MEDICAL GRAND ROUNDS

PARKLAND MEMORIAL HOSPITAL

September 16, 1965

ACUTE ALCOHOLIC FATTY LIVER SYNDROMES

CASE 1, [redacted]

The patient is a 32-year-old [redacted] with a background of emotional instability. She had been hospitalized 3 years previously after an attempted suicide. Several EOR visits since then were for suicide gestures or beatings. Admission to Surgery on [redacted]/65 was precipitated by a history of RUQ pain, nausea and vomiting of 3 days duration. Symptoms of intermittent RUQ pain, with nausea and vomiting had been present for one year. Dark urine was noted for the past month, whereas darkening of the skin and yellow eyes had been present for 7 to 10 days. Appetite had been poor for several months. The husband indicated that whereas his wife had been drinking heavily 3 years ago, she consumed only 2 to 3 beers a day now. The patient admitted to intake of vodka and gin, and had taken a drink on the morning of admission. Physical examination revealed an acutely ill woman with T 100.2, P 96, BP 118/80. Scleral icterus and 4 fingerbreadth, very tender hepatomegaly were the only described abnormal findings. Neurological exam was normal.

Abdominal pain, fever to 101.6 and nausea persisted. Laporotomy was performed on [redacted] with a preoperative diagnosis of acute cholecystitis. The gall bladder was normal. An enlarged pale yellow liver was encountered. Edema was described in the region of the head of the pancreas and transverse mesocolon. Cholecystotomy and liver biopsy were performed.

Liver biopsy S65-3813 revealed severe fatty metamorphosis, some bile stasis and focal areas of necrosis with acute inflammatory reaction. Some alcoholic hyaline was observed. No increased fibrous tissue or histologic evidence of cholangitis was detected.

Hospital course was highlighted by tremulousness and disorientation beginning on [redacted], intermittent fever, nausea and vomiting. Patient received predominantly I.V. fluids till [redacted]. Folic acid, vitamins and food were started at this time.

Following discharge, she complained of intermittent RUQ pain. Her last EOR visit on [redacted]/65 mentions that the patient is drinking alcohol again.

CASE I - LAB DATA

	[redacted] 1965	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted] 1965
Hgb.	10.5	8.7-9.4	10.6	9.2	8.8	9.3	9.9	10.5			10.8	
WBC	11,700	10,600	13,600			10,000		13,500			11,700	
Plts.		277,500					570,000				637,500	
Retics.							7.2	8.6			3.4	
Bilirubin- 1 min/Total	3.2/5.0	2.6/4.8	3.2/5.0	3.6/5.8	3.0/5.2	3.2/5.6	2.5/6.2	1.6/3.2		0.9/2.5	0.9/1.6	0.5/1.1
Ceph.Floc.	2+/3+	2+/3+			3+/3+	N/1+				1+/3+	N/1+	1+/2+
Thymol Turbidity	12.0	12.5			5.9	6.7		8.0			9.8	14.8
Alk. P'tase. Bodansky Units	9.4	8.7	10.3	6.0	6.2	6.7	5.4	9.7		7.4	6.9	8.4
SGOT	394	264	228	234	118	332			239		192	186
Prothrombin time		12.5 sec							13.5 sec.			
Amylase	427	<320	582 <320	<320		<320	<320			<320		
Total protein	8.2	6.5					6.1				7.4	8.8
Albumin		3.3					3.3				3.4	3.7
Globulin		3.2					2.8				4.0	5.1
Cholesterol		240										Coombs neg.
Urine bile	1+											
Urobilinogen	1+											
			↑ Laporotomy									

CASE 2, [redacted]

A 58-year-old unemployed [redacted] was admitted [redacted]/65 because of jaundice of 4 days duration. The patient had been a chronic alcoholic for 30 years. His drinking increased markedly after his wife's death 7 months previously. Food intake was poor. Two weeks ago his ankles then abdomen began to swell. Dark urine and jaundice were noted for 4 days. He denied nausea, vomiting, hematemesis, melena or abdominal pain. On physical examination the patient was in no acute distress. T 100.2, P 104, R 16, BP 114/65. Liver down 7 cm, firm, nontender. No spleen. Flank dullness, but no fluid wave. Edema of abdominal wall, and 3+ leg edema. Neurological exam normal.

