Alcoholic Related Gastrointestinal and Liver Diseases

Pisaln Mairiang MD
Department of Internal Medicine
Khon Kaen University Thailand

Complication associated with chronic alcoholic drinker

Neurologic disorders

- Intoxication
- Addiction
- Withdrawal syndrome
- Seizures
- Delirium tremens
- Wernicke – Korsakoff syndrome
- Alcoholic cerebellar degeneration
- Peripheral neuropathy
- Ischemic stroke
- Intracranial hemorrhage

Malignancy

- Oral and pharyngeal
- Laryngeal
- Esophageal
- Stomach
- Breast
- Liver
- Colon

Cardiac disorders

- Hypertension
- Cardiomyopathy
- Arrhythmias

Hematologic disorders

- Bone marrow suppression
- Nutritional and blood loss anemia

Complication associated with chronic alcoholic drinker

Hepatic dysfunction
- Cirrhosis
- Alcoholic hepatitis

Immune system disorders
- Impaired immune system
- More frequent infections

Gastrointestinal disorders
- Gastritis
- Esophagitis
- Duodenitis
- Peptic ulcer disease
- Pancreatitis

Psychiatric
- Psychiatric comorbidities are exacerbated
- Suicide risk increases

Musculoskeletal
- Alcoholic myopathy
- Osteoporosis

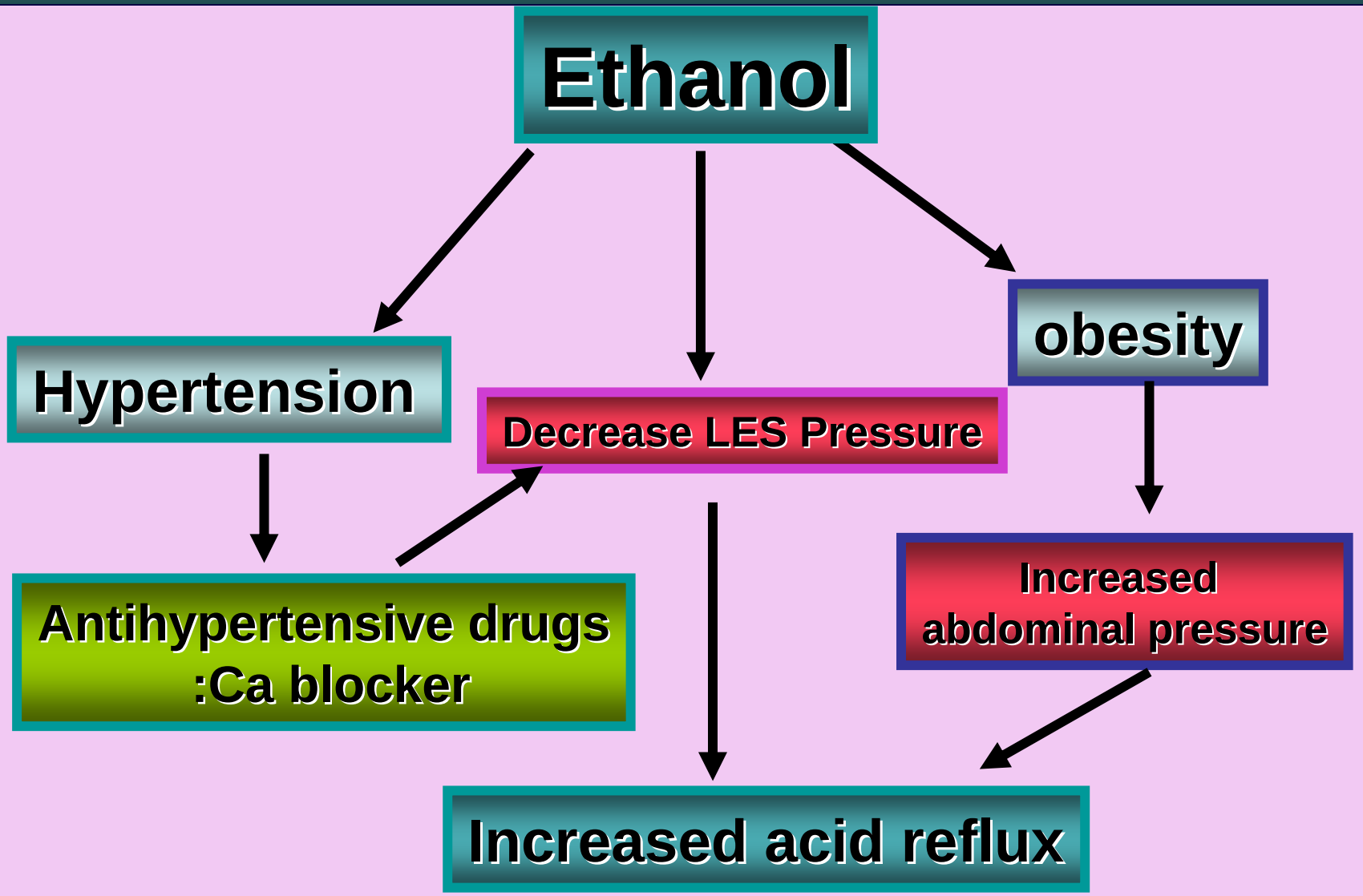
Others
- Sleep disturbance
- Sexual dysfunction
- Obstructive sleep apnea
- Periodic limb movement disorders
- Accidents and injury (to self and others)

GI complications associated with alcohol

- Esophagitis
- Peptic ulcer diseases
- Pancreatitis
- Alcoholic liver diseases
- Malignancy
  - Esophagus
  - Liver
  - Colon

Esophagus

Alcoholic induced esophagitis



Risk factors for erosive esophagitis analysis of 6215 cases

Risk factors	OR (95% CI)	*P* - Value
Male gender	2.177 (1.576 – 3.008)	< 0.0001
Age > 60 yr.	1.869 (1.115 – 3.314)	0.0177
BMI > 25 – 30 kg/m^2	1.703 (1.237 – 2.344)	0.0011
BMI > 30 – 40 kg/m^2	1.971 (1.327 – 2.926)	0.0008
Regular alcohol intake	1.706 (1.232 – 2.362)	0.0013
Duration of disease > 1 – 5 yr.	1.475 (1.067 – 2.040)	0.0187
Duration of disease > 5 yr.	1.607 (1.137 – 2.272)	0.0072
Smoker / ex – smoker	1.333 (1.004 – 1.771)	0.0469
Single	1.638 (1.184 – 2.265)	0.0029
Retired	0.615 (0.390 – 0.967)	0.0354
H. Pylori positive	0.610 (0.440 – 0.845)	0.0029

Labenz J, et al. Am J Gastroenterol 2004;1652-6..

Alcohol and Esophageal cancer

- Alcohol increase risk of squamous cell carcinoma not adenocarcinoma
- Subjects who consumed more than 4 can of beer/day for 20 years, have a **9.7 fold higher risk (95%CI =4.3-22.0)**

  Wu MT et al Br J Cancer 2001;85:658-60
- Genetic polymorphisms of alcohol and aldehyde dehydrogenases is related to the increasing risk of squamous cell cancer

  Wu CF et al World J Gastroenterol 2005;11:5103-08

Joint effect of ADH2 and ALDH2 genotypes on esophageal cancer risk

ADH2	ALDH2	Case (%) n=134	Control (%) n=237	OR (95% CI)	AOR (95% CI)
1/2 or *2/2*	*1 / *1	23 (17.2)	112 (47.3)	1	1
*1 / *1		9 (6.7)	8 (3.4)	4.20 (1.49 – 11.81)	3.54 (0.93-13.53)
*1/*2 or *2/*2	*1/*2	69 (51.5)	98 (41.4)	2.63 (1.58 - 4.37)	4.81 (2.17-10.70)
*1 / *1		30 (22.4)	7 (3.0)	16.00 (6.40 - 39.99)	36.79 (9.36-144.65)
*1/*2 or *2/*2	*2/*2	3 (2.2)	11 (4.6)	1.02 (0.27 – 3.88)	3.40 (0.63-18.33)
*1/*1		0	1 (0.4)	-	-

Aldehyde level determines the risk of cancer

Wu CF, et al. World J Gastroenterol 2005. 11(33):5103-08.

