have both been associated with elevation of liver transaminases, a surrogate marker for acute liver injury. From these reports it has been assumed that **paracetamol use should be restricted or the dosage reduced in patients with chronic liver disease**
- inadvertent under-dosing may result in concentrations too low to enable efficacy

acetaminophen overdose

- Acetaminophen overdose is the most common cause of acute liver failure in the U.S. and other Western countries.
- During the 10-year interval, 1543 patients were hospitalized for acetaminophen overdose; 34% were alcohol abusers, 3% had liver disease, and 13% overdosed unintentionally. **Seventy patients (4.5%) developed hepatotoxicity. 15** 人死亡 **(1%)**

- **Unintentional overdoses 5.18; 3.00-8.95),**
- **alcohol abuse OR, 2.21**;, (1.30-3.76),
- **underlying liver disease OR, 3.50**;(1.57-7.77),
- **N-acetylcysteine treatment OR, 6.75;(2.78-16.39)**

- **During a median follow-up of 5.2 years (range, 1 day-11.0 years), 79 patients (5.1%) died.** 死因是可以避免的原因(如自殺,濫用藥物等)

41,肝移植是解救肝衰竭病人的的最終手段

- **(1963 the first in the world,1984 in Taiwan)**
- **The first liver transplant operation was performed in March, 1963 in Denver, Colorado by Dr Tom Starzl. Throughout the 1960's and 1970's, liver transplantation was performed in only a handful of centres worldwide and the results were very disappointing.**
- **1984年**—陳肇隆完成亞洲首例成功的肝臟移植手術,1994年6月—在高雄長庚醫院完成台灣首例活體肝臟移植手術.2013年時累積換肝手術已達1193例，其中活體肝臟手術1037例。
- 1989年台大醫院完成第一例屍體肝臟移植,1997年完成第一例活體部分肝臟移植, 至2011年底共完成活體肝臟移植410例.

Criteria for emergency liver transplantation

King's College criteria

ALF due to paracetamol

- Arterial pH <7.3 after resuscitation and
  >24 hours since ingestion
- Lactate >3 mmol/L or
- The 3 following criteria:
  - HE >Grade 3
  - Serum creatinine >300 µmol/L
  - INR >6.5

ALF not due to paracetamol

- INR >6.5 or
- 3 out of 5 following criteria:
  - Aetiology: indeterminate aetiology, hepatitis, drug-induced hepatitis
  - Age <10 years or >40 years
  - Interval jaundice encephalopathy >7 days
  - Bilirubin >300 µmol/L
  - INR >3.5

Liver transplantation

- Evaluation of patient prognosis is key at the earliest opportunity

Recommendations	Grade of evidence	Grade of recommendation
Prognostic assessment should take place not only in the transplant centre but also at the site of first presentation, as decisions in relation to patient transfer to a specialist centre must be made at the earliest opportunity	III	1
Development of encephalopathy is of key prognostic importance, with onset indicating critically impaired liver function. In subacute presentations, even low-grade encephalopathy may indicate extremely poor prognosis	II-2	1
Prognosis is worse in patients with more severe liver injury, extrahepatic organ failure and subacute presentations	II-3	1
Transplantation should be considered in those patients fulfilling Clichy or King's College Criteria	II-2	1

Liver transplantation criteria

King's College Hospital criteria

for liver transplantation in acute liver failure[17]

Patients with paracetamol toxicity

pH < 7.3 or

Prothrombin time > 100 seconds and

serum creatinine level > 3.4 mg/dL (> 300 µmol/l)

if in grade III or IV encephalopathy

Other patients

Prothrombin time > 100 seconds or

Three of the following variables:

- Age < 10 yr or > 40 years
- Cause:
  - Hepatitis C or E
  - halothane hepatitis
  - idiosyncratic drug reaction
- Duration of jaundice before encephalopathy > 7 days
- Prothrombin time > 50 seconds
- Serum bilirubin level > 17.6 mg/dL (> 300 µmol/l)

