

William Bernal<sup>1\*</sup>, Mark J. McPhail<sup>1</sup>

<sup>1</sup>Liver Intensive Therapy Unit, Institute of Liver Studies, King's College Hospital, Denmark Hill, London SE5 9RS, United Kingdom

\*Corresponding author: Liver Intensive Therapy Unit, Institute of Liver Studies Kings College Hospital, Denmark Hill, London SE5 9RS, United Kingdom; Tel.: +44 203 299 4468.

E-mail address: william.bernal@kcl.ac.uk (W. Bernal).

## A rare, complex critical illness

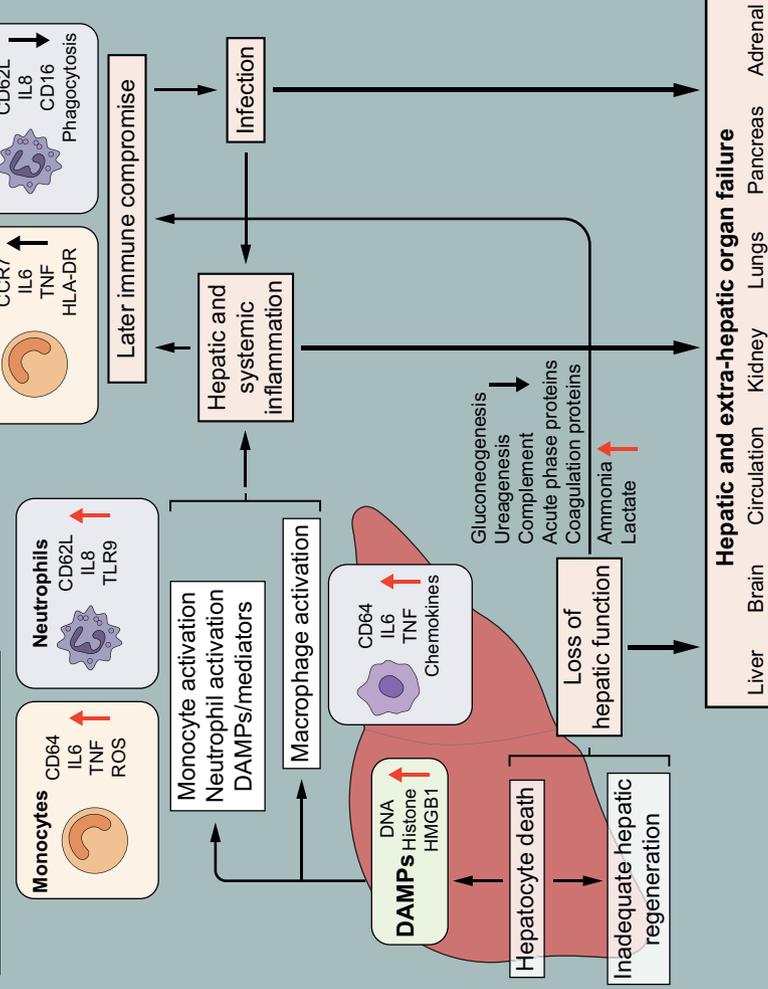
Massive liver cell death in a previously normal liver may result from apoptotic, necrotic or necroptotic mechanisms, depending on the cause of liver injury.<sup>1</sup> The clinical phenotype of acute liver failure (ALF) reflects the nature and extent of liver damage, its rate of evolution and adequacy of hepatic regeneration.

Globally, cases with rapid onset from viral or drug-induced injury are most common with complex immune dysregulation and multiorgan failure (MOF).<sup>2</sup>

1. Hepatocyte death triggers release of Damage-associated molecular patterns (DAMPs) that activate immune cells in the liver and circulation.
2. Loss of hepatic function with hyper-ammonaemia and "spill over" of intra-hepatic inflammatory mediators cause systemic effects with hepatic encephalopathy (HE) and extra-hepatic organ dysfunction.
3. Immune compromise follows, with complicating sepsis a major cause of later morbidity and mortality.