Stomach

Peptic ulcer disease and alcohol

- **Wine and beer are potent gastric acid secretagogues.**
- **Alcohol induced superficial mucosal injury not ulcer.**
- **Mallory Weiss tear .**
- **Drinking moderate alcohol seemed to protect against active *H pylori* infection**

Relation of smoking and alcohol and coffee consumption to active H pylori infection

			Odds ratio (95% CI)	
	No of subjects	No (%) with infection	Crude	Adjusted*
Smoking:				
Never smoked	220	40 (18.2)	1.00	1.00
Former smoker	110	28 (25.5)	1.54 (0.89 to 2.66)	1.48 (0.81 to 2.72)
Current smoker	116	25 (21.6)	1.24 (0.71 to 2.16)	1.57 (0.81 to 3.05)
Alcohol consumption (g ethanol/week)† :				
None	152	35 (23.0)	1.00	1.00
75	152	38 (25.0)	1.11 (0.66 to 1.89)	0.90 (0.51 to 1.59)
> 75	141	21 (14.9)	0.59 (0.32 to 1.06)	0.33 (0.16 to .68)**
Coffee consumption (cups/day):				
None	120	14 (11.7)	1.00	1.00
< 3	138	26 (18.8)	1.76 (0.87 to 3.55)	1.49 (0.71 to 3.12)
3	188	53 (28.2)	2.97 (1.57 to 5.65)	2.49 (1.23 to 5.03)§

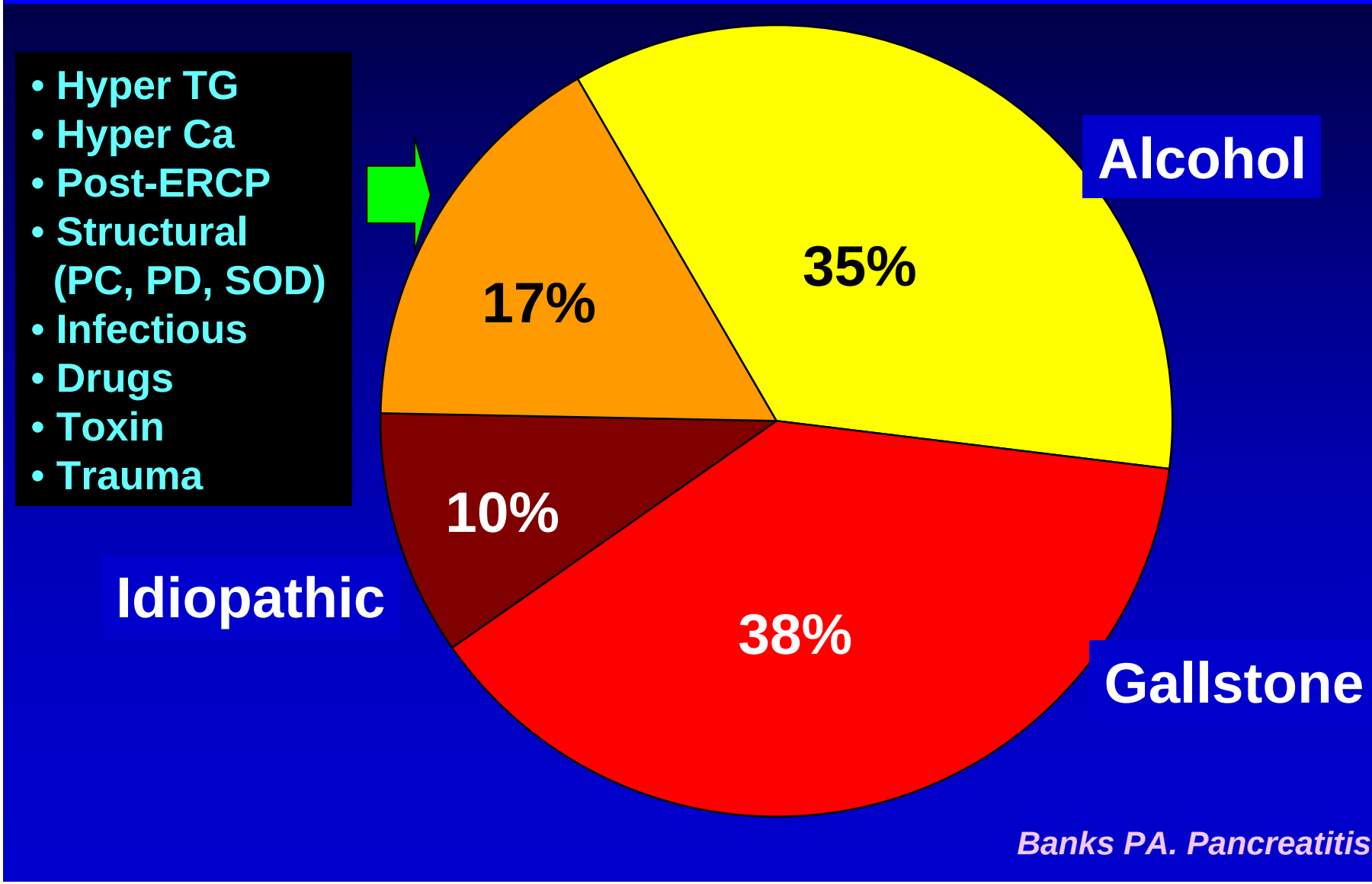
*Adjusted for other variables listed in table and for sex, age, nationality, school education, and parental history of ulcer.
†Assuming that 1 litre of beer and 0.5 l of wine contain on average 50 g ethanol in south Germany.
** P value for trend in multivariable analysis 0.005.
§P value for trend in multivariable analysis 0.007

Hermaan Brenner. BMJ 1997;315:149-92.

Alcoholic related pancreatitis

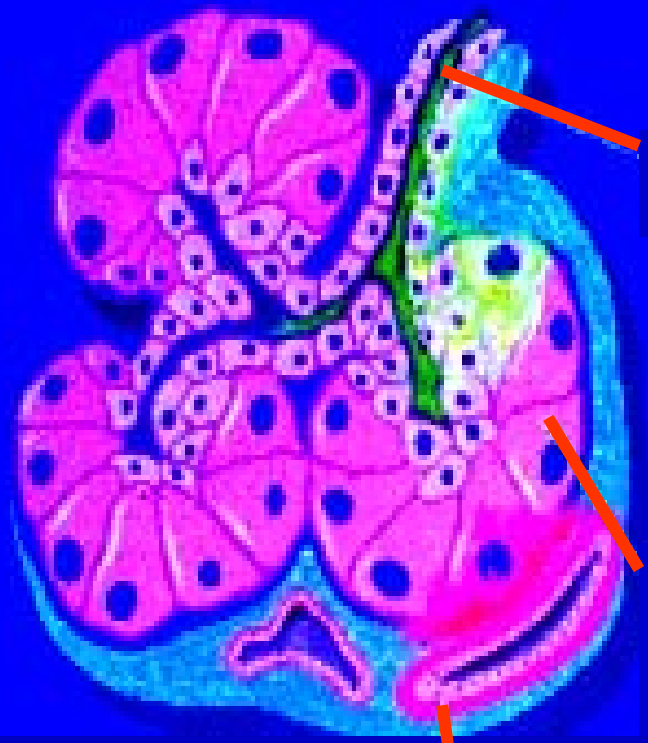
Causes of Acute Pancreatitis

(n = 6,749)