活體肝臟捐贈者的風險與恢復

- 肝臟移植會以**捐贈者的安全為第一優先考慮，因此至少會留下百分之三 十五的肝臟，至於需**捐出多少的肝臟，必須視受贈者之體重而定，一般 而言，捐贈重量至少是受贈者體重的百分之零點八至百分之一.
- 手術後七天至十天可以出院，肝功能約二至三週可以恢復正常，術後三 至四個月可以恢復勞力工作，**半年後可以再生回原有肝臟體積的百分之 七十左右。**
- 因施行肝臟捐贈手術而死亡者 為百分之零點六至百分之一

那些情況不適合肝臟移植

- 年齡65歲以上，健康狀況不佳者
- 有無法控制的感染者
- 愛滋病帶原者
- 肺結核未完全治療者
- 有惡性腫瘤者（除原發性肝腫瘤之外）
- 心智不正常者或無法長期配合藥物治療者
- 嚴重心肺功能障礙者
- 嚴重腦血管或週邊血管病變
- 免疫系統不全或自體免疫疾病
- 藥癮患者
- 酒癮戒除未滿半年者

liver transplant may be from different sources

- **Toronto man gets liver transplant from different source after cousin turned back at airport (Oct. 20, 2015)**
- A Toronto man who was waiting for a liver transplant has received the lifesaving procedure. But his cousin, a potential donor, was prevented from entering Canada, and the transplant came from another source. Christina Stevens reports.
- Diego Menendez' cousin, who was hoping to donate part of his liver, was prevented from entering Canada by Canada Border Service Agency officers earlier this month.
- Menendez was on the liver transplant waitlist for two years. The lifesaving call that a suitable cadaveric liver was available finally came on Friday.(Oct. 16)

42,肝移植是解救兒童肝衰竭病人的最有效的治療

Liver transplantation in children with ALF

- LTx is the only proven treatment that has improved outcomes in children with ALF who fulfil poor prognostic criteria

Liver transplantation criteria in paediatric ALF
Indications (accepted, not validated) • INR >4 and total bilirubin >300 µmol/L (17.6 mg/dl) irrespective of HE
Contraindications • Fixed and dilated pupils • Uncontrolled sepsis • Severe respiratory failure (ARDS)

Liver transplantation and artificial liver devices

Considerations for future studies

Liver transplantation

- Prospective studies of high methodological quality and sufficient size, enrolling from multiple centres, to assess the current natural history of ALF
- Avoid the assumption that transplantation equals non-survival for prognostic modelling purposes
- Definition and validation of contraindications to transplant in patients with ALF
- Definition and validation of futility of LTx in patients with ALF
- Clarification of the role of auxiliary LTx in patients with ALF
- Definition of long-term outcomes including quality of life in both transplant recipients and spontaneous survivors
- Biomarkers of regenerative capacity

Artificial and bioartificial liver devices

- Well-designed RCTs of new liver support systems in well-defined patient cohorts
- Development of dynamic measures of liver function to assess metabolic and synthetic capacity
- Antimicrobial clearance and dosing when utilizing various liver support systems such as PE

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EASL CPG ALF. J Hepatol 2017;66:1047–81

Hepatol Int. 2025 Feb 17;19(1):1–69. doi: 10.1007/s12072-024-10773-4

Acute-on-chronic liver failure (ACLF): the 'Kyoto Consensus'—steps from Asia

Ashok Choudhury [1], Anand V Kulkarni [2], Vinod Arora [1], A S Soin [3], Abdul Kadir Dokmeci [4], Abhijeet Chowdhury [5], *Et al*

- 慢加急性肝衰竭 (ACLF) 是一種如果不進行肝臟移植會導致高死亡率的疾病。世界各地對此提出了不同的定義。亞太地區肝病研究協會 (APASL) 工作小組於 2004 年就 ACLF 制定了第一份共識報告，該報告於 2009 年發布. 「APASL ACLF 研究聯盟 (AARC)」於 2012 年成立.
- APASL主動邀請全球利益相關方，包括來自亞洲的意見領袖、EASL和AASLD以及ACLF領域的其他研究人員，共同確定關鍵問題並制定基於證據的共識文件。該共識文件於 2024 年 3 月在京都舉行的 APASL 年會上以混合形式提交。

