对中国酒精性肝病负担的思考

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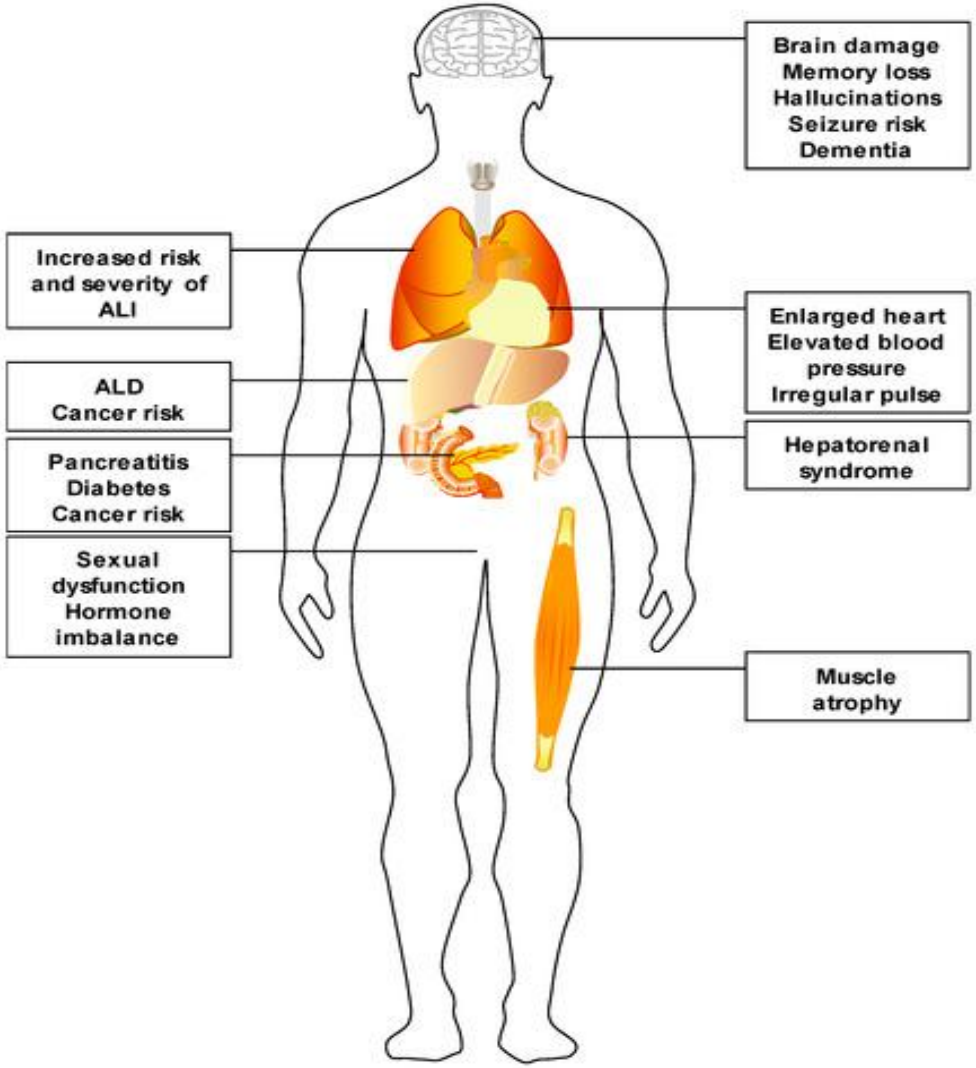
广州 • 2019-5-25

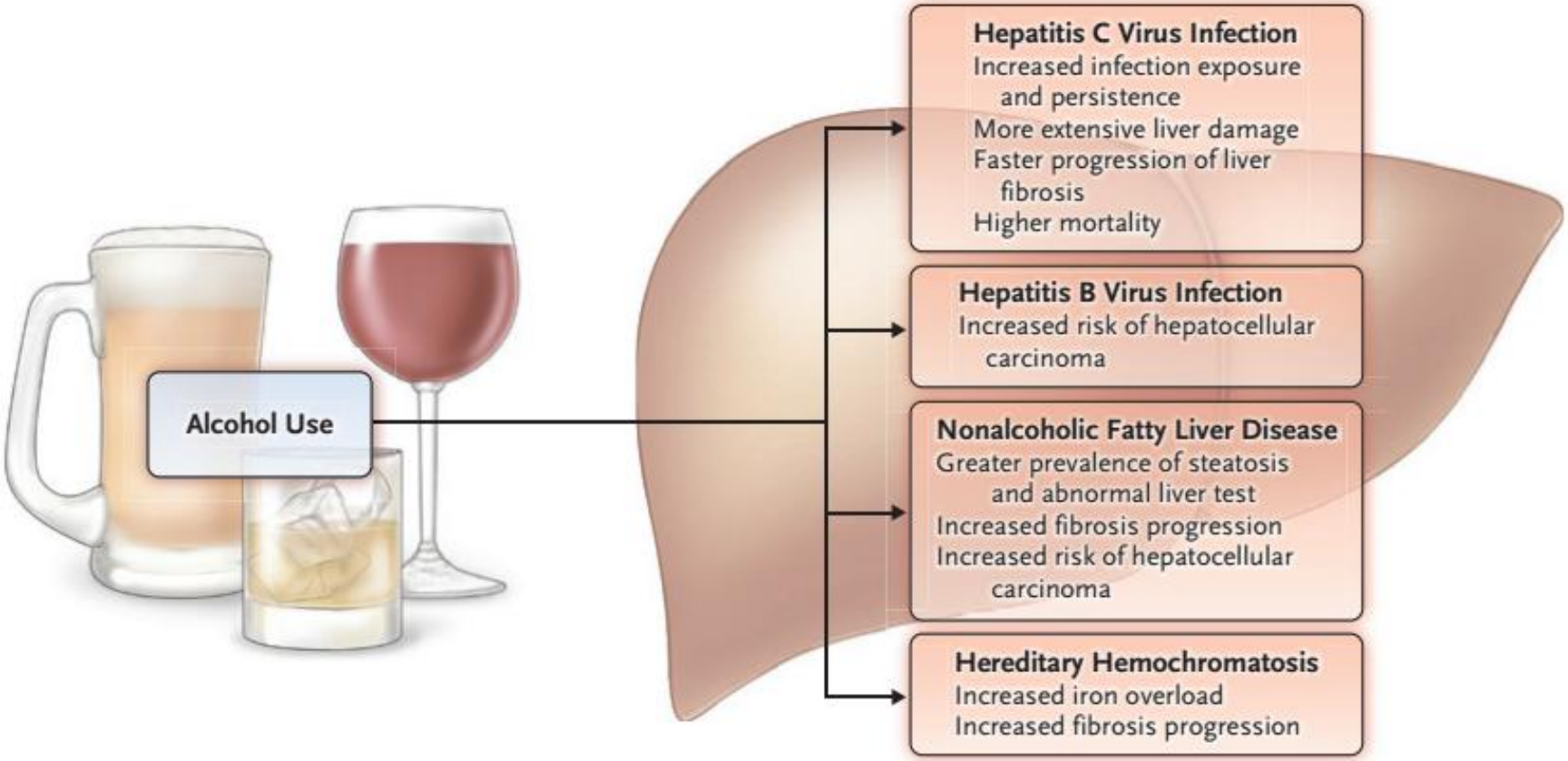
Alcoholic Liver Disease is a World Health Problem

- **493,000 deaths in 2010**
- **0.9% of all deaths**
- **47.9% of all cirrhotic deaths**
- **ALD-associated liver cancer: 80,600 deaths**

Rehm J et al. Global burden of alcoholic liver diseases. J. Hepatol 2013; 59: 160-168



Lauren G. Poole, Christine E. Dolin and Gavin E. Arteel. Organ–Organ Crosstalk and Alcoholic Liver Disease Biomolecules 2017, 7(3), 62