Banks PA. Pancreatitis 1999

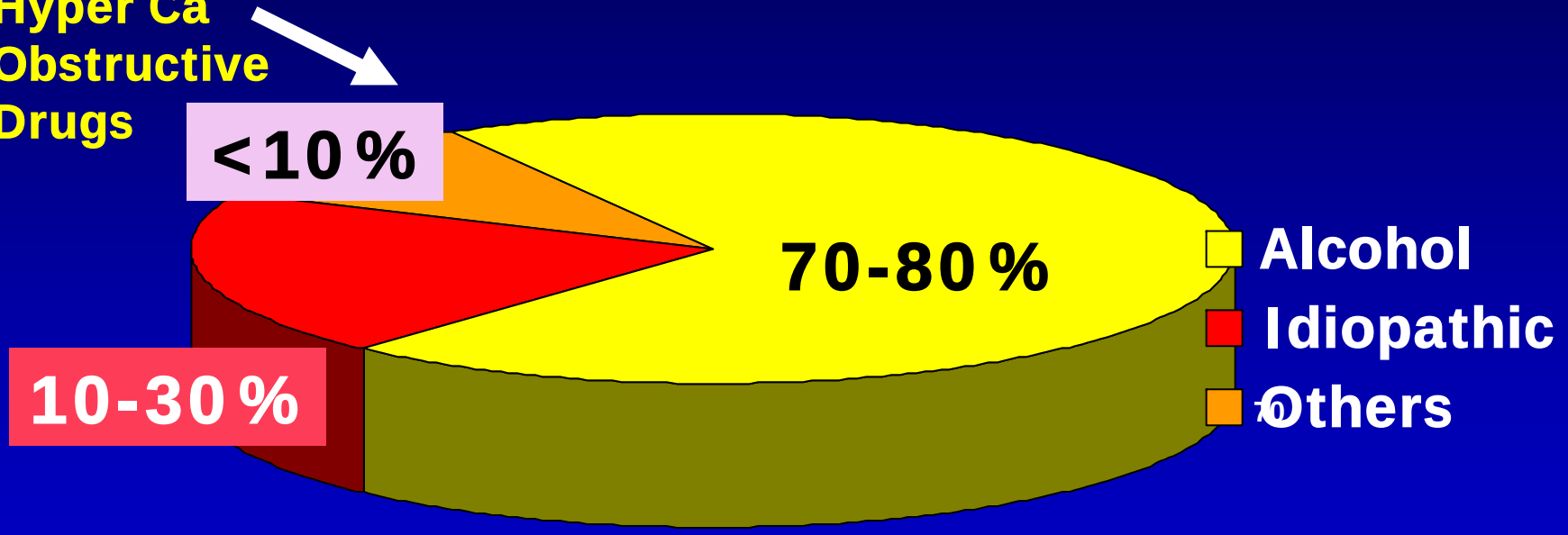
Pathophysiology of inflammation



	Cause	Effect
Duct	Bile reflux **Alcohol** Hypercalcemia Obstruction	↑ Permeability Damage to ducts and acini
Acina cell	**Alcohol** Drugs Infection Hyperlipidemia	Disruption of cell membrances
Blood vessel	Hypotension	Ischemia

Causes of CP

- Hereditary
- Tropical CP
- Hyper Ca
- Obstructive
- Drugs

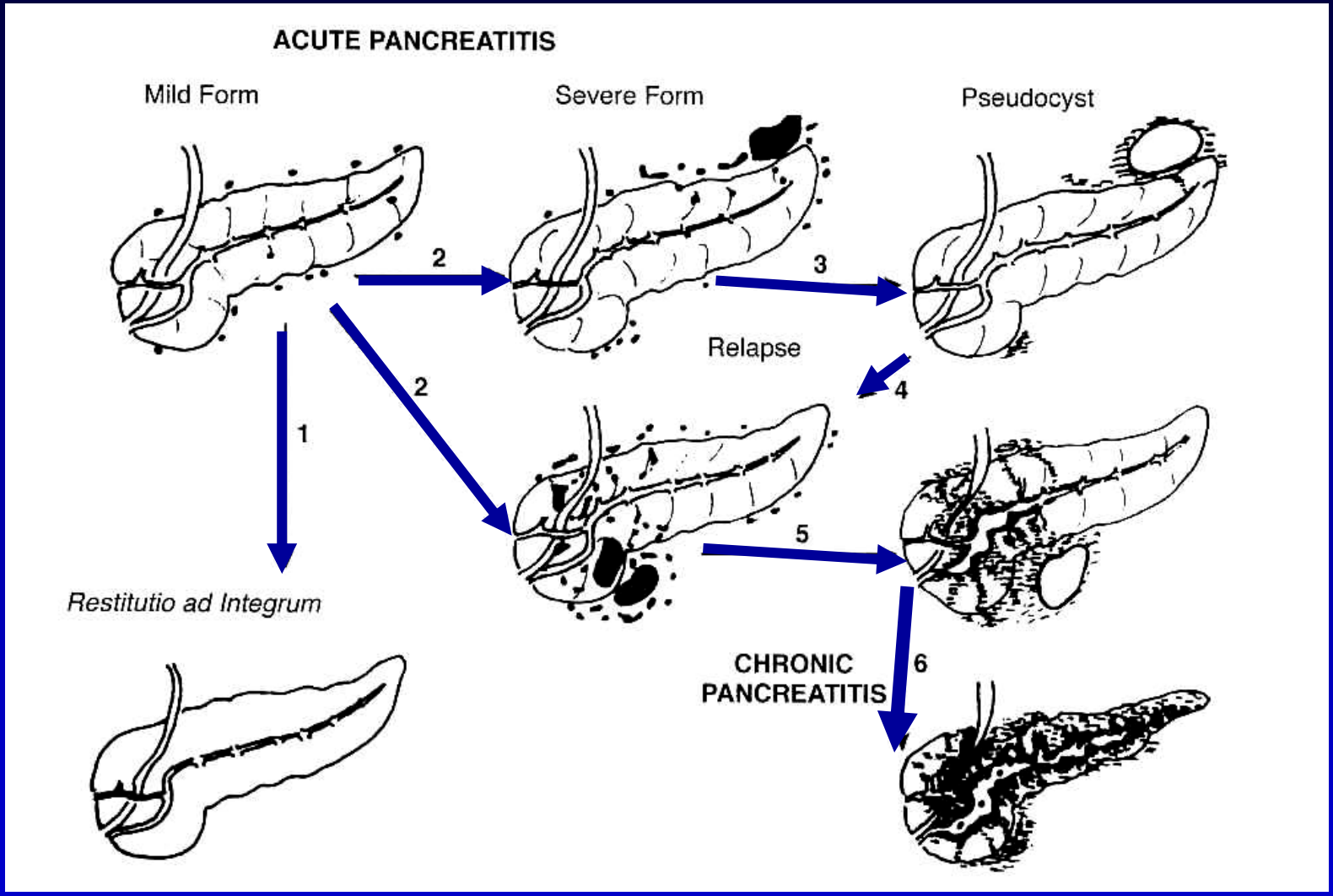


Alcoholic Chronic Pancreatitis (ACP)

- Most common cause of CP
- < 10 % of alcoholics have CP
- No definite threshold amount of alcohol to cause CP (differs from cirrhosis)
- Arbitrary amount used:
  - 50 g[2] - 80 g/day for 5 years in male and smaller amount in female[1]