Cirrhosis, compensated or decompensated

- 肝硬化的自然病程分為兩個不同的階段：代償期和失代償期。代償期是無症狀的時期，中位存活期為 10 年或更長。第二階段稱為失代償性肝硬化，其特徵是存在症狀，中位存活期為 1-2 年。 從代償期到失代償期的肝硬化轉變會導致死亡風險增加.
- Decompensation: 包括膽紅素> 3 mg/dl、臨床上可偵測到的腹水、明顯的 HE 或門靜脈高壓出血。

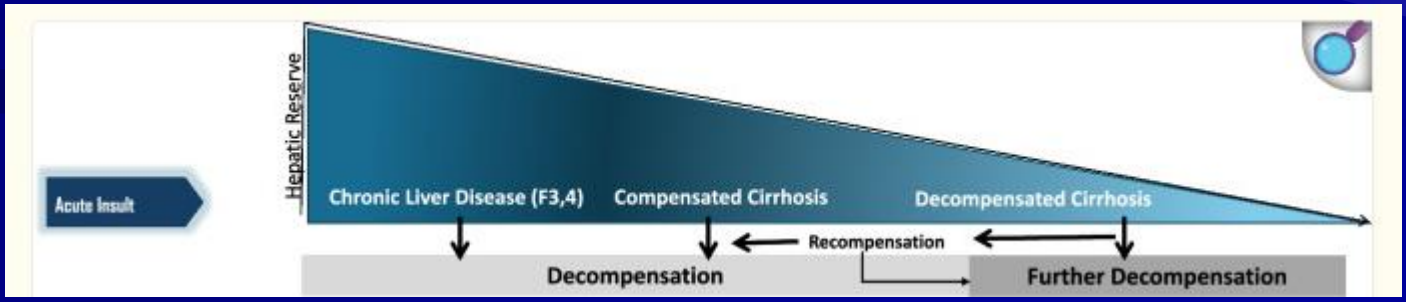

Table 1. Management of extrahepatic organ failure in patients with acute liver failure.

	What to do	What not to do
Central nervous system	Encephalopathy should be monitored frequently Maintain serum sodium levels between 140 and 145 mmol/L Monitoring of blood glucose will probably be required at least every 2 hours Tracheal intubation and sedation in the event of progressive HE (Glasgow < 8) Practices to minimise the depth of sedation are recommended Transcranial Doppler ultrasound ICP: no specific treatment	Administration of sedatives such as benzodiazepines and psychotropic drugs (such as metoclopramide) Use of treatments (lactulose, rifaximin) to lower ammonia levels

Respiratory system	Standard lung protective ventilator strategy (according to specific recommendations)
Cardiovascular system	Assessment of volume status, cardiac output and cardiac function (right and left-sided function) Fluid expansion using crystalloid fluids as first choice Norepinephrine infusion for refractory hypotension

What not to do

Renal system	Renal replacement therapy according to specific recommendations	Use of nephrotoxic drugs, including non-steroidal anti-inflammatory drugs
Gastrointestinal system	Stress ulcer prophylaxis according to specific recommendations	
Coagulation		Routine correction of coagulation: restrict clotting factors administration unless active bleeding
Immune system	Empirical broad spectrum antibiotics should be administered to patients with worsening HE or signs of SIRS	

6. Question 1: In patients with acute liver failure, which etiological exams should be performed to reduce morbidity and mortality?

R1 – In patients with severe acute liver failure, we recommend the determination of serum acetaminophen levels, serology for Hepatitis A (IgM VHA) and Hepatitis B (HBsAg and anti-HBc IgM) viruses, urinary toxins (amphetamine, cocaine), and the performance of an echocardiography and hepatic echo-Doppler.