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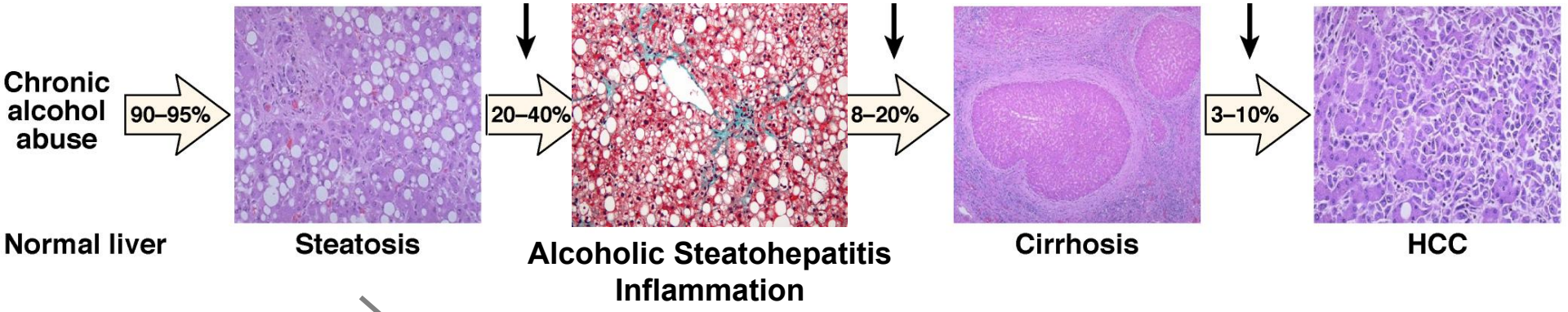
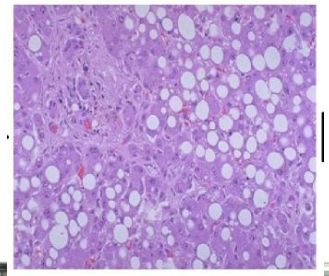
Spectrum of Alcoholic Liver Disease (ALD)

Alcohol drinking is a leading cause of chronic liver disease, accounting for 30-40% cirrhosis and 20-30% liver cancer in the USA

Gao and Bataller. *Gastroenterology* 2011, 141:1572-85

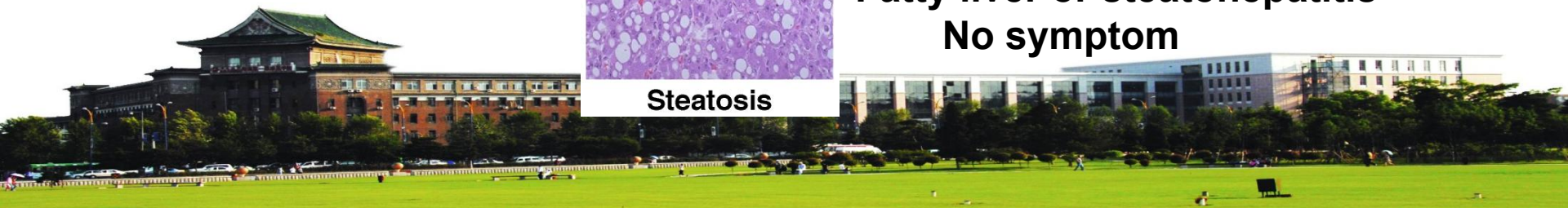


60-80%



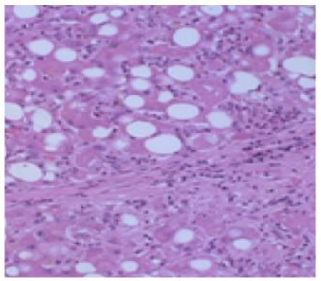
Steatosis

Fatty liver or steatohepatitis
No symptom



Alcoholic Hepatitis

Overt Alcoholic Hepatitis



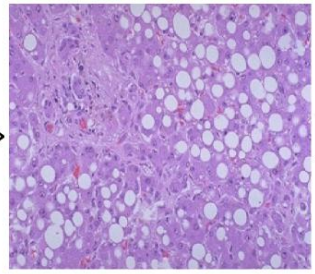
Alcoholic hepatitis

AH: Clinical diagnosis:

- Chronic drinking plus recent excessive binge
- Symptoms: Jaundice, hepatomegaly, fever
- Lab test: AST: ALT ratio >2, neutrophilia
- Severe form with **a high mortality**
- Liver histology may help rule out other causes

Chronic alcohol abuse

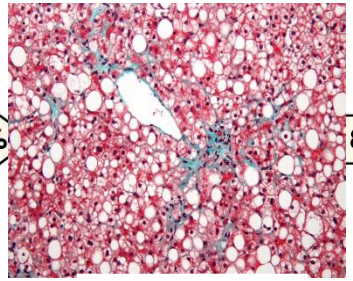
90–95%



Normal liver

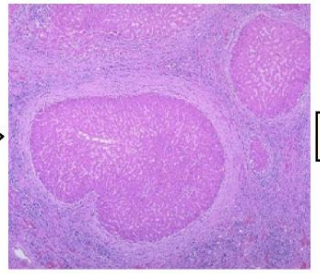
Steatosis

20–40%



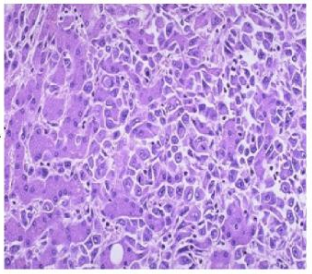
Alcoholic Steatohepatitis
Inflammation

8–20%



Cirrhosis

3–10%

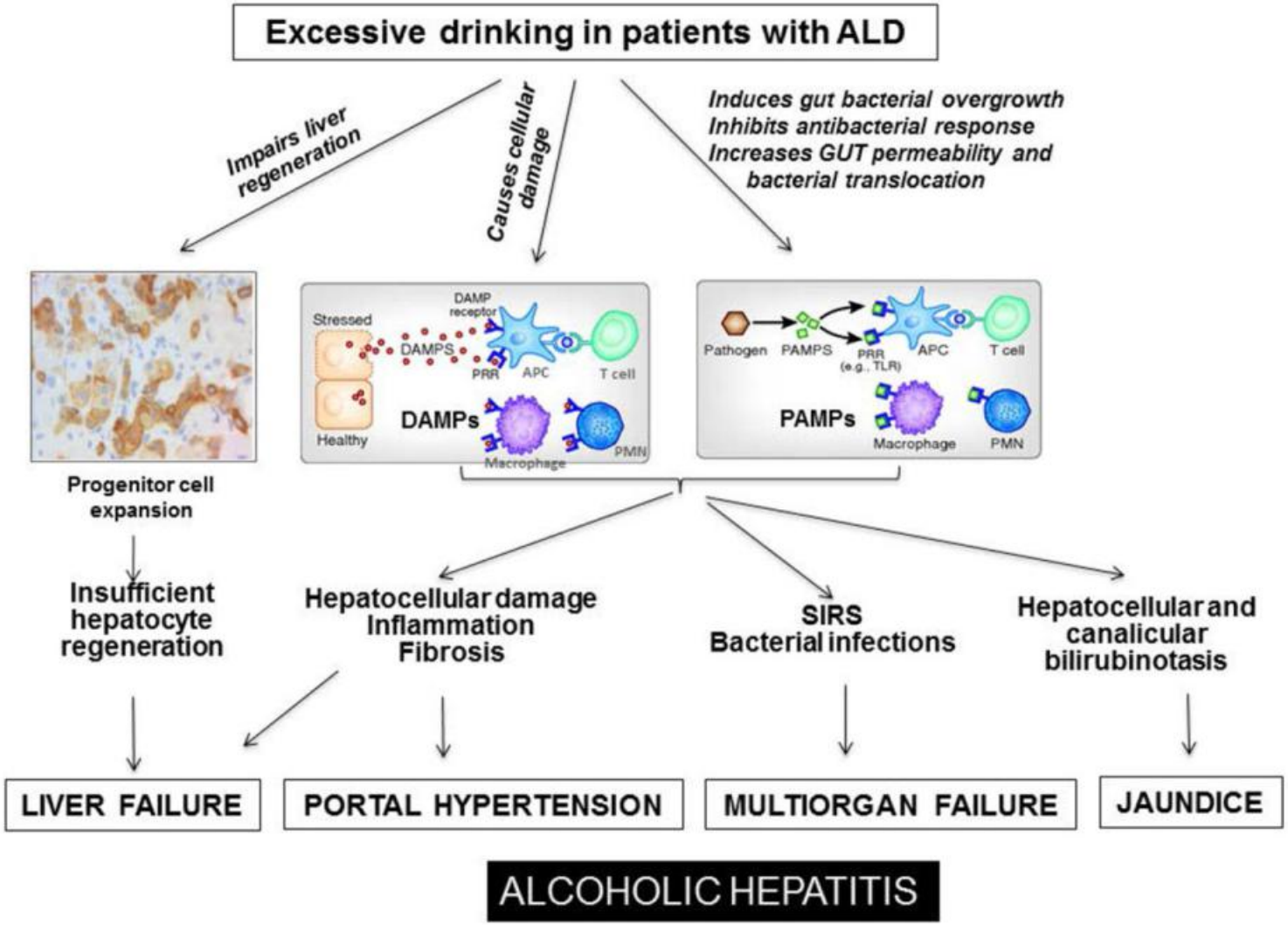


HCC

Subclinical Steatohepatitis
Walking alcoholic hepatitis

ASH: Pathologic diagnosis:

- Steatosis, lobular inflammation (neutrophil infiltration)
- Ballooning degeneration, Mallory bodies
- Chicken wire fibrosis


Excessive drinking in patients with ALD
Impairs liver regeneration
Causes cellular damage
Induces gut bacterial overgrowth
Inhibits antibacterial response
Increases GUT permeability and bacterial translocation
Stressed
DAMP receptor
DAMPS
PRR
APC
T cell
Healthy
DAMPs
Macrophage
PMN
Pathogen
PAMPS
PRR (e.g., TLR)
APC
T cell
PAMPs
Macrophage
PMN
Progenitor cell expansion
Insufficient hepatocyte regeneration
Hepatocellular damage
Inflammation
Fibrosis
SIRS
Bacterial infections
Hepatocellular and canalicular bilirubinotasis
LIVER FAILURE
PORTAL HYPERTENSION
MULTIORGAN FAILURE
JAUNDICE
ALCOHOLIC HEPATITIS

Formulas for scores used in alcoholic hepatitis

Scoring system	Formula
mDF	mDF = 4.6 × (prothrombin time − control time) + bilirubin in mg/dL
MELD	MELD = 3.78 × ln[serum bilirubin (mg/dL)] + 11.2 × ln[INR] + 9.57 × ln[serum creatinine (mg/dL)] + 6.43
MELD-Na score	MELD-Na = MELD + 1.59 (135-Na), with maximum and minimum Na of 135 and 120 mEq/L, respectively
GAHS	Age (years), WBC (109/L) , Urea (mmol/L) ,Bilirubin (μmol/L)
ABIC score at 90 days	(age × 0.1) + (serum bilirubin × 0.08) + (serum creatinine × 0.3) + (INR × 0.8)
ECBL	Bilirubin levels at day 7 lower than at baseline, on corticosteroid therapy
Lille's model	Exp(−*R*)/[1 + Exp(−*R*)], Where *R* = [3.19 − (0.101 × age in years)] + (1.47 × albumin at day 1 in g/dL) + [0.28215 × (bilirubin at day 1 − bilirubin at day 8 in mg/dL)] − [0.206 × (if creatinine ≥1.3 mg/dL at day 1)] − [0.11115 × bilirubin at day 1 in mg/dL] − (0.0096 × prothrombin time in seconds at day 1)
MELD + Lille combination model	MELD variables + Lille variables

OUTLINE

- EPIDEMIOLOGY OF ALD IN CHINA
- RISK FACTORS FOR ALD IN CHINA
- MANAGEMENT OF ALD IN CHINA

In China

- Beer production increased by 2.27 times over 18 years from 1987.67 tons in 1998 to 4506.44 tons in 2016
- The percentage of the Chinese population that reported weekly regular alcohol drinking increased by more than 33% between 2004 and 2008
- The annual consumed volume of alcoholic beverages per capita in the general Chinese population increased from 4.9 L in 2003-2005 to 7.2 L in 2016, with regular Chinese drinkers consuming an average of 12.9 L per capita in 2016

Table 1 population-based surveys of alcohol consumption in China

Author	Year	Area	*n*	Age (yr)	Habitual drinking (%)	Excessive drinking (%)
Li *et al*[19]	2000	Zhengjiang	18237 (M 66.0%)	38.3 ± 12.3	27.0 (M -, F -)	14.8
Lu *et al*[20]	2000	Xi'an	3613 (M 60.6%)	36.0 ± 13.0	35.2 (M 52.2, F 8.9)	-
Huang *et al*[21]	2005	Hu'nan	18828 (M 69.2%)	42.1 ± 13.4	37.8 (M -, F -)	-
Chen *et al*[22]	2007	Liaoning	6598 (M 62.2%)	39.3 ± 11.1	27.0 (M 38.3, F 5.6)	-
Wang *et al*[9]	2011	Shandong	7295 (M 48.2%)	44.7 ± 13.9	42.76 (M 74.5, F 11.3)	-
Yan *et al*[23]	2015	Shanxi, Gansu, Xinjiang	2300 (M 75.0%)	38.1 ± 13.3	66.2 (M 77.9, F 31.2)	-
Guo *et al*[24]	2016	Guizhou	9280 (M 47.9%)	42.7 ± 25.5	32.1 (M 52.8, F 13.2)	-
Chang *et al*[25]	2016	Tianjin	3137 (M 45.1%)	-	32.2 (M 55.9, F 12.6)	-

Excessive drinking: alcohol consumption ≥ 40 g/d for over 5 years. M: Male; F: Female; "-": Unavailable.

Wang WJ, Xiao P, Xu HQ, Niu JQ, ***Gao YH***. Growing burden of alcoholic liver disease in China: A review. World J Gastroenterol 2019 March 28; 25(12): 1445-1456.

Table 2 population-based surveys of alcoholic liver disease in China

Author	Year	*n*	Morbidity rate of ALD (%)	ALD			
				MALD (%)	AFL (%)	AH (%)	AC (%)
Li *et al*[19]	2000	18237	4.34 (M 6.36, F 0.36)	1.21	0.94	1.51	0.68
Lu *et al*[20]	2000	3613	2.27 (only one female)	-	2.16	-	0.11
Huang *et al*[21]	2005	18828	4.36 (M 6.00, F 0.52)	1.21	0.97	1.50	0.68
Chen *et al*[22]	2007	6598	6.82 (M 9.75, F 2.00)	4.29	4.29	2.18	0.35
Wang *et al*[9]	2011	7295	8.55 (M 15.76, F 1.42)	6.23	1.71	0.42	0.17
Yan *et al*[23]	2015	2300	8.74 (M 10.08, F 4.70)	4.22	3.74	0.48	0.30

ALD: Alcoholic liver disease; MALD: Mild ALD; AH: Alcoholic hepatitis; AC: Alcoholic cirrhosis; "-": Unavailable.

Wang WJ, Xiao P, Xu HQ, Niu JQ, ***Gao YH***. Growing burden of alcoholic liver disease in China: A review. World J Gastroenterol 2019 March 28; 25(12): 1445-1456.

- The percentage of regular alcohol drinkers among the general adult population in different areas increased from 27.0% in 2000 to 66.2% in 2015
- The percentage of heavy drinkers increased from 0.21% in 1982 to 14.8% in 2000, a 70-fold increase in < 20 years
- There is a notable parallel between the increased male drinking population and the increased ALD prevalence in males
- The 2.27% ALD prevalence in 2000 was increased to 8.74% in 2015
- The frequencies of different ALD stages differ significantly between the general Chinese population and heavy Chinese drinkers: 0.94%-3.74% (general population) vs 50% (heavy drinkers) with alcoholic fatty liver, 0.42%-2.18% vs 10% with alcoholic hepatitis (AH), and 0.11%-0.68% vs 10% with alcoholic cirrhosis

OPEN

Disease spectrum of alcoholic liver disease in Beijing 302 Hospital from 2002 to 2013

A large tertiary referral hospital experience from 7422 patients

Ang Huang, MD, PhD[a,b], Binxia Chang, MD, PhD[a,b], Yin Sun, MD, PhD[a,b], Huiming Lin, MB[a,b], Baosen Li, MB[a,b], Guangju Teng, MM[a,b], Zheng-Sheng Zou, MD, PhD[a,b,*]

Abstract

Alcohol consumption in China has substantially in
disease (ALD) is rising at an alarming rate. However,
available. The aim of this study is to assess the cur
referral hospital, Beijing 302 Hospital.