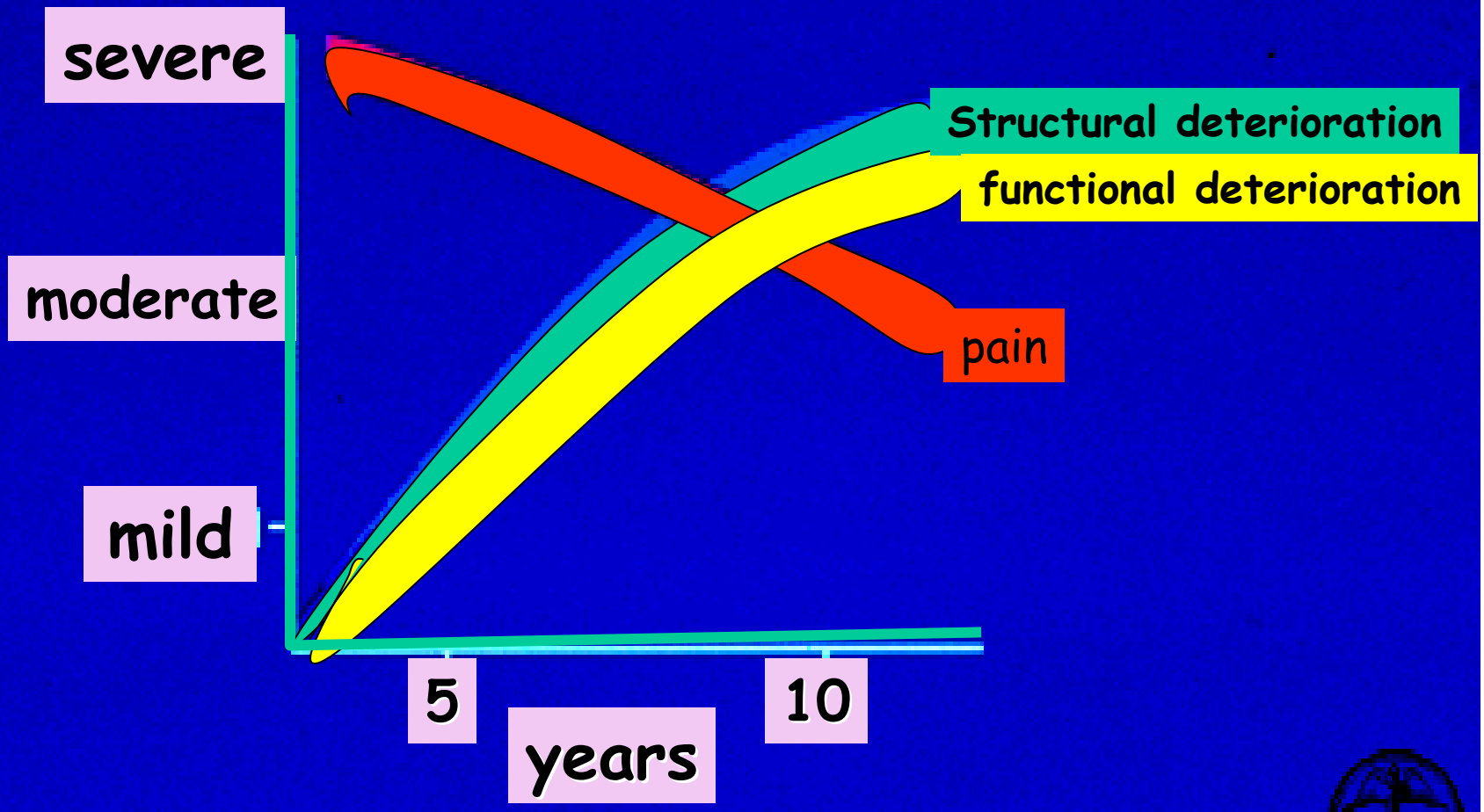
[1]Ammann RW, et al. Pancreas 1997
[2]Layer P, et al. GE 1994