(GRADE 1+), STRONG AGREEMENT

7. Question 2: In patients with acute liver failure, which specific treatments should be initiated rapidly to reduce morbidity and mortality?

R2.1 – In patients with acetaminophen-induced acute liver failure, we recommend the initiation of N-acetylcysteine therapy without waiting for, and regardless of, the results of serum acetaminophen determinations.

(GRADE 1+) STRONG AGREEMENT

R2.2 – In patients with acute liver failure whatever the aetiology, we suggest the initiation of N- acetylcysteine therapy to improve morbidity and mortality.

(GRADE 2+) STRONG AGREEMENT

R2.3 – In patients with acute liver failure, whatever the aetiology, the experts suggest that advice should be obtained from a liver transplantation centre in order to discuss:

1. Second-line aetiological investigations if the results of first-line examinations (see R1) are negative

2. An indication for liver transplantation

EXPERT OPINION, STRONG AGREEMENT

8. Question 3: In patients with acute liver failure, which symptomatic treatment should be initiated to reduce morbidity and mortality?

R3 – In order to reduce morbidity and mortality in patients with acute liver failure, the experts suggest that extrahepatic organ failure should be treated early and any aggravating factors should be prevented, as shown in the Table below.

EXPERT OPINION, STRONG AGREEMENT

8.1.3. Liver support devices

Two well-designed RCT including 115 patients with ALF (not related to hypoxic hepatitis) failed to demonstrate a significant reduction in mortality (pooled data: RR=0.82; 95% CI 0.42–1.59) [59], [60]. The place of liver support systems in the management of patients with ALF need to be better defined. In any case, these techniques should not delay transfer to a liver transplantation centre.

Patients with ALF have increased susceptibility to infections. Bacterial infections have been documented in 60%–80% of patients with ALF, and fungal infections occur in one third of patients [64]. Empirical broad-spectrum antibiotics should be administrated to ALF patients if there are signs of sepsis and/or of worsening encephalopathy [65]. These broad-spectrum antibiotics should cover common organisms such as enterobacteria, staphylococcal or streptococcal species, or as a function of the ecology in the unit [64].

9. Question 4: In patients with cirrhosis, which criteria should be used to guide admission or non-admission to an ICU to improve their prognosis?

R4–We do not suggest denying the admission of patients with cirrhosis to the ICU solely because of their underlying cirrhotic condition.

(GRADE 2–) STRONG AGREEMENT

10. Question 5: In patients with cirrhosis hospitalised in an ICU, which specific measures to manage acute kidney injury should be used to reduce morbidity and mortality?

R5.1 – To define and assess the severity of acute kidney injury (AKI) in patients with cirrhosis, the experts suggest:

1. Using the modified KDIGO criteria specifically refined by the International Club of Ascites

2. Managing AKI according to its severity and to the algorithm proposed (Fig. 2)

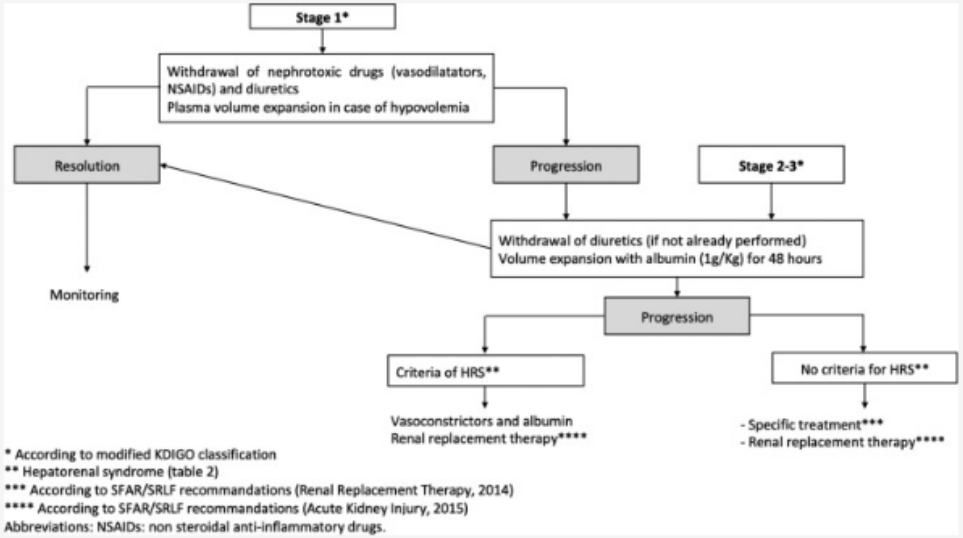

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Fig. 2. Algorithm for the management of acute kidney injury according to modified KDIGO classification in patients with cirrhosis.

3. Not contraindicating renal replacement therapy in these patients just because of their underlying cirrhotic condition.

About acute kidney injury

EXPERT OPINION, STRONG AGREEMENT

表 3 .肝腎症候群的診斷標準（必須遵守所有標準才能保留 HRS）。

肝硬化腹水的診斷
根據 KDIGO 標準診斷為急性腎損傷第 2 期或第 3 期
連續2天停用利尿劑並以白蛋白（1g /kg體重）擴容後無反應
無休克
近期未使用腎毒性藥物（非類固醇抗發炎藥、氨基糖苷類、碘化造影劑...）
無宏觀結構損傷跡象定義為
無蛋白尿（> 500mg /天）
無鏡下血尿（每高倍視野> 50 個紅血球）
腎臟超音波檢查結果正常

11 .問題 6：對於入住 ICU 的肝硬化患者，應採用哪種特定的膿毒症治療方法來降低發病率和死亡率？

R6 – 為了降低肝硬化重症患者的發病率和死亡率，無論症狀和器官衰竭如何，我們建議：

1. 進行系統性感染檢查，包括對腹水進行微生物學和細胞學檢查（腹水中多形核細胞濃度> 250/mm^3將確診自發性細菌性腹膜炎），

2. 儘早開始經驗性抗生素治療，治療方案應根據疑似感染部位、已確定的致病病原體以及當地生態狀況進行調整

2 級以上，強烈認同

12 .問題7：對於入住ICU的肝硬化患者，何時應注射濃縮白蛋白以降低發病率和死亡率？

R7.1 – 對於入住 ICU 的肝硬化患者，我們建議在大量腹水穿刺（抽取超過 4 至 5 公升腹水）後使用濃縮白蛋白輸注

1+級，強烈認同

大量腹水穿刺以不超過兩公升腹水為原則

R7.2 – 對於入住 ICU 的肝硬化患者，我們建議在發生自發性細菌性腹膜炎 (SBP) 時應使用濃縮白蛋白輸注

2 級以上，強烈認同

13 .問題 8：對於入住 ICU 的肝硬化患者，應採取哪一種急性上消化道出血治療措施以降低發病率和死亡率？

R8.1.1 – 對於肝硬化和急性上消化道出血患者，我們建議盡快引入靜脈血管活性藥物治療（奧曲肽、生長抑素或特利加壓素）和預防性抗生素治療。

1+級，強烈認同

octreotide, somatostatin or terlipressin

R8.1.2 – 對於肝硬化和急性上消化道出血患者，我們建議盡快使用質子幫浦抑制劑。

2 級以上，強烈認同

R8.1.3 – 對於肝硬化和急性上消化道出血患者，我們建議盡快進行上消化道內視鏡檢查。

1+級，強烈認同

R8.3–In patients with cirrhosis and acute upper gastrointestinal bleeding, we suggest to consider Transjugular intrahepatic portosystemic shunt (TIPS) with a covered stent within 24 to 72 hours of the bleeding for episodes in Child–Pugh class C patients (< 14) or in Child–Pugh class B patients with initially active bleeding at endoscopy (early TIPS).