Data were retrospectively recorded from patien
spectrum and biochemical parameters of each pa

The patients with ALD accounted for 3.93% (74
number of patients hospitalized with ALD increased
all patients hospitalized with liver diseases was risin
patients with ALD were male. Age distribution of AL
subjects. Notably, the annual proportion of severe
highest levels of mean corpuscular volume, th
international normalized ratio, and alkaline phos
cholinesterase were significantly decreased in SAH
Alcoholic cirrhosis (ALC) is the most common ALD,

The number of hospitalized patients with ALD and
Hospital from 2002 to 2013. More attention shou

Abbreviations: AFL = alcoholic fatty liver, AH = a
disease, ALP = alkaline phosphatase, ALT = alanin
GGT = gamma-glutamyl transferase, HBV = hepati
alcoholic hepatitis, MDF = Maddrey's discriminan
alcoholic hepatitis, TBIL = total bilirubin.

Keywords: alcoholic hepatitis, alcoholic liver dis

Changing trends of hospitalisation of liver cirrhosis in Beijing, China

Xiao-Yuan Bao,[1] Bei-Bei Xu,[1] Kai Fang,[2] Yan Li,[3] Yong-Hua Hu,[2] Guo-Pei Yu,[1]

ABSTRACT

Objective: To examine if the hospitalisation trends of liver cirrhosis are changing with the changes of risk factors of the disease in China.

Design: Secondary analysis of hospitalisation records in the 31 top-ranking hospitals in Beijing.

Results: Between 2006 and 2010, hospitalisation from viral hepatitis cirrhosis (VHC) decreased by 10% (95% CI=5–14%, p<0.001), but non-viral hepatitis cirrhosis (NVHC) and alcoholic cirrhosis (AC) increased by 35% (26–46%, p<0.001) and 33% (19%– 47%, p<0.001), respectively. The age patterns of hospitalisation varied with different types of liver cirrhosis. The hospitalisation risks for patients with VHC and AC were significantly high in the age groups 40–49 and 50–59 years, but risks for those with NHVC were high in all age groups of 40 years or above. Overall male-to-

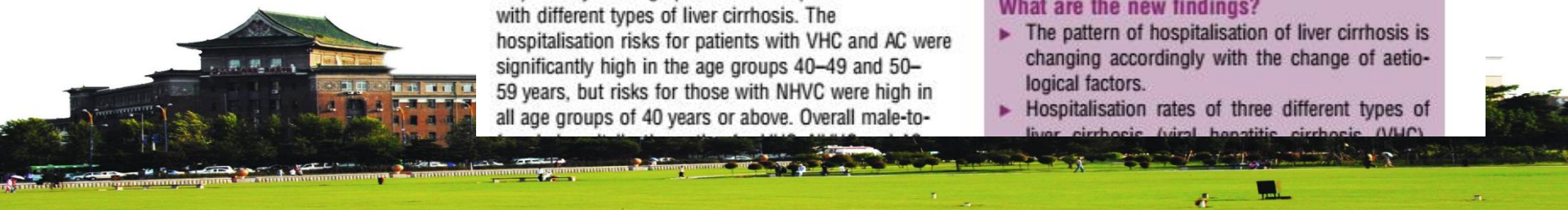
Summary box

What is already known about this subject?

- The change of hospitalisation of liver cirrhosis in time has been studied generally with a small number of patients in China.
- Evidence of the change of hospitalisation of liver cirrhosis as an outcome of the change of aetiological factors is relatively weak.
- Sex ratio of hospitalisation has not been well studied as different types of liver cirrhosis.

What are the new findings?

- The pattern of hospitalisation of liver cirrhosis is changing accordingly with the change of aetiological factors.
- Hospitalisation rates of three different types of liver cirrhosis (viral hepatitis cirrhosis (VHC)



- A hospitalization summary report (HSR) showed that viral hepatitis related cirrhosis hospitalization declined by 10% and alcoholic cirrhosis-related hospital stay was increased by 33% after categorizing approximately 2.3 million hospitalized patients in 31 Grade 3A hospitals in Beijing between 2006 and 2010. Male patients accounted for 98% of ALD cases and 71% of viral hepatitis cases, respectively

- Similarly, the percentage of hospitalized ALD patients among all those hospitalized for liver diseases increased from 1.7% in 2002 to 4.6% in 2013, and the annual incidence of severe alcoholic hepatitis (SAH) increased by 2.43 times from 2002 to 2013, as reported by the 302 Hospital in Beijing

2012 年 3 月 1 日至 2017 年 8 月 31 日吉林大学第一医院肝胆胰内科住院的 HBV 相关性肝癌、HCV 相关性肝癌、酒精性肝癌、自身免疫性肝癌患者共 1423 人，其中 HBV 相关性肝癌 1074 人（占 75.4%），HCV 相关性肝癌 262 人（占 18.4%），酒精性肝癌 70 人（占 4.9%），自身免疫性肝癌 17 人（占 1.2%），见图 4.8。

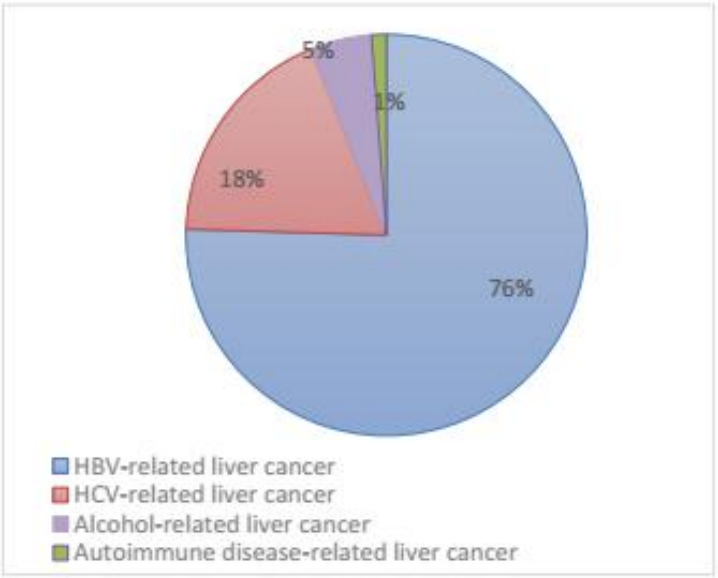


Figure 4.8 Distribution of causes on 1423 patients with PLC

OUTLINE

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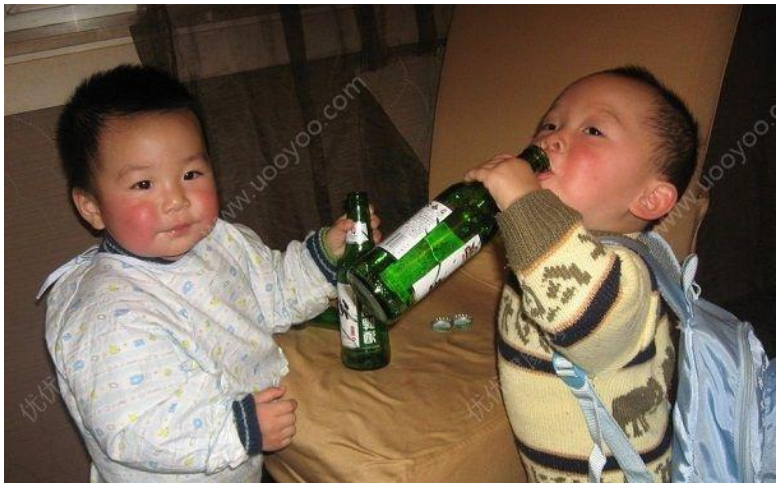
Age

The 2017 Annals of Chinese Health and Family Planning showed the constituent ratio of ALD patients aged between 15 to 44 years old who were discharged from hospitals, and the percentages significantly increased from 20% among 45-59 year olds to 48.8% among 60 year olds and 31.2% among those > 60 years old.