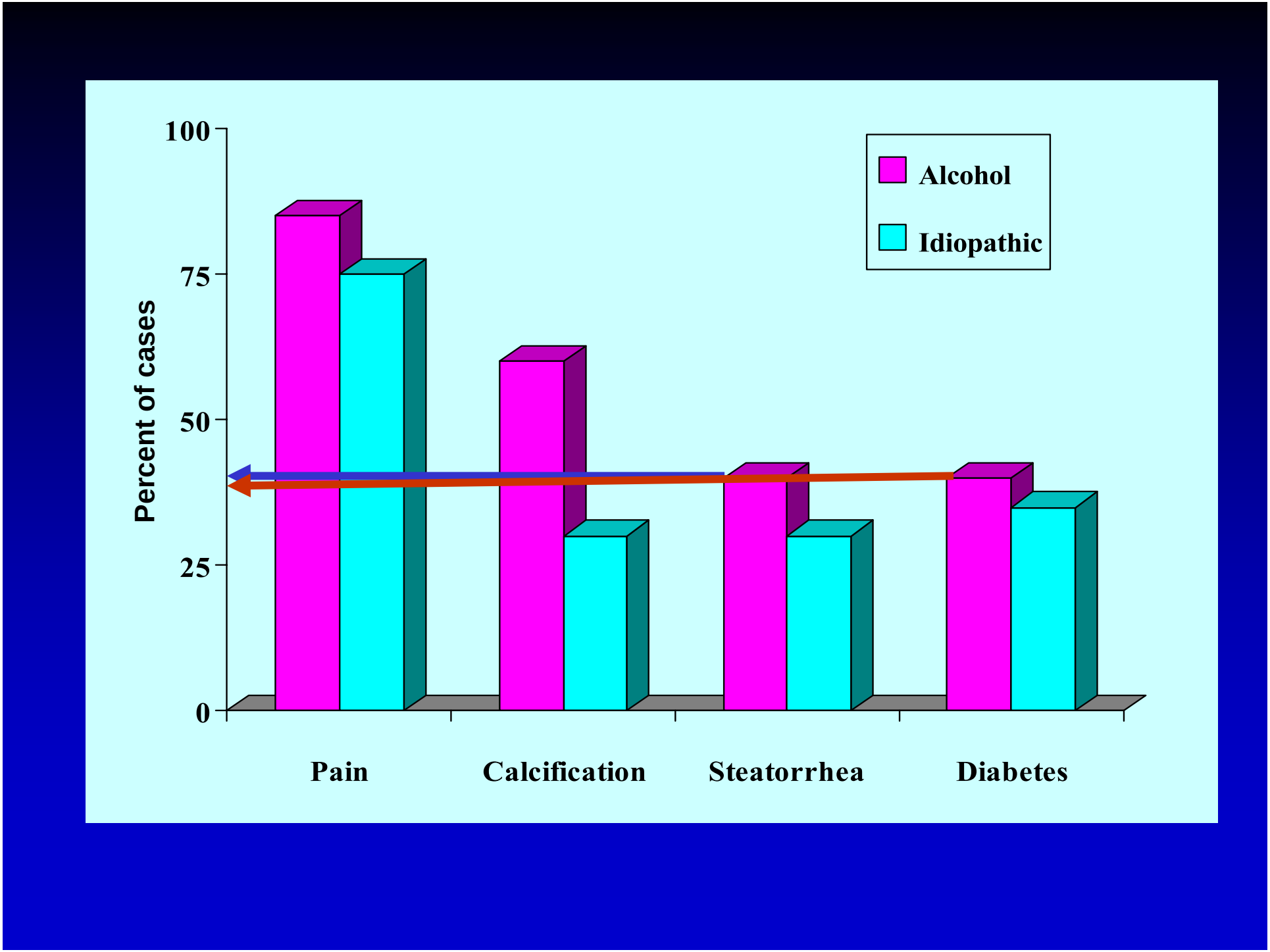
Necrosis-Fibrosis Theory



Kloppel G, et al. Hepatogastroenterol 1991

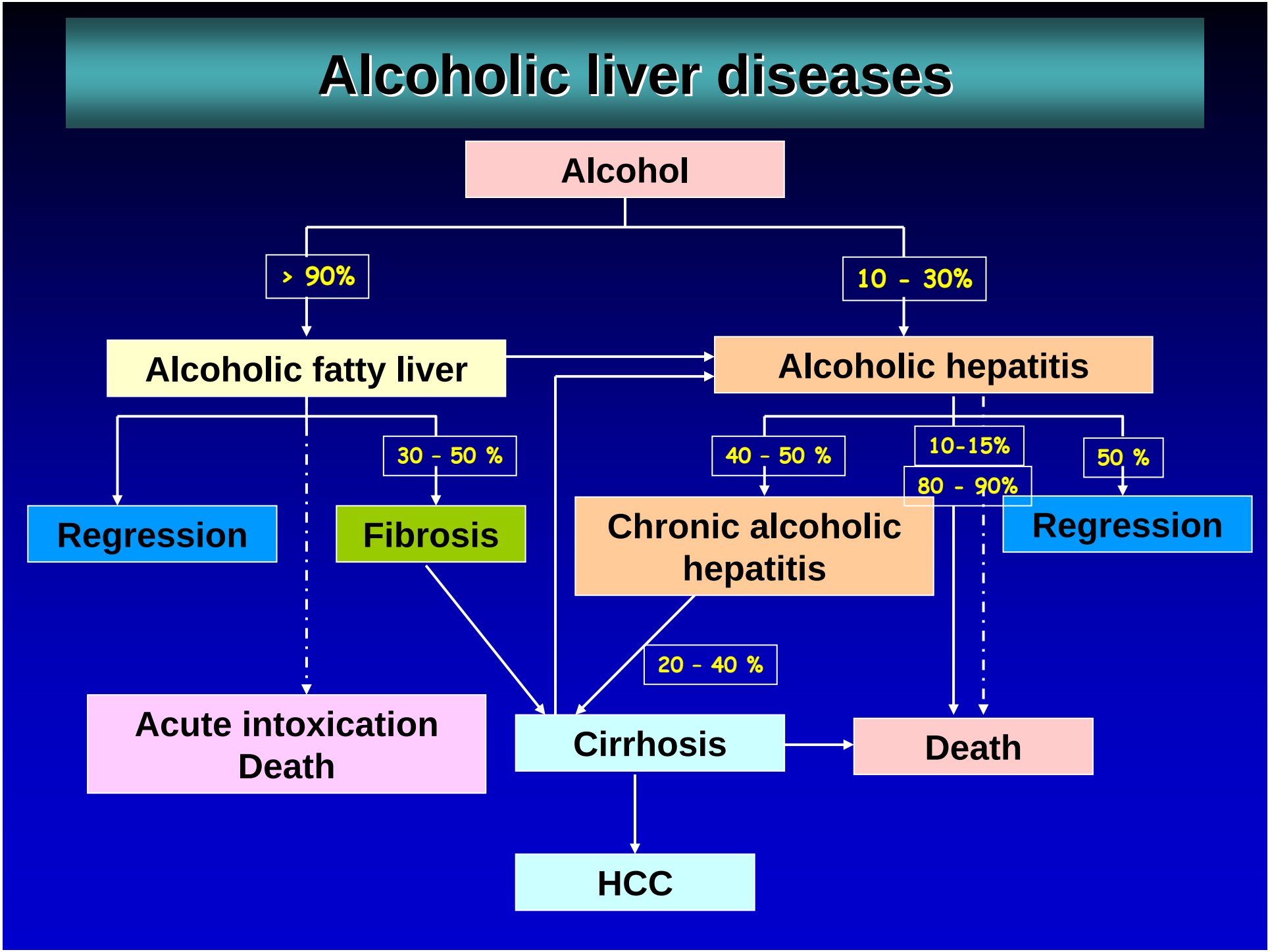
Natural History of Alcoholic Pancreatitis

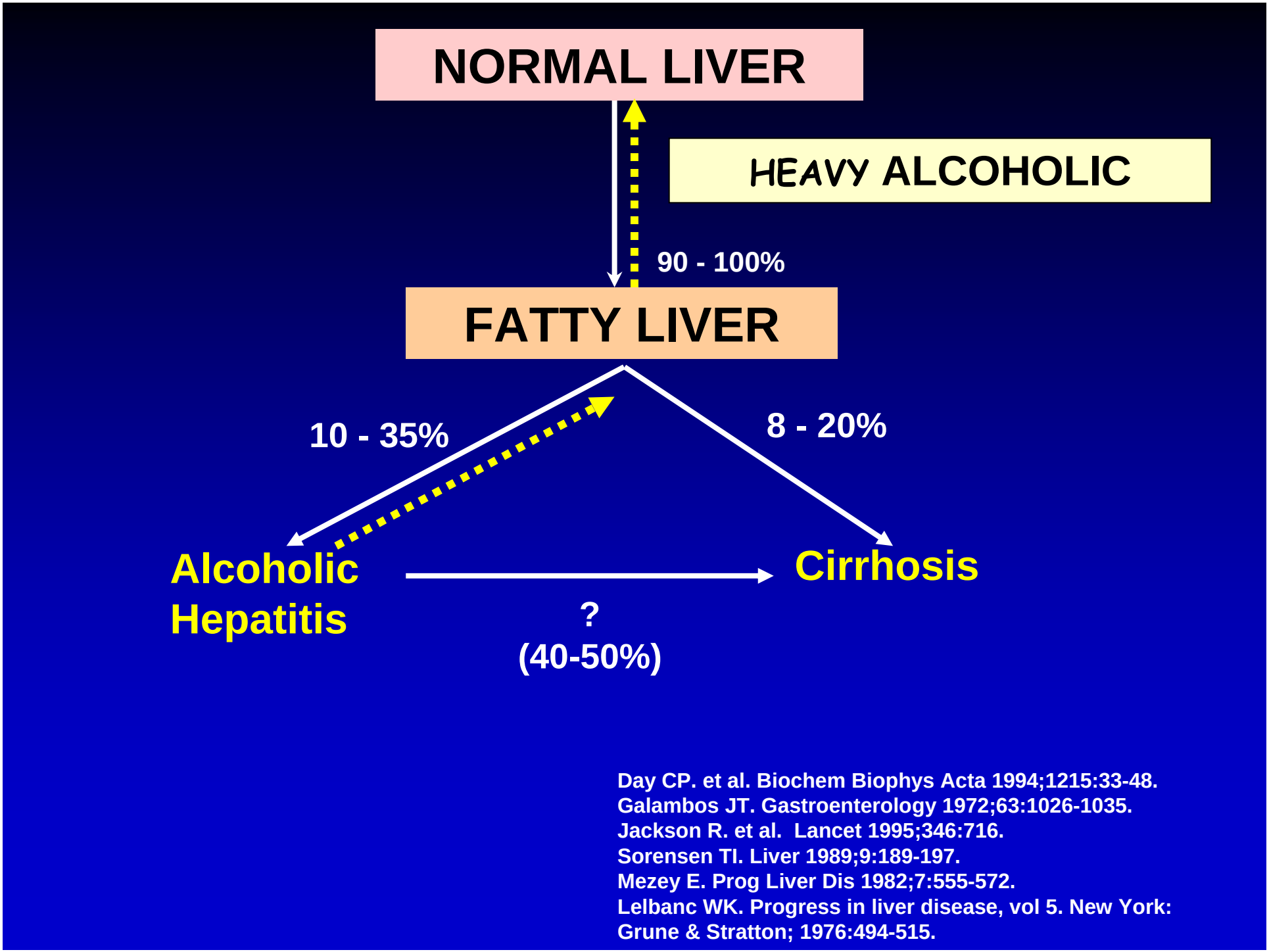



100
75
50
25
0
Percent of cases
Alcohol
Idiopathic
Pain
Calcification
Steatorrhea
Diabetes