GRADE 2+, STRONG AGREEMENT

R8.4–In patients with cirrhosis and acute upper gastrointestinal bleeding, the experts suggest considering emergency Transjugular intrahepatic portosystemic shunt (TIPS) with a covered stent in the event of variceal bleeding refractory to endoscopic treatment (salvage TIPS).

EXPERT OPINION, STRONG AGREEMENT

14. Question 9: In patients with cirrhosis hospitalised in the ICU, which measures to manage haemostasis should be initiated to reduce morbidity and mortality?

R9 – The experts suggest that routine prophylactic fresh frozen plasma, platelets or fibrinogen concentrates should not be systematically administrated before invasive procedures in cirrhotic patients in order to reduce bleeding.

EXPERT OPINION, STRONG AGREEMENT

14 .問題 9：對於入住 ICU 的肝硬化患者，應採取哪些止血措施來降低發病率和死亡率？

R9 – 專家建議，為了減少出血，肝硬化患者在接受侵入性手術前不應系統性地給予常規預防性新鮮冷凍血漿、血小板或纖維蛋白原濃縮物。

專家意見，強烈認同

15 .問題 10：對於入住 ICU 的肝硬化患者，應何時尋求專家建議以降低發病率和死亡率？

R10 – 專家建議，對於入住 ICU 的肝硬化患者，應尋求專家建議：

1. 入院時，如果病人已經在肝臟移植等候名單上。

2. 入住 ICU 後不久，討論根據器官衰竭的數量及其病程所提供的護理強度。

3. 討論肝臟支持技術的益處。

4. 離開ICU時，安排肝病管理，以備潛在的肝臟移植

專家意見，強烈認同

Liver transplantation: final

3. 在 ACLF 情況下適當使用的人工肝臟支持可能包括：

（1）允許肝臟再生（恢復橋樑），或（2）使用支持療法直至肝臟移植（移植橋樑）。

迄今為止，最著名的設備是基於白蛋白透析的原理。 MARS® 和 Prometheus® 系統在法國得到了最廣泛的研究。兩項針對急性失代償患者的歐洲多中心隨機研究將 MARS® 或 Prometheus® 與標準藥物治療進行了比較。這些研究並未證明其對 28 天和 90天存活率有任何益處[230]、[231]。然而，事後分析顯示，使用 MARS 與標準藥物治療相比，白蛋白透析在肝性腦病變和肝腎症候群方面有顯著改善。值得注意的是，這兩項研究的納入標準是失代償性肝硬化，但不知道是否有 ACLF。因此，這些研究能夠納入無器官衰竭（ACLF 0 級）或多重器官衰竭（ACLF 3 級）的急性失代償患者，他們的預後和死亡率有顯著差異，從 4% 到 80% 不等[68]。人工支持系統最初用於治療重度肝病和多重器官衰竭患者。最近，這些系統被用作等待肝臟移植的支持療法。一項觀察性研究[232]和一項薈萃分析[233]表明，使用人工肝支持系統與 ACLF 和多重器官衰竭患者的短期存活率（14 天和 28 天）提高有關。這種短期改善可以使這些患者獲得肝臟移植，而肝臟移植仍是末期肝病患者的基本治療方法[225]、[227]、[228]。現有數據表明，肝臟支持系統可能有助於為最終治療提供「橋樑」。其適應症有待探索，這些設備的未來需要新的研究方案。因此，專家建議，患者應在肝硬化失代償後儘早轉診至專家中心。

4. 肝硬化患者轉出ICU時仍存活者預後不良，若不接受肝臟移植，1年存活率不足25% [114]。因此，應系統性地將這些患者轉診至肝臟移植科。

摘要(2025.09.26)

- 肝衰竭代表肝功能喪失其代謝解毒之功能&肝昏迷是肝衰竭之具體表現。
- 減少 Ammonia之產生是公認對肝昏迷有效之療法。改善電解質之平衡也很重要。
- 找出原因,再針對原因治療是最快收效的治療方法。
- 讓肝恢復其原有功能必需一個月或更久,因此massive liver necrosis 只好依賴肝臟移植度過難關。人工肝臟只有輔助功能。