Adolescents

- The percentages of adolescents drinkers were highest among vocational high school students (44.7% for males, 28.8% for females).
- Alcohol consumption rates in high school students were higher (36.5% for males, 21.2% for females) than those in middle school students (23.6% for males and 15.3% for females).
- The percentages of drinkers among males were significantly higher in all three types of schools compared with those among females.
- Although prevalence estimates among Chinese students were generally lower than those reported in Western countries, an increasing trend has been observed in recent decades

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儿子，干！
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Gender

- The prevalence rates of current drinking among women in the World Health Organization Western Pacific Region were 39.3%, 36.4%, 42.0%, and 40.7% in 2000, 2005, 2010, and 2016, respectively
- In China specifically, the total, including recorded and unrecorded, per capita alcohol consumption for women was 2.2 (95%CI: 1.9-2.5) and 2.5 (95%CI: 2.4-2.6) in 2014 and 2018, respectively
- The age-standardized death rates for liver cirrhosis in females were 5.8 and 8.3 per 100000 population (15+) in 2012 and 2016

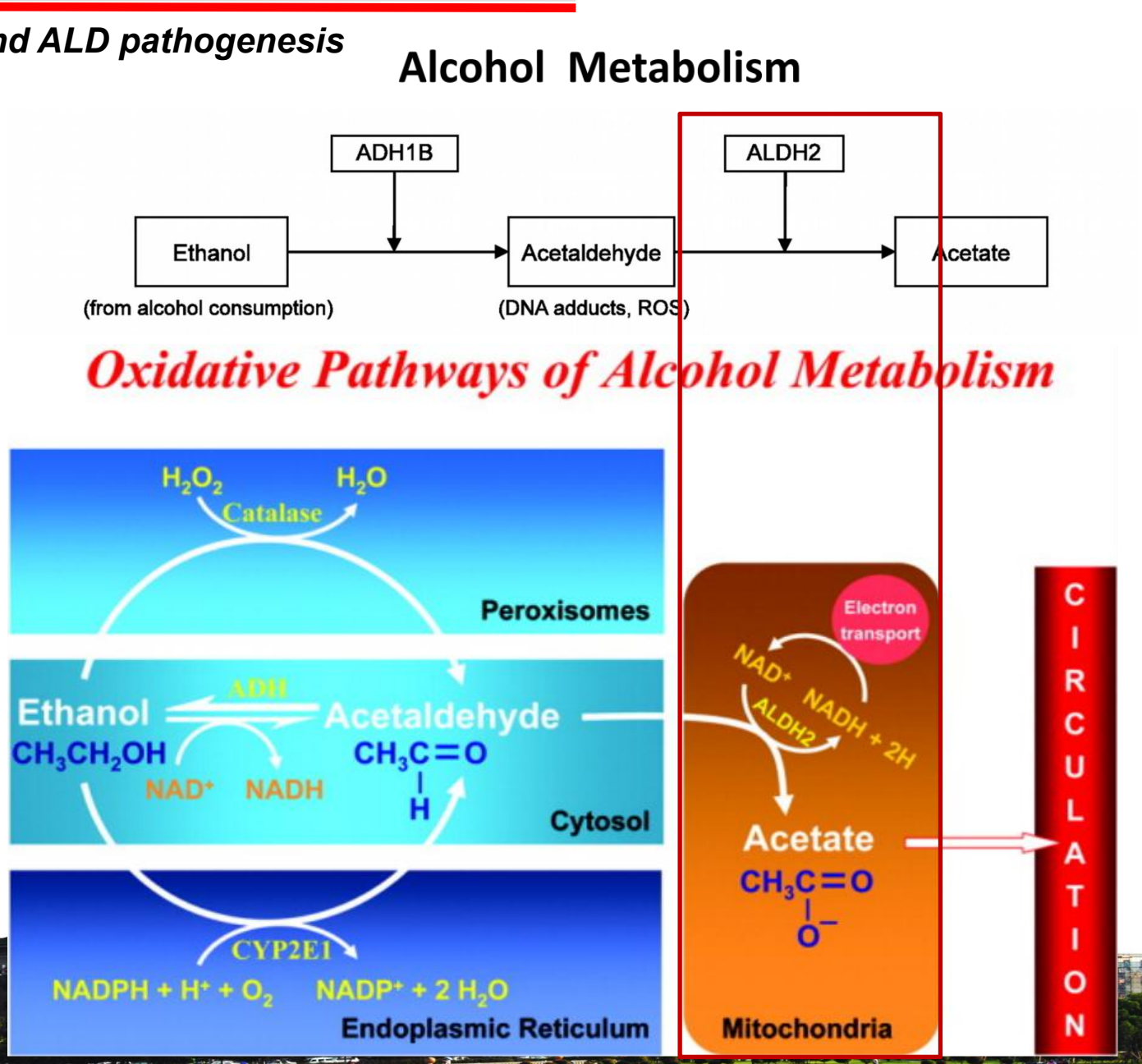
Types of alcoholic beverages ingested

- In China, spirits make up about 70% of the alcoholic beverages consumed, and it is estimated that up to 25% of the consumed alcohol is not registered
- Homemade wines including rice wines, which are not subject to taxation, are distilled by farmersin their family workshops
- A cross-sectional survey found that the three most commonly consumed alcoholic beverages in rural regions in Hunan province were homemade alcoholic beverages, beer, and high alcohol liquors. In Henan, they were beer, high and low alcohol liquors. Traditional distilled spirits (bai jiu) are the most popular unrecorded alcohols, and the production volume is often underestimated by official statistics

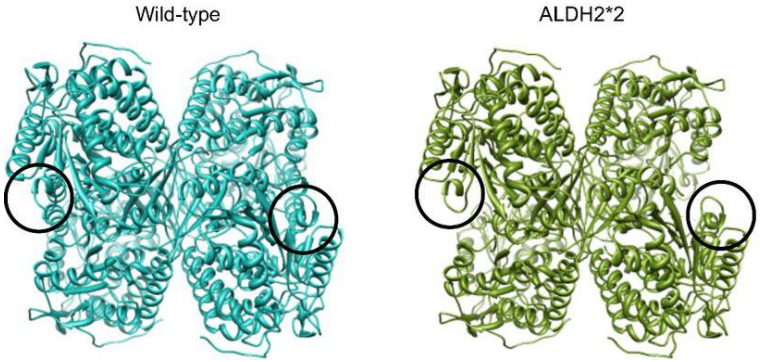



It is of importance to include home brews in the drinking surveys in both China and other countries. The main concern regarding homemade alcoholic beverages is the easy access to high alcohol drinking at an exceedingly affordable price. Furthermore, Newman et al commented that the major health risks posed by unrecorded Chinese bai jiu include not only the high concentration of alcohol but also the presence of toxic impurities including heavy metals and acetaldehyde.

Genetics and ALD pathogenesis



European



Acetaldehyde accumulation

Vasodilation

"Facial Flushing"

This so-called alcohol flushing response is also known as *"Asian flush"* or *"Asian glow"*.

In East Asians, up to 40% have a polymorphism of ALDH2 in which glutamate is substituted for lysine at position 487.