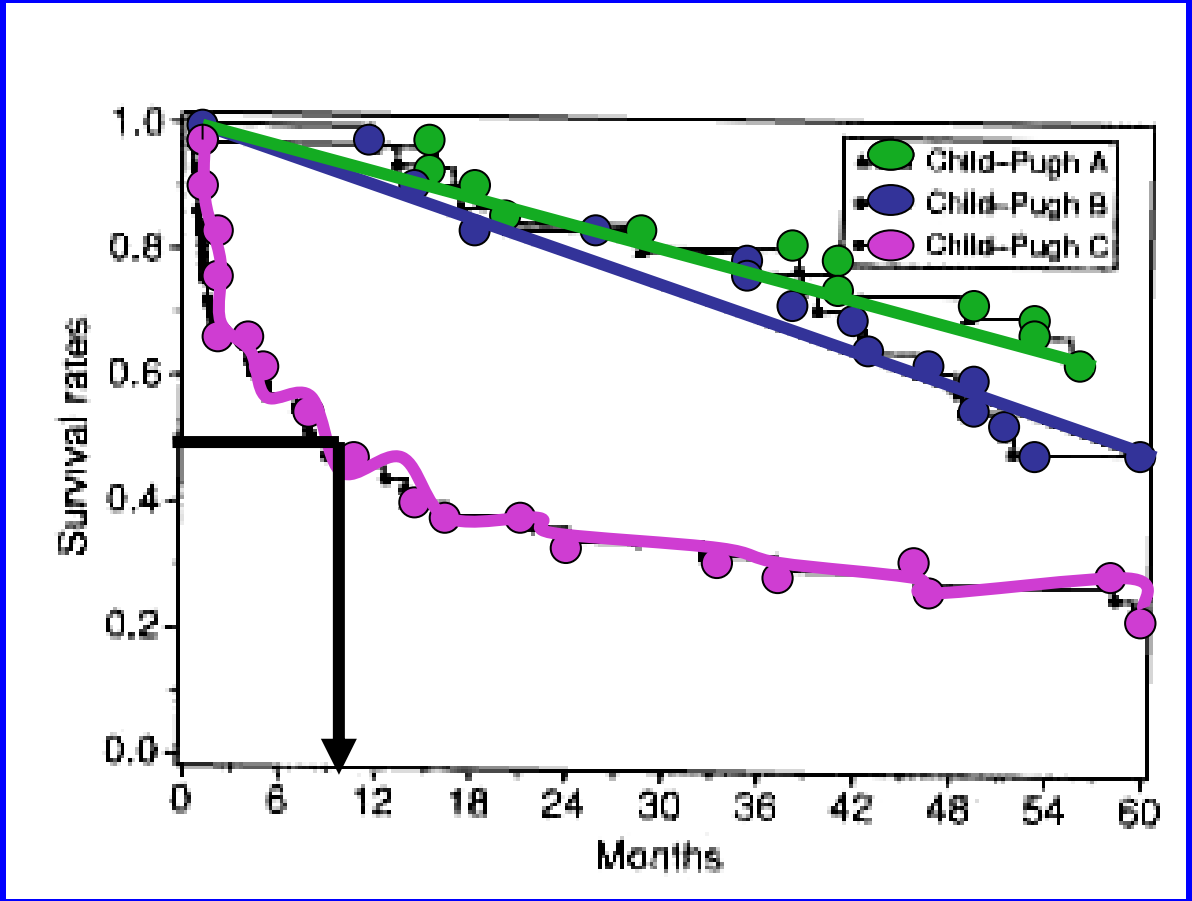
Alcoholic liver disease

Alcoholic liver diseases



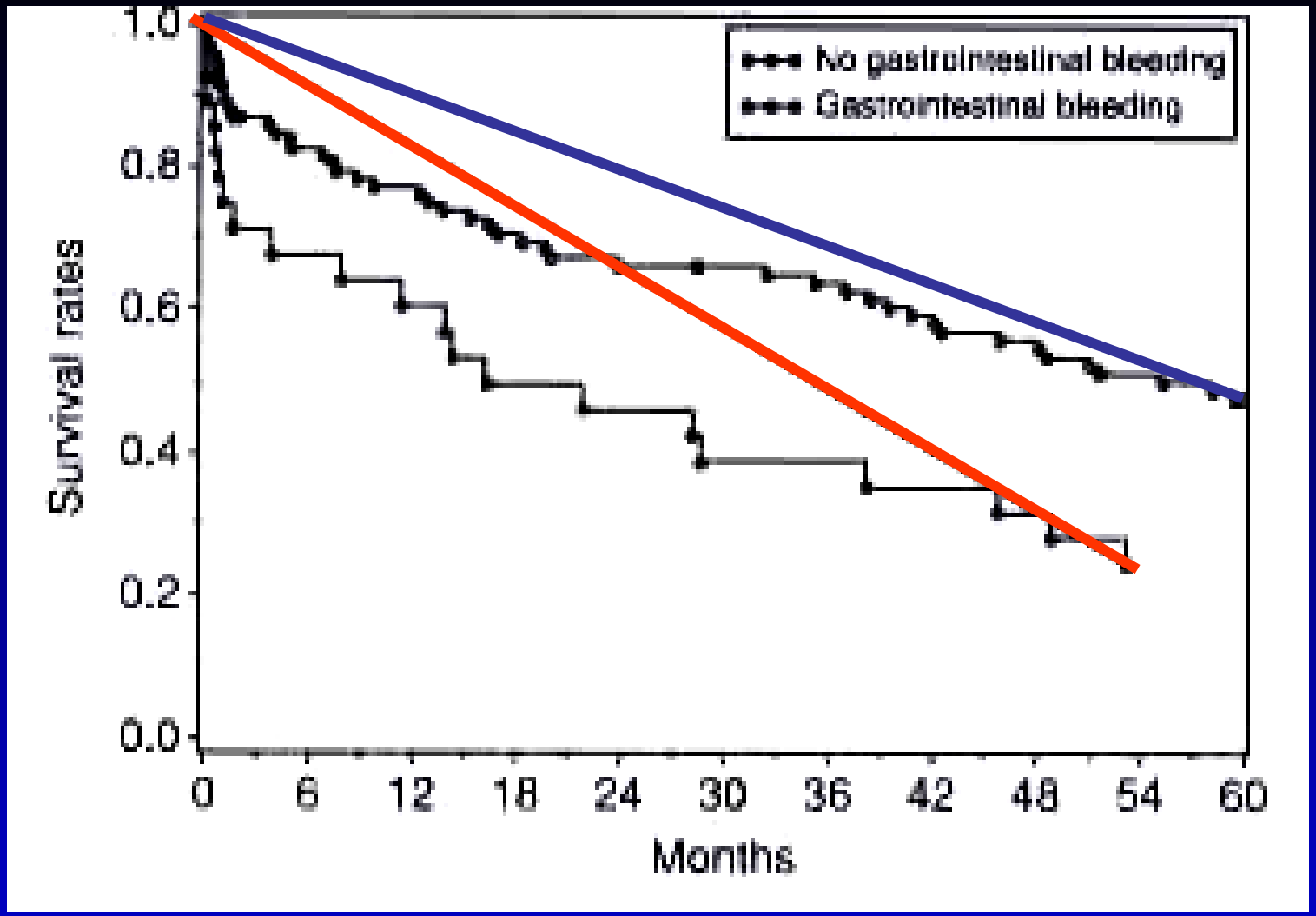


Day CP. et al. Biochem Biophys Acta 1994;1215:33-48.
Galambos JT. Gastroenterology 1972;63:1026-1035.
Jackson R. et al. Lancet 1995;346:716.
Sorensen TI. Liver 1989;9:189-197.
Mezey E. Prog Liver Dis 1982;7:555-572.
Lelbanc WK. Progress in liver disease, vol 5. New York: Grune & Stratton; 1976:494-515.



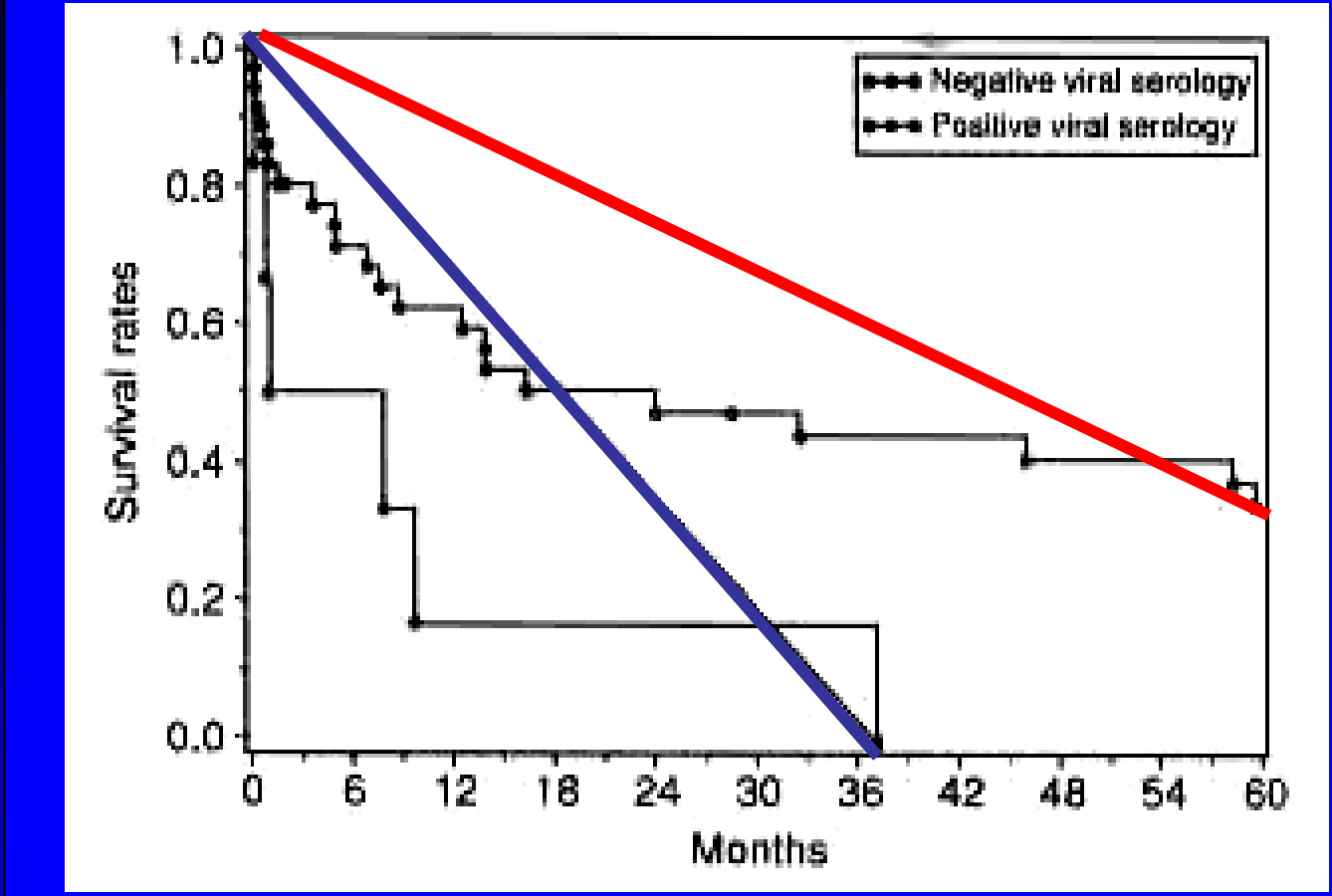
Five - year survival curves of 122 patients with excessive alcohol intake and cirrhosis, according to Child-Pugh class at including