Red cells were macrocytic. No hypersegmented neutrophiles were noted. Bone marrow described as megaloblastoid, megaloblastic by different observer. Excess iron was present. Vitamin B_{12} level > 900 μμg/cc. No comments about hyperlipemia early in course. No cholesterol determinations. Placed on diet alone. Folic acid added on [redacted]. Proctoscopy, barium enema, GI series were negative.

Liver biopsy [redacted] S65-2873. Intense diffuse fatty metamorphosis. Increased portal fibrosis.

On last clinic visit he appeared well and had apparently stopped drinking.

CASE 2 - LAB DATA

	[redacted] 1965	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted] 1965	[redacted] 1965
Hgb.	6.7	5.7	5.9	7.0	8.0	7.5	8.8	8.9	11.2
Hct.	20.5	19.5	19.0	24.0	27.0	27.0	31.0	31.5	
Retics.		5.1	9.2	14.9	8.4		8.2	2.4	1.2
WBC	16,300	16,900	12,500	10,200		6,850	8,700		7,850
Platelets			672,500					445,000	
Bilirubin-1 min.		8.4			5.9			2.4	
Total		15.0			13.2			4.8	0.5
Ceph. Floc		1+/2+			1+/2+			+/2+	N/2+
Thymol Turbidity		3.7			3.9			2.4	3.0
Alk. P'tase		12.2			6.3			8.2	6.1
SGOT		342	323		222			194	24
Prothrombin time		15.0/12.5	14.0/12.5					11.5/12.5	
Total protein		6.2	5.9						7.2
Albumin			2.8						4.2
Globulin			3.1						3.0
Serum iron/TIBC		263/263							
Amylase	<320								
Stool guaiac		3+	Neg.			Neg.	Neg.	Trace	
Gastric aspiration				Free acid					

CASE 3, [redacted]

A 47-year-old man, [redacted] claimed he consumed a fifth or more of whiskey a day for 20 years. Food intake varied, but for 3 to 4 months he ate poorly, usually a bowl of soup on occasion. Abdominal swelling began 8 days before admission. He stopped drinking 5 days ago. Jaundice was noted the next day. The patient was told he had diabetes in 1953. Initially, he used insulin, but had changed to Orinase 1-2 pills per day with apparent satisfactory control. He denied bouts of abdominal pain.

Physical examination revealed an obese markedly jaundiced male in no distress. T 98.4, P 90, R 18, BP 104/75. Bilateral paratoid enlargement. Fundi negative. Very obese abdomen - question of some ascites. Liver massively enlarged, firm somewhat tender. Spleen not palpable. KJ diminished, AJ absent. Vibratory and position sense impaired in feet.

Liver biopsy [redacted]/63 S 63-3591 reveals a florid alcoholic necrosis and fatty metamorphosis. Extensive swelling and necrosis of liver cells with many Mallory bodies are noted. A delicate fibrosis is present.

Despite food and supplemental vitamins, course was characterized by worsening jaundice, progressive renal failure and death 2 days after massive hematemesis, which was controlled by esophageal tamponade.

CASE 3 - LAB DATA

	[redacted] 1963	[redacted]	[redacted]	[redacted] 1963	[redacted]	[redacted]	[redacted]	[redacted]
Hgb.	12.3	12.7	12.0	13.0	12.1			
Hct.	40.5	42.5	37.5					
Retics.	5.0	3.7	4.1	1.6				
WBC	9,200	9,300	83,000	15,750	15,150			14,250
Platelets	115,000	200,000	180,000	182,500				
Bilirubin-1 min.	17.2	25.6	28.0	29.0	24.5	24.4	21.2	
Total	28.8	41.6	39.6	50.0	36.0	38.0	36.0	30.4
Ceph. floc.	0/1+	0/1+		3+/4+	2+/0	2+/2+	1+/3+	
Thymol Turbidity	4.9	3.5	6.7	3.9	4.6	2.9	2.2	
Alk. P'tase	8.3	7.1	7.8	7.5		9.4	11.8	
SGOT	118	111	65	171	145	120	100	
Prothrombin time	13/12.5	13.5/12.5			16/13			
Amylase	<320				<320		<320	
Cholesterol	247							