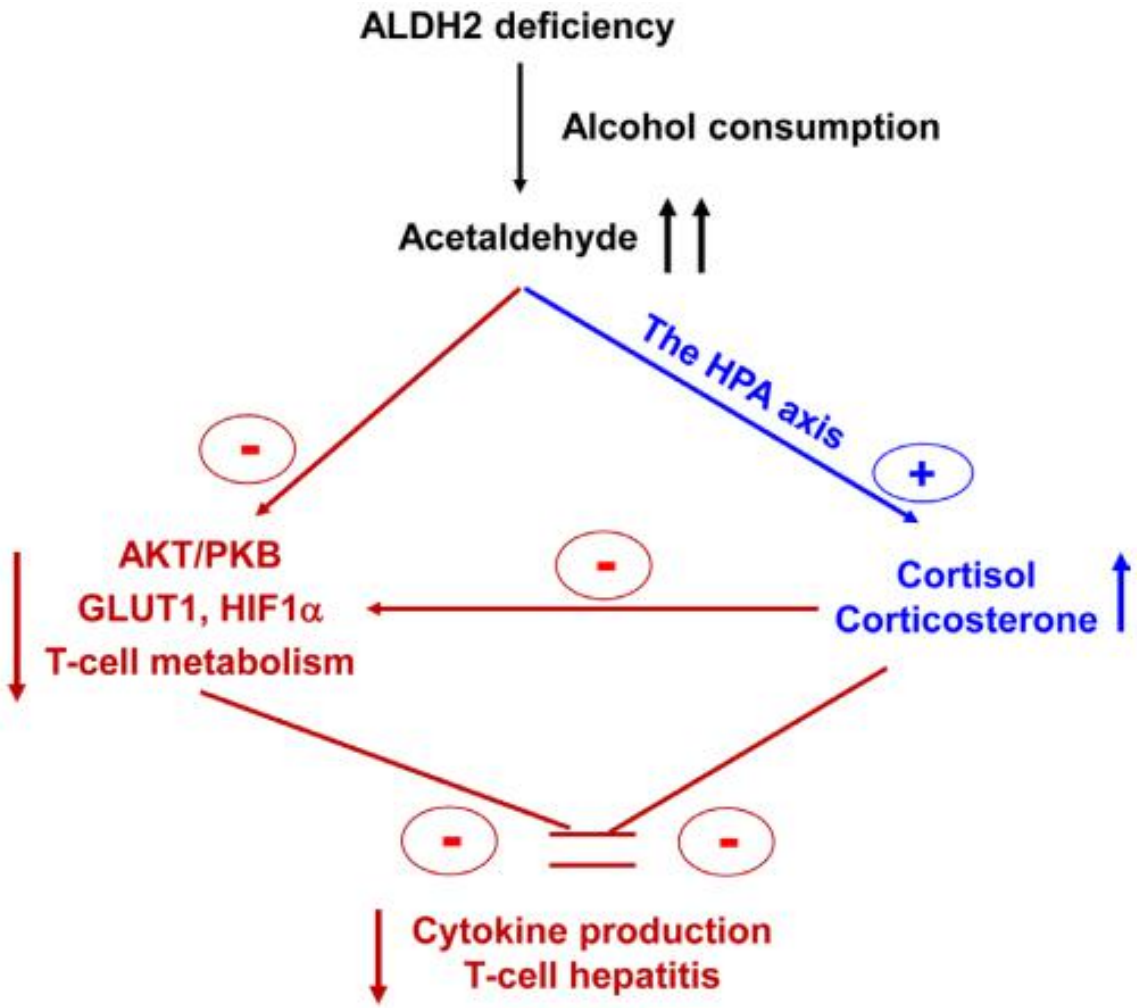
Asian

Except ALDH2, other enzymes can also remove acetaldehyde from the body

- **Glyceraldehyde-3-phosphate(G3P) dehydrogenases**
- **Aldehyde and Xanthine oxidases**
- **Cytochrome P450**

"the king of the hill"

ALDH2



Gao Y, Zhou Z, Ren TY, et al. Gut. 2018 Aug

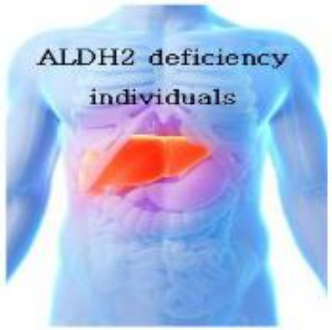
ALDH2 knockout Mice

ETOH-fed

Acetaldehyde ↑

Corticosterone ↑

ConA induced T cell response



Chronic alcohol consumption

OR

Non alcohol consumption

Acetaldehyde ↑

Other aldehydes ↑

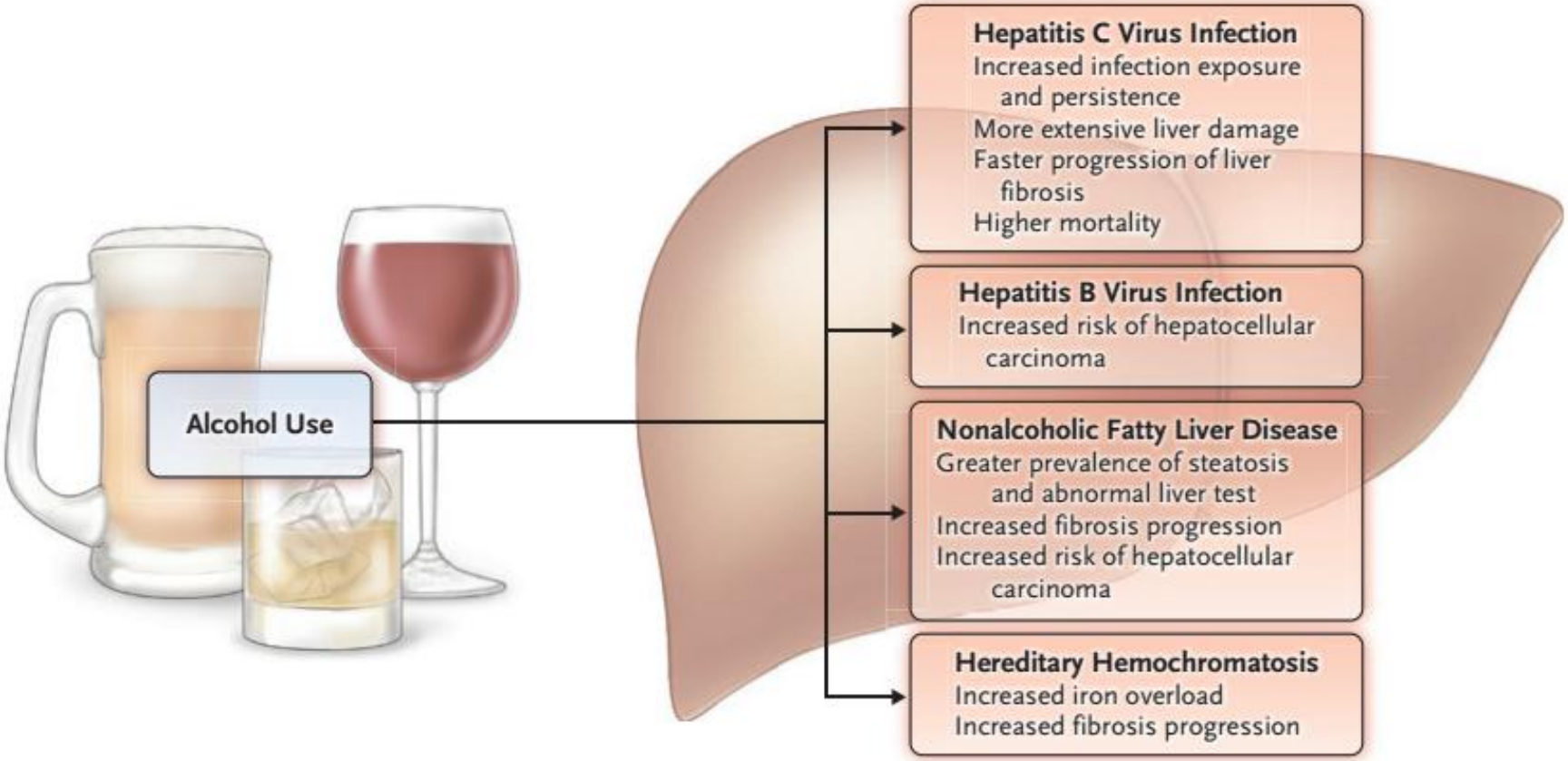
Viral infection

Hepatic cirrhosis

Hepatocarcinoma

HBV or HCV infection

- A combination of excessive alcohol consumption and endemic chronic HBV/HCV infection may promote advancement of chronic liver diseases, regardless of the initial etiology, and increase the ALD and chronic HBV infection (CHB) burden in China
- Alcohol consumption by chronic HBV- or chronic HCV-infected patients is an additional risk factor for accelerated progression of chronic hepatitis to liver cirrhosis, HCC, or liver-related mortality
- Alcohol consumption may thus enable HCV evasion from the immune response and facilitate HCV replication
- Further studies should be directed at exploring the impact of ALD on the long-term outcomes of antiviral therapy



N ENGL J MED 379;13 NEJM.ORG SEPTEMBER 27, 2018

OUTLINE

- EPIDEMIOLOGY OF ALD IN CHINA
- RISK FACTORS FOR ALD IN CHINA
- MANAGEMENT OF ALD IN CHINA

All treatment of alcohol-associated liver disease begins with

abstaining from drinking

- International guidelines from China, the United States, and Europe, as well as questionnaires including the Alcohol Use Disorders Identification Test (AUDIT), the Michigan Alcoholism Screening Test (MAST), and the CAGE alcohol screening questionnaire, emphasize the discrimination of alcohol dependence or abuse.