Pessione F, et al. Liver International 2003;23:45-53.



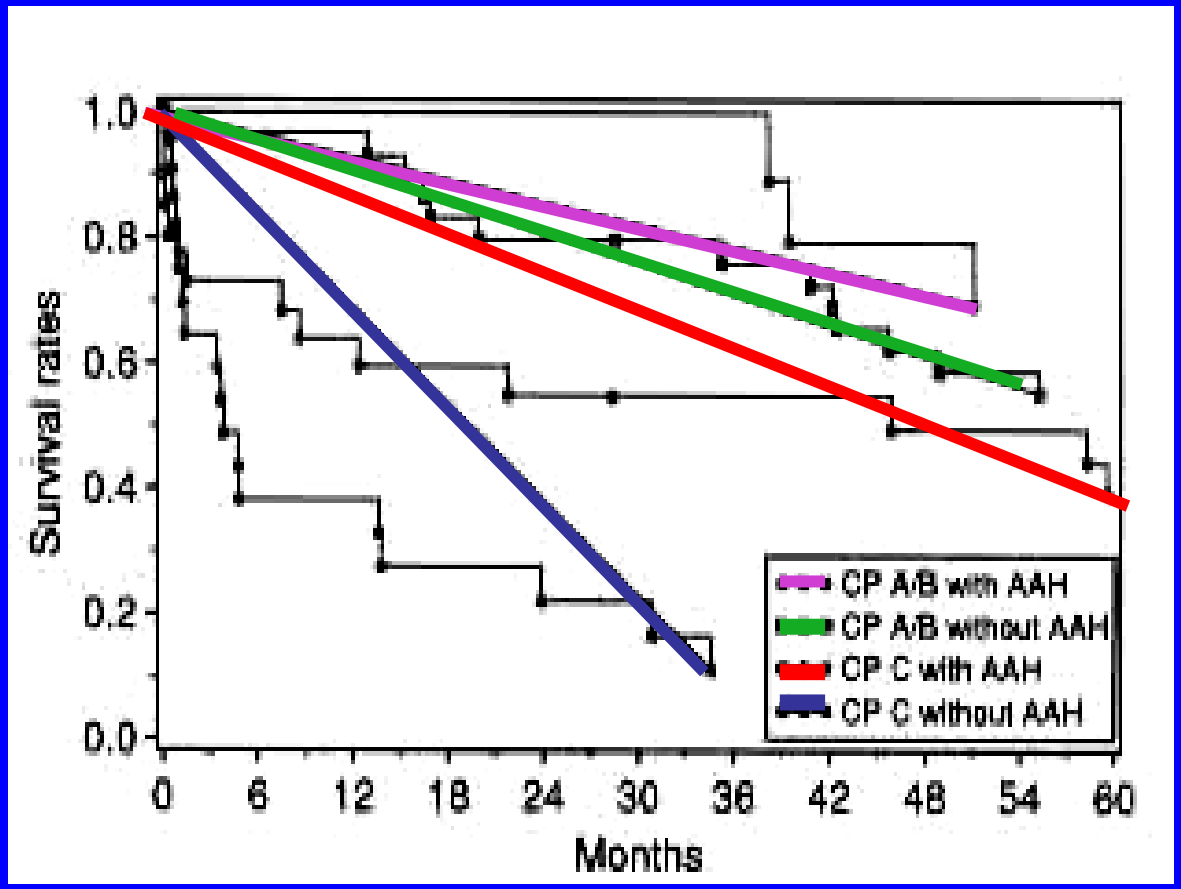
Five - year survival curves of 122 patients with excessive alcohol intake and cirrhosis with and without gastrointestinal bleeding at entry

Pessione F, et al. Liver International 2003;23:45-53.



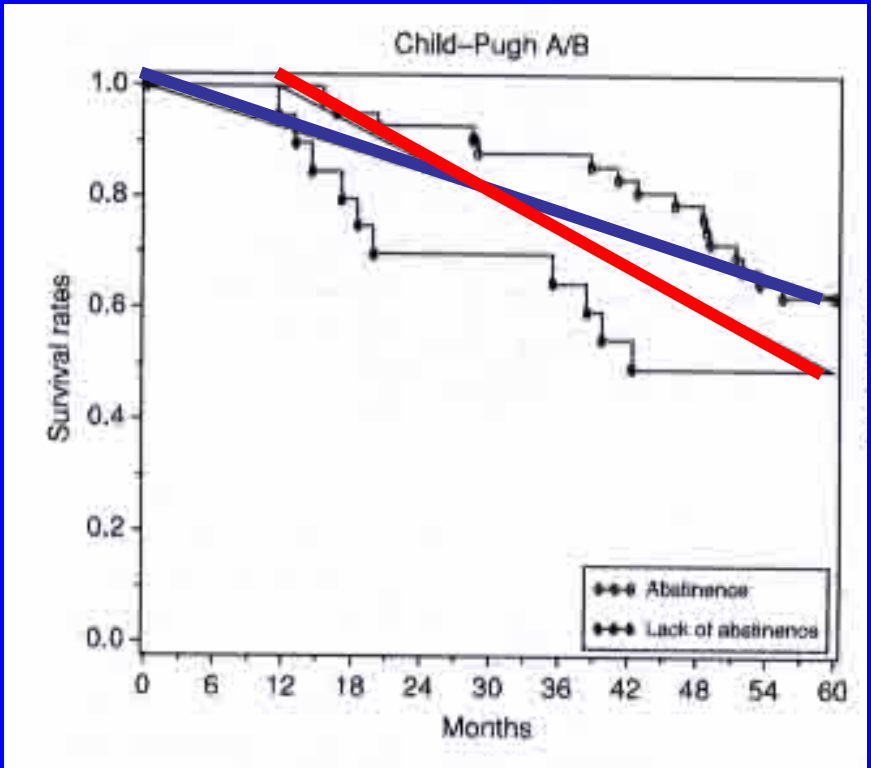
Five - year survival curves of Child-Pugh class C patients with excessive alcohol intake and cirrhosis with and without HBsAg and/or anti - HCV