CASE 4 [redacted]

A 42-year-old [redacted] woman chronic alcoholic, consumed approximately 1 pint of whiskey daily for at least 10 years. Dietary intake was poor. One trial on Antabuse was unsuccessful. Patient had been hospitalized elsewhere on several occasions for tarry stools and/or hematemesis. She denied alcohol intake for the past 6 months, yet told another physician that her alcohol intake increased to at least a fifth of vodka daily for a month since the death of her mother. Six days before admission, she began to vomit, eventually bringing up coffee ground material then bright red blood. Her stools became black.

Physical examination revealed her to be in no acute distress, BP 130/86, P 120, R 16, afebrile. The liver was huge, down 6 fingerbreadths almost to the iliac crest and was tender. Spleen down 2 fingers. There was questionable ascites and no peripheral edema.

During the first few days in the hospital, attention was directed to fluid and electrolyte problems, fever to 102. On [redacted] she developed full-blown DT's. Evidence of pneumonia on [redacted] - multivitamin Rx started soon after admission, folic acid on [redacted]. Mentation remained poor. Liver biopsy on [redacted] S64-2879 revealed florid cirrhosis, considerable alcohol hyaline, marked fatty metamorphosis. Steroids started on [redacted]. Gradual increase in oral intake from [redacted] on to finally a high protein diet in June. Ascites noted on [redacted]. Liver biopsy [redacted] - slight increase portal fibrous tissue. Necrotic liver cells surrounded by polymorphonuclear leukocytes. Marked decrease in fat content.

Gradually improved, but course punctuated by intermittent diarrhea, ascites, occasional elevations of temperature to 100.6.

Proctoscopy and barium enema were negative. GI series revealed esophageal varices.

Following discharge in [redacted], the patient did well as an outpatient. In [redacted] she talked about her turmoil at home. Drinking was resumed about this time. An increased SGOT was apparent in [redacted]. When seen in the EOR in [redacted], ascites and ethanol odor on her breath were detected. The patient did not return to clinic subsequently.

CASE 4 - LAB DATA

[redacted] 1964	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted].	12.2	10.9	9.2	7.5	10.0	9.9	7.5	12.5	11.8	11.2	10.7	11.7	11.5	12.6	12.0	12.5	12.7
Hct.	37	34	27	26	33.0			39.5			36.0	35.0		40.0			40.0
Retics.			0 0.1	8.1	5.7	2.3		5.1		2.4	4.1						
WBC	9,800	7,200	3,100	17,800		28,600	19,000	22,000		35,000	20,000	7,600		6,000	6,400	9,700	5,550
Platelets			68,000	297,000		345,000		290,000						152,000			
BSP	Blood alcohol, methyl, ethyl, isopropyl negative			36%													
Bilirubin=1 min			0.8	2.2	4.2	6.8	9.0	5.0	3.6	2.2	1.2	0.7	0.6			0.4	
Total			1.7	3.4	6.2	10.6	15.2	9.0	6.8	6.6	2.8	2.7	1.6		2.4	2.8	
Ceph. Floc.	Reinsch test - negative for heavy metal		1+/2+	N/1+	N/N	1+/4+	2+/3+	N/N	3+/3+		2+/3+		1+/3+	1+/1+	N/1+	2+/3+	
Thymol turbidity			3.5	1.9	3.9	12.0	8.2	6.8	9.4	9.5	5.2	10.2	4.9	5.6	4.4	12.0	
Alk. P'tase			12.7	16.1	8.5	16.0	10.5	6.8	24.1	24.1	18.6	10.0	12.0	9.4	8.4	25.5	
SGOT			34	138	93	57	63	76	112	80	50	33	24	19	12	295	
Total protein			6.1	4.7		4.5				5.4	5.3	5.6	6.2	5.0	6.6	7.6	
Albumin			3.3	2.6							2.7	2.7	3.2	3.6	3.8	4.0	
Globulin			2.8	2.1							2.6	2.9	2.8	1.4	2.8	3.6	
Prothrombin time			13.0	12.5					16.5			15.0		13.5			
Urine bile		Trace	+														
Urobilinogen		Trace	Neg.														
TSI/TIBC			44/175	31/100													
Amylase	400	<320								<320							
Stool guaiac	3+	4+	3+	N	N			N				N					
Prednisolone							45	20			15	10		10 Stopped			