- Currently, a combination of drug therapy, psychosocial interventions, and medical management is recommended.

Pharmacotherapy to Control Drinking

- **Disulfiram:** potentially toxic in cirrhosis
- **Naltrexone:** black box warning
- **Acamprosate:** not studied in cirrhosis,
- doubts about efficacy
- **Topiramate:** not studied in cirrhosis
- **Baclofen:** efficacy in 1 RCT in cirrhosis, sleepiness

Nutriti

- Malnu
- Good r

Achieven ...educes complicati

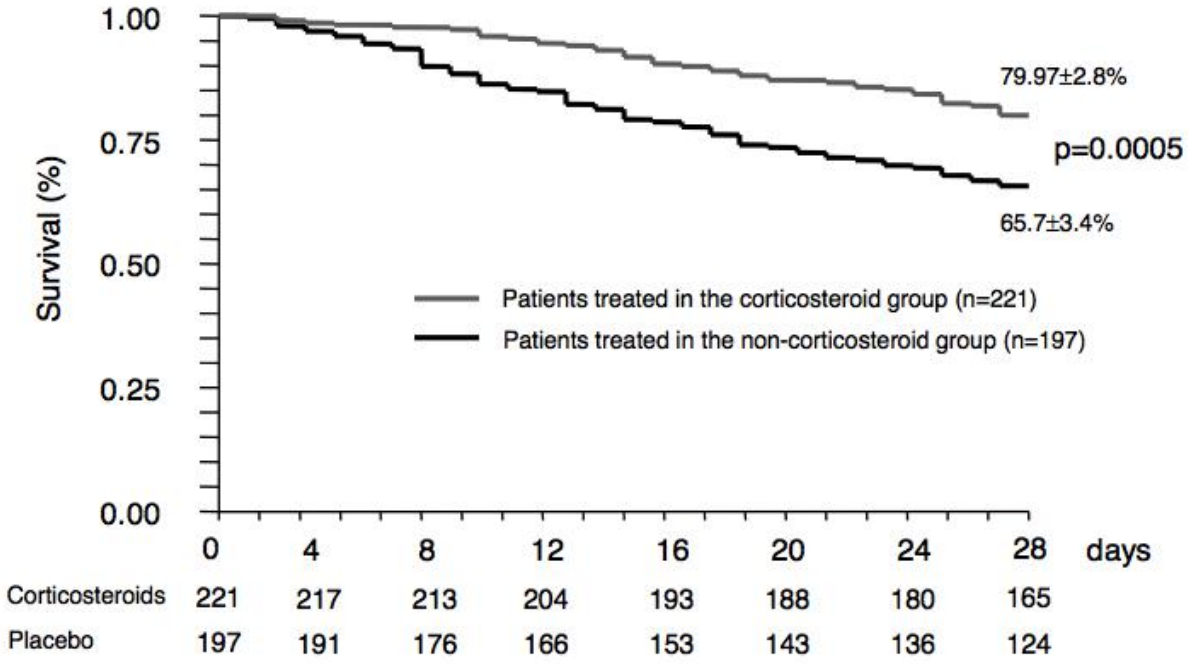
- Encourage voluntary oral intake when possible
- Enteral support with dietary supplements is strongly preferred over parenteral support
- Feeding tubes should be used only when absolutely necessary
- Evidence is lacking to support use of parenteral nutrition
- Protein 1.5 g/kg body weight
- Total calories of 30 kcal/kg body weight (minimum)
  - 50–55% as complex carbohydrates
  - 25–30% as fat, preferably avoiding polyunsaturated fat
  - 20% as protein
- Provide night time snack of 500–700 kcal to avoid hepatic glycogen depletion
- B complex multiple vitamins daily
- Thiamine 100 mg daily
- Zinc 220 mg/kg unless patients have renal insufficiency
- Correct magnesium deficiency
- Correct hypokalemia
- Correct hyponatremia cautiously
- Use of probiotics is unproven, but may be beneficial if patients are on broad spectrum antibiotics

Anti-inflammation therapy

- **Corticosteroid is the only treatment proven to reduce mortality from severe alcoholic hepatitis (SAH)**
- **Corticosteroid therapy improves short-term survival but has no effect on long-term survial in SAH patients**
- **AASLD guideline recommends prednisolone 40 mg daily or the equivalent *dose* of methylprednisolone, 32 mg daily.**
- **Glucocorticoids should be discontinued in patients who fail to improve based on Lille criteria within 7 days.**

Meta Analysis of Individual Data from 4 RCTs of Corticosteroids in Patients with Severe Alcoholic Hepatitis

Mathurin et al. GUT 2010



Corticosteroid Therapy: Cautious!

- ***The increased risk of infection*** leads to no change in survival at 90 days and 1 year after diagnosis. Infections often precede development of AKI and MOF, which has a high mortality rate
- Some patients ***do not respond to glucocorticoids therapy***

Levels of GR-B, an alternatively spliced form of GR that essentially acts as a dominant negative inhibitor of glucocorticoid action

Antioxidant therapy

Pentoxifylline

S-adenosylmethionine (SAMe) therapy

Early Liver transplantation for AH

- AASLD recommends at least 6 months is needed for stop drinking before liver transplantation
- Many SAH patients survive less than 6 months.
- It is worth paying attention to early liver transplantation for this group of patients

Liver Transplantation for Severe Alcoholic Hepatitis, Updated Lessons from the World's Largest Series

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CONCLUSIONS: In the largest cohort of patients reported, outcomes after liver transplantation for SAH had excellent 1-year outcomes, similar to those seen in patients who received transplants with 6 months of sobriety. Recidivism was similar in the 2 groups. Early liver transplantation for SAH represents life-saving therapy for patients with otherwise high mortality, calling into question the utility of the 6-month rule in predicting outcomes in patients receiving transplants for alcoholic liver disease. (J Am Coll Surg 2018;226:549–557.

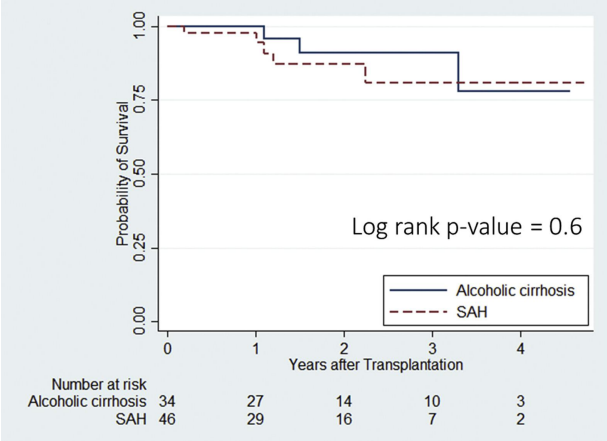

Figure 1. Kaplan-Meier estimates of patient survival. Recipients transplanted for severe alcoholic hepatitis (SAH) (dashed line) had similar survival estimates compared with those transplanted for alcoholic cirrhosis (solid line) (p = 0.6).

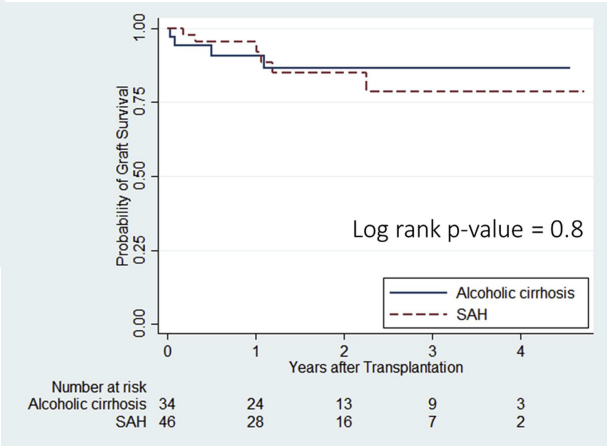

Figure 2. Kaplan-Meier estimates of graft survival. Recipients transplanted for severe alcoholic hepatitis (SAH) (dashed line) had similar graft survival estimates compared with those transplanted for alcoholic cirrhosis (solid line) (p = 0.8).