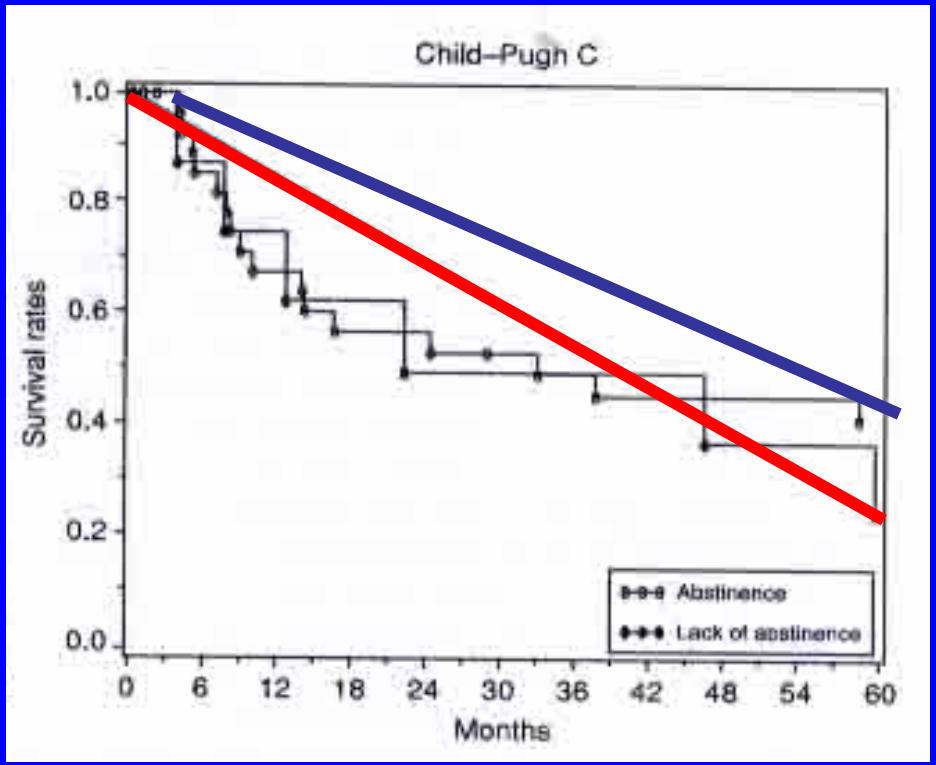
Pessione F, et al. Liver International 2003;23:45-53.



Five - year survival curves of patients with excessive alcohol intake and cirrhosis with and without biopsy - proved acute alcoholic hepatitis, according to Child – Pugh class

Pessione F, et al. Liver International 2003;23:45-53.





Five - year survival curves patients with excessive alcohol intake and cirrhosis with and without abstinence, according to Child – Pugh class. In this bi – variable analysis a difference appears only in class A and B, whereas in multivariable analysis the differences are significant in class

A and B (*P*=0.002) and C (*P*=0.04) patients

Pessione F, et al. Liver International 2003;23:45-53.

Effect of alcohol on natural history of HCV

- Increase risk of cirrhosis
- Increase risk of HCC

Alcohol increase risk of cirrhosis in HCV

Factors associated with increased risk

- **Age at infection older than 40 years**
- **Consumption more than 260 g / week**
- **Male gender**

RR=3.6 (95% CI,1.73-7.52)

1. *Poynard T et al Lancet 1997;349:825-32*
2. *Thomus DL et al JAMA 2000;284:450-6*

Alcohol increase risk of HCC in HCV (odds ratio)

No liver disease	HCV	HCV +Alcohol >80g/day	HCV+HBV +Alcohol
1	26.3 (15.8-44)	126 (42.8-373)	132 (15.3-890)

Tager A et al Int J Cancer 1999;81:695-9

Alcohol and Hepatocellular carcinoma

	P value for significance	*P* value for residual	Odds ratio for heavy drinking
All ages			
Male	0.005	0.936	4.4 (1.4 to 14.1)[1]
Female	0.81	0.362	1.6 (0.3 to 9.3)
> 40 years			
Male	0.003	0.74	4.4 (1.3 to 16.6)
Female	0.853	0.426	1.4 (0.2 to 9.6)
< 40 years			
Male	0.82	0.976	1.6 (0.1to 18)
Female	-[2]	-	-

[1] 95% confidence interval, -[2] Sample size to small

Abdulla E, et al. Int J Cancer 1992;51:537-41.

Alcohol and colon

Alcohol and Colorectal cancer

Likely increase incidence	Likely decrease incidence
High – caloric diet	High – fiber diet
High red meat intake	Antioxidant vitamins
Overcooked re meat	Fresh fruits / vegetables
High saturated fat intake	Nonsteroidal anti - inflammatory drug use
Excess alcohol consumption	High calcium intake
Smoking	
Sedentary lifestyle	
Obesity	

Alcohol and Colorectal cancer

	Cases	Person-Month	Minimally Adjusted (95% CI)	Fully Adjusted (95%CI)
Alcoholic beverages				
No	63	45,734	1.00	1.00
Yes	48	40,177	1.26 (0.85, 1.89)	1.29 (0.86, 1.95)
Nondrinkers	63	45,734	1.00	1.00
< 1 Drink/day	22	23,301	1.04 (0.63, 1.71)	108 (0.65, 1.79)
≥ 1 Drink/day	26	16,587	1.67 (1.03, 2.70)	1.69 (1.03, 2.79)
Trend *P* value			0.04	0.04
Beer consumption				
Nondrinkers	76	53,672	1.00	1.00
< 1 Drink/day	27	25,639	1.03 (0.65, 1.64)	1.04 (0.65, 1.66)
≥ 1 Drink/day	8	6,601	1.10 (0.51, 2.35)	1.09 (0.51, 2.34)
Trend *P* value			0.82	0.84
Wine consumption				
Nondrinkers	77	51,292	1.00	1.00
< 1 Drink/day	31	31,585	1.02 (0.66, 1.57)	1.04 (0.67, 1.61)
≥ 1 Drink/day	3	3,035	0.83 (0.26, 2.63)	0.78 (0.24, 2.49)
Trend *P* value			0.97	0.67
Liquor consumption				
Nondrinkers	63	50,154	1.00	1.00
< 1 Drink/day	33	30,339	1.44 (0.93, 2.23)	1.48 (0.95, 2.31)
≥ 1 Drink/day	15	5,419	2.28 (1.28, 4.06)	2.48 (1.66, 4.53)
Trend *P* value			0.01	<0.01

Su, LJ, et al. Nutrition and Cancer 2004;50(2):111-9.

Impact of alcohol related disease and inpatient work among gastroenterologist in Scotland

- 25% (337/1367) were admitted because of alcohol related illness
- 15% (201/1363) have alcoholic liver disease
- 10% of beds were occupied because of delayed discharge related to alcoholic

Hislop WS, Heading RC.Scott Med J 2004;49:57-60.

Cohort study of alcoholic cirrhosis in Srinagarind hospital, KKU

- Follow up time 74 months (July 2000-September 2006)
- Male 74,Female 8
- Co-morbid: HCV19,HBV6,HCV+HBV1,DM22
- Child status:A19,B19,C44

Cohort study of alcoholic cirrhosis in Srinagarind hospital, KKU

- Death 12(Child C=11,B=1) septicemia10,rupture HCC1, UGI Bleeding1,Electrolyte imbalance 1.
- **Continue drinking 58, death 10** vs **Stop drinking 24,death 2 (p<0.05)**
- Hepatocellular carcinoma 5
- Child status improved4(C → B,3(1),B → A,1(1))
- UGI Bleeding 60 episodes, SBP 21episodes, Hepatic encephalopathy 12, Alcoholic withdrawal 11,Liver failure 1

Cohort study of alcoholic cirrhosis in Srinagarind hospital,KKU

Infection(43)

- Septicemia 13,septic shock 8,pneumonia 17, Cellulitis and soft tissue infection 5.

Renal(25)

- ARF 25,Hepatorenal syndrome 1

CNS(12)

- DT 7,Rum fit 2, psychosis 1,Head injury1,CVA1

CVS(2)

- Cardiomyopathy 1, AMI 1,

Metabolic

- Hypokalemia 1→VT (death), Hypoglycemia 2

Conclusion 1

- Alcohol is associated with many gastrointestinal and hepato-pancreatic pathologies such as esophagitis ,gastric mucosal injury, pancreatitis and alcoholic liver diseases.
- Alcohol is also associated with increased risk of GI malignancies such as squamous cell carcinoma of esophagus, hepatocellular carcinoma and carcinoma of colon.
- Abstinence of alcohol prevent or delay the progression of alcoholic liver disease.

Conclusion 2

- Alcohol is associated with the increased risk of cirrhosis and hepatocellular carcinoma among chronic HCV and HBV.
- High physician work load and large amount of budget are spent on treatment various medical complications associated with alcoholic liver diseases.

THANK YOU FOR YOUR ATTENTION