Introductory Articles to the Subject of Alcohol and Liver

1. Klatskin, G. Alcohol and its relation to liver damage. Gastroenterol. 41:443, 1961.

2. Patek, A.J. Jr. Portal cirrhosis (Laennec's cirrhosis). Chap. 16 in Diseases of the Liver, Ed., Schiff, L., J.B. Lippincott Co., 1963.

3. Isselbacher, K.J., and Greenberger, N.J. Metabolic effects of alcohol on the liver. New Eng. J. Med. 270:351, 402, 1964.

   Best review article on the subject.

Fatty Liver Associated with Alcohol Administration, Experimental Studies

A. Acute Studies

4. Mallov, S., and Block J.L. Role of hypophysis and adrenals in fatty infiltration of liver resulting from acute ethanol intoxication. Am. J. Physiol. 184:29, 1956.

   Single doses of ethanol in fed rats produce increased hepatic lipid. Intact pituitary-adrenal system required. Pretreatment with very large doses of choline reduces but does not prevent fat accumulation.

5. Di Luzio, N.R. Effect of acute ethanol intoxication on liver and plasma lipid fractions of the rat. Am. J. Physiol. 194:453, 1958.

   Increased liver lipid after single dose of ethanol to fasted rat is triglyceride. No change in liver phospholipid or cholesterol content. Choline does not prevent increased liver triglyceride nor affect phospholipid metabolism. Increase in plasma triglyceride and phosphatide noted when compared to saline controls at 16 hours.

6. Maling, H.M., Horning, M.G., Butler, W.M.J., Highman, B. and Brodie, B.B. Triglyceride deposition in rat liver through derangement of fat transport by various chemical agents. Fed. Proc. 19:229, 1960 (Abstract).

   Increased liver triglyceride after ethanol has same percentage of linoleic acid as adipose triglyceride. Suggests increased fat mobilization from adipose tissue since linoleic acid not synthesized by mammalian liver. Hypophysectomy and dibenamine reduce lipid deposition in liver.

7. Feigelson, E.B., Pfaff, W.W., Karmen, A., and Steinberg, D. The role of plasma free fatty acids in development of fatty liver. J. Clin. Invest. 40:2171, 1961.

   Infusions of norepinephrine into the femoral vein produce sustained elevations of FFA and increase in liver TG in dogs. Norepinephrine infusion into portal vein causes slight increase in FFA and no rise in liver TG presumably because of hepatic metabolism of norepinephrine. Studies of fatty acid composition of liver TG, plasma FFA and adipose tissue TG suggest that newly formed liver TG is synthesized from plasma FFA mobilized from adipose tissue.

8. Elko, E.E., Wooles, W.R., and Di Luzio, N.R. Alterations and mobilization of lipids in acute ethanol-treated rats. Am. J. Physiol. 201:923, 1961.

   Increased liver TG after single dose of ethanol not accompanied by increased plasma FFA or TG when compared to rats receiving isocaloric glucose or saline. Suggest alteration in liver TG metabolism.

9. Mallov, S. Effect of ethanol intoxication on plasma free fatty acids in the rat. Quart. J. Stud. Alcohol 22:250, 1961.

Increase in plasma FFA observed within 4 hours of single dose of ethanol, persists up to 20 hours.

10. Lieber, C.S., and Schmid, R. The effect of ethanol on fatty acid metabolism; stimulation of hepatic fatty acid synthesis in vitro. J. Clin. Invest. 40:394, 1961.