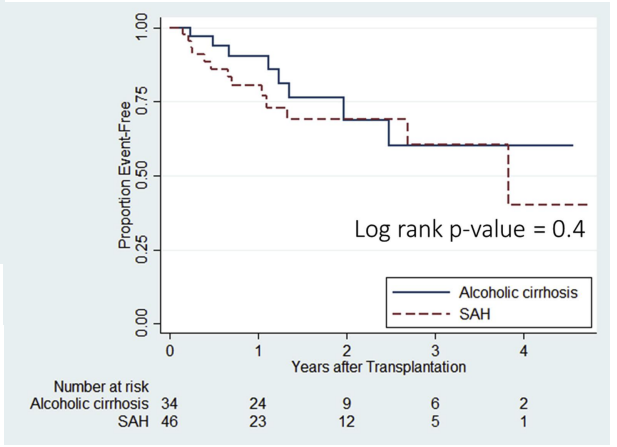

Figure 3. Kaplan-Meier estimates of alcohol recidivism. Recipients transplanted for severe alcoholic hepatitis (SAH) (dashed line) did not have significantly different relapse to alcohol than those transplanted for alcoholic cirrhosis (solid line) (p = 0.4).

No difference in patient or graft survival or in alcohol relapse for SAH patients compared with cirrhosis patients receiving transplants for alcoholic cirrhosis under standard of 6 months of sobriety

Future therapy of AH

- Anti-inflammation
- Anti-oxidants and hepatoprotection
- Nuclear receptor agonists
- Gut microbiota

Pathology	Therapeutic target	Therapy	Trial ID: clinicaltrials.gov, EudraCT, PMID
Portal translocation of gut microbiota	Intestinal dysbiosis	Oral Rifaximin	NCT02116556 2014-002264-33
		Oral vancomycin, gentamycin, meropenem	NCT03157388
		Faecal microbiota transplant	NCT03091010 NCT02458079
		Probiotics Lactobacillus *spp.*	NCT01922895 NCT02335632
	Intestinal mucosal integrity	Zinc	NCT01809132
Enterohepatic circulation of bile acids	Farsenoid receptor	Obeticholic acid	NCT02039219
Hepatic inflammation	IL-1β	Anakinra Rilonacept Canakinumab	NCT01809132 NCT01903798 2017-003724-79
	IL-22	F-652 (recombinant fusion protein of IL-22 and IgG2-Fc)	NCT02655510
	TLR-4 Non-specific	Anti-LPS IgG with Bovine colostrum	NCT02473341 NCT01968382
		Mycophenolate mofetil	NCT01903798
Hepatocellular injury and repair	Oxidative stress	S-Adenosyl methionine	NCT00851981 NCT02024295
		Metadoxine	NCT02019056 NCT02161653 PMID 24756009
		N-acetylcysteine	NCT00863785 PMID 22070475
	Hepatocyte regeneration	GCSF	NCT01820208 NCT02971306 NCT02442180 NCT01341951 NCT02776059
Complications	Infection	GCSF	NCT01820208 NCT02971306 NCT02442180 NCT01341951 NCT02776059
		Augmentin	NCT02281929
		Ciprofloxacin	NCT02326103
		N-acetylcysteine	NCT03069300
	Kidney injury	Terlipressin	2006-002837-19

Active published clinical trials for alcoholic hepatitis listed by the U.S.

National Library of Medicine at clinicaltrials.gov

European Clinical Trials Database at: EudraCT.ema.europa.eu

IL-22: the unique feature

- IL-22 is probably only cytokine that is produced by immune cells but does not target immune cells
- IL-22 mainly targets epithelial cells
- IL-22 is a key survival factor for hepatocytes
- IL-22 signal is simple and specific: predominantly activates cell survival signal STAT3
- IL-22 levels are not elevated in many types of liver diseases (ALD, NAFLD, DILI)(elevated in viral hepatitis)
- Additional Benefits: Anti-bacteria, protection against gut and renal epithelial injury
- rIL-22 protein is currently on a phase IIb trial for alcoholic hepatitis (Dr. Shah, Mayo; Dr. Gao, NIAAA)

Combination therapy: new hope for alcoholic hepatitis (AH)?

Bin Gao, MD PhD, Chief, Lab of Liver Diseases, NIAAA, NIH
Vijay Shah, MD, Chief, Division of Gastroenterology, Mayo Clinic

Clinics and Research in Hepatology and Gastroenterology 2015

Alcoholic Hepatitis

Inflammation

Immune cells:
Neutrophils, Macrophages, T, B, DC, NKT and NK cells

Inflammatory mediators
TNF-α, IL-1, IL-17, IL-6
CXCL3, CXCL4, CXCL5, CXCL6, CXCL10, TNFRSF12A (Fn14), CXCL1, IL-8, MCP-1, Osteopontin, CCL5, TNFRSF1, TRAF1, TRAF3, TRAILR1 and TNFSF12 (TWEAK), ……

Steroids

Patients with a modified Maddrey's discriminant function score > 32 or hepatic encephalopathy should be considered for treatment with prednisolone 40 mg daily for four weeks followed by a taper

Impaired liver repair

Ethanol direct inhibition of liver regeneration by blocking regenerating signals eg. STAT3

Ethanol direct inhibition of liver progenitor cell proliferation

Steroids inhibit liver regeneration

IL-22: Hepatoprotection

Protects against liver injury
Promotes liver regeneration
Ameliorates steatosis
Ameliorates liver fibrosis
Few side effects:
Promotes liver cancer cell growth

Complications

- Bacterial infection
- Renal failure
- Intestinal epithelial cell injury

IL-22: additional benefits

Inhibits bacterial infection,

Epithelial protection in many organs

Treatment of alcoholic liver disease (ALD) and alcoholic hepatitis (AH)

STOP drinking Help from family members and drugs

Mild to moderate Early ALD

Hepatoprotection

Recovery

Severe AH

Prednisolone 40 mg daily for 4 weeks followed by a taper

Clinical trials:

IL-1 inhibitor; gut microbiota and gut barrier (probiotics, Zinc, antibiotics); ASK1 inhibitor

IL-22, G-CSF
Antibiotic

End-stage AH Multiple organ failure

Liver transplantation

6–month abstinence

Early transplantation (< 6 months)

Traditional Chinese Medicine

- Many ALD patients in China, especially those who fail to respond to treatment with small molecule drugs, pursue traditional Chinese medicine (TCM) as an adjunct or alternative therapy. Several TCM formulae are known to be effective at mitigating hepatic fibrosis. Several herbal medicines, including Cnidium monnieri (L.) Cusson (Apiaceae), and Curcuma longa L. (Zingiberaceae), have been used for ALD treatment in China
- TCM formulae consist of multiple components with complex chemistry and pharmacology characteristics, they could be made more effective once the active components and their underlying mechanisms are clearly elucidated. The potential side effects of TCM must be evaluated through large-sample, randomized, double-blind clinical trials that are consistent with the principles of evidence-based medicine


重磅出击
HEAVY ATTACK


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调控

Regulation of alcohol consumption

Alcohol consumption is impacted by alcohol and taxation policies as well as social and cultural norms.
In China, the alcohol taxes were increased in 2002, and the alcohol sale restrictions and the license requirement were implemented in 2004. In 2007, the laws that punish drunk drivers began to be enforced, and restrictions on alcohol advertisements took effect in 2010.

However, the alcohol policy in China is weaker than those in its neighboring countries in many aspects, which favors alcohol consumption, leading to consequent alcohol-related problems:(1)There are no minimal legal age requirements for purchasing or selling alcoholic beverages;(2) No restrictions on home-made alcohol beverages, no enforceable regulations on alcohol sponsorship/sale promotion;(3)No legal requirements for warning labels on alcohol advertisements/containers in China.

We advocate a strong and sensible alcohol policy that effectively regulates alcohol production quality and consumption to reduce the occurrence of ALD in China.


THANK YOU.