Cases with gradual onset are rarer, often of indeterminate cause, and have much less prominent systemic features until a very late stage of illness. However, liver regeneration is often inadequate and liver transplantation life saving.<sup>3</sup>

## Immune dysregulation in the pathogenesis of ALF

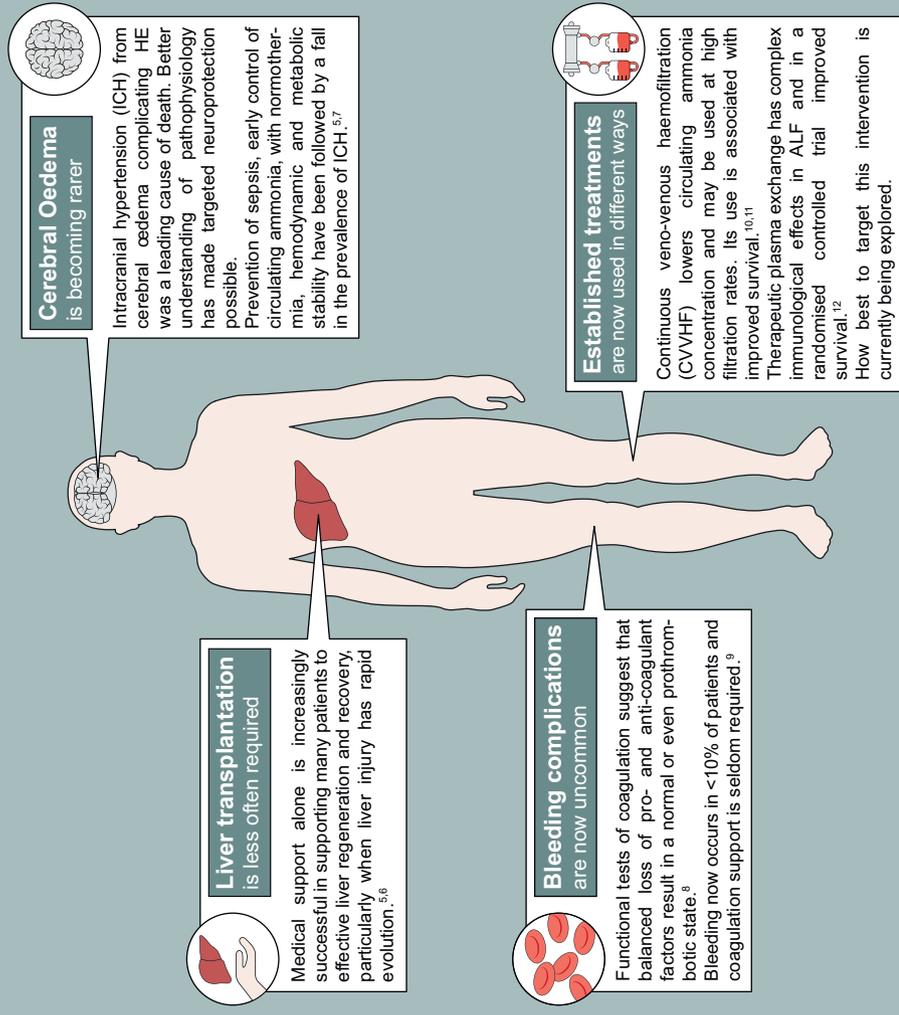


## Clinical care focuses on<sup>4</sup>

1. Early recognition and limitation of hepatic injury by addressing its cause and cofactors.
2. Intensive care measures to address MOF, limit complications and optimise hepatic regeneration.
3. Continuous assessment of hepatic function and likelihood of native liver recovery.
4. Emergency liver transplantation when liver recovery is not expected.

## The illness is changing and survival is improving

Though ALF remains a critical illness with significant mortality, in recent years patient survival has markedly improved.<sup>5,6</sup>



# Hepatology Snapshot

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## Conflict of interest

The authors declare no conflicts of interest that pertain to this work.

Please refer to the accompanying ICMJE disclosure forms for further details.

## Authors' contributions

Both authors contributed to the content, design and execution of the figure.

## Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jhep.2021.01.037>.

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