Incubation of liver in vitro with ethanol a) increases net synthesis of fatty acids, b) increases incorporation of trace amounts of acetate-1-C^{14} into FA when compared to equivalent amounts of acetate or glucose. Stimulation of hepatic FA synthesis may be result of excess DPNH formed on ethanol oxidation. Ethanol may exert inhibitory effect on FA oxidation.

11. Rebouças, G., and Isselbacher, K.J. Studies on the pathogenesis of the ethanol-induced fatty liver. I. Synthesis and oxidation of fatty acids by the liver. J. Clin. Invest. 40:1355, 1961.

Ethanol in rats stimulates incorporation of acetate-1-C^{14} into liver lipids. Glucose and sorbitol also stimulate without producing an increase in liver fat.

Nicotinamide injection prior to ethanol depresses acetate-1-C^{14} incorporation into lipid but does not affect extent of fatty liver. Hypophysectomy and cordotomy prevent fatty liver, but acetate-1-C^{14} incorporation into liver lipid remains increased.

Ethanol increases liver DPNH and decreases DPN/DPNH ratio. Similar changes induced by sorbitol, but sorbitol does not produce a fatty liver.

Palmitate-1-C^{14} oxidation to $C^{14}O_2$ decreased by ethanol in vivo and in vitro.

Prior treatment with nicotinamide prevents inhibitory effect but does not prevent fatty liver. Glucose also decreases palmitate oxidation but does not induce a fatty liver.

Concludes - Although ethanol induces increased FA synthesis and decreased FA oxidation, these are probably unimportant in genesis of steatosis since other compounds produce same changes but not a fatty liver.

12. Maickel, R.P., and Yamada, K. Dynamic processes involved in the production of of a fatty liver, in Advances in Enzyme Regulation, Vol. 1, P. 235, Ed., Weber, G., Pergamon Press, MacMillan Co., 1963.

Excellent summary of studies indicating that increased liver TG after ethanol is dependent upon integrity of both the sympathetic nervous system and the pituitary-adrenocortical system. Sympathetic nervous system controls the activity of adipose tissue lipase and thus the mobilization of FFA from adipose tissue TG. Pituitary-adrenocortical system has action on responsiveness of adipose tissue to lipolytic agents. Large doses of ACTH and cortisone alone given to intact animals produce increase in liver TG.

13. Maling, H.M., Wakabayaski, M., and Horning, M.G. Alterations in hepatic lipid biosynthetic pathways after ethanol, ethionine and carbon tetrachloride, in Advances in Enzyme Regulation, Vol. 1, P. 247, Ed., Weber, G., Pergamon Press, MacMillan Co., 1963.

Ethanol increases incorporation by liver homogenates of palmitate-1-C^{14} into triglycerides and decreases incorporation into phospholipids. Homogenates from hypophysectomized rats incorporate less palmitate into TG and more into PL than intact rats.

14. Nikkila, E.A., and Ojala, K. Role of hepatic L-a-glycerophosphate and triglyceride synthesis in production of fatty liver by ethanol. Proc. Soc. Exp. Biol. Med. 113:814, 1963.

Single dose ethanol is followed by significant increase in hepatic glycerophosphate concentration and in incorporation of I.V. injected palmitic acid-1-C^{14} into liver TG.

15. Schapiro, R.H., Drummey, G.D., Shimuzu, Y., and Isselbacher, K.J. Studies on the pathogenesis of the ethanol-induced fatty liver. II. Effect of ethanol on palmitate-1-C^{14} metabolism by the isolated perfused rat liver. J. Clin. Invest. 43:1338, 1964.

Ethanol in high concentration did not affect palmitate-1-C^{14} uptake by liver, but was associated with a decrease in rate of appearance of C^{14} labeled TG in perfusion fluid. Did not resolve whether latter is due to decreased release of TG from liver, or increased uptake of circulating TG by liver.

16. Hartroft, W.S., Porta, E.A., and Suzuta, M. Effects of choline chloride on hepatic lipids after acute ethanol intoxications. Quart. J. Stud. Alcohol 25:427, 1964.

Choline does not prevent increased liver TG after single dose of ethanol.

17. Scheig, R., and Isselbacher, K.J. Pathogenesis of ethanol-induced fatty liver. III. *In vivo* and *in vitro* effects of ethanol on hepatic fatty acid metabolism in rat. J. Lipid Res. 6:269, 1965.

Effects of ethanol added *in vitro* to liver slices probably not germane to the induction of fatty liver, since they were not observed after ethanol administration to the whole animal. FA accumulating in liver after oral administration of ethanol consist primarily of unsaturated fatty acids similar to those found in adipose tissue. FA synthesized *in vitro* when ethanol is added to liver slices are primarily saturated. Incorporation of circulating FFA into hepatic TG is increased *in vivo*. Amount and rate of TG formation from FA significantly increased in liver homogenates and microsomes after ethanol administration *in vivo*, but not upon *in vitro* addition of ethanol to liver slices.

18. Zakim, D., Alexander, D., and Sleisenger, M.H. The effect of ethanol on hepatic secretion of triglycerides into plasma. J. Clin. Invest. 44:1115, 1965 (Abstract).

Evidence for increased hepatic secretion of TG and phospholipid after single dose of ethanol. Increased plasma phospholipid primarily in choline fraction.

Chronic Studies

19. Ashworth, C.T. Production of fatty infiltration of liver in rats by alcohol in spite of adequate diet. Proc. Soc. Exp. Biol. Med. 66:382, 1947.

Fed low and high casein diets to rats for 50-60 days. Alcohol rats received alcohol by stomach tube and in drinking water. Controls received same food but no alcohol. Fatty liver detected histologically in all rats on low casein diets, and in animals on high casein diet with alcohol. No fat detected in high casein controls.

Concludes - alcohol permits accumulation of fat in liver. This effect operates separately from extensive deficiency of lipotropic factors.

20. Best, C.H., Hartroft, W.S., Lucas, C.C., and Ridout, J.H. Liver damage produced by feeding alcohol or sugar and its prevention by choline. Brit. Med. J. 2:1001, 1949.

Rats maintained on a diet marginal in lipotropic activity and on a fluid intake of 15 per cent alcohol, developed fatty infiltration and fibrosis of the liver. Similar lesions observed in pair-fed controls given isocaloric equivalents of sucrose instead of alcohol, but not in pair-fed controls given neither sucrose nor alcohol supplements. Alcohol and sucrose effects appeared to be identical and were abolished by supplements of choline, methionine or casein.

Concludes - addition of alcohol and sucrose calories to a diet of marginal lipotropic activity creates a relative choline deficiency.

21. Klatskin, G., Gewin, H.M., and Krehl, W.A. Effects of prolonged alcohol ingestion on the liver of rats under conditions of controlled adequate dietary intake. Yale J. Biol. Med. 23:317, 1951.

Administration of 15 per cent alcohol as sole source of drinking water to rats for 6 months did not produce histologic evidence of significant fatty infiltration or cirrhosis when the diet contained protein, calories, and vitamins sufficient to prevent fatty infiltration in ad libitum fed controls. On chemical analysis, the fat content of the liver, while still in the normal range, was greater than in ad libitum, pair-fed or isocalorically-fed controls receiving no alcohol.

22. Klatskin, G., Krehl, W.A., and Conn, H.O. The effect of alcohol on the choline requirement. I. Changes in the rat's liver following prolonged ingestion of alcohol. J. Exp. Med. 100:605, 1954.

Rats maintained for 7 months on fluid intake of 15 per cent alcohol and a diet marginal in lipotropic activity developed fatty infiltration and mild fibrosis of liver. Similar changes observed in pair-fed controls given isocaloric equivalent of sucrose instead of alcohol but not in pair-fed controls receiving neither alcohol nor sucrose supplements. When sucrose from the last diet was replaced by isocaloric ethanol equivalent to that consumed in the original ethanol rats, fatty liver developed despite no increased caloric intake. Choline or methionine abolished the effects of both alcohol and sucrose supplements.

Concludes - alcohol increases the choline requirement of the rat. Does not support Best's conclusion that the alcohol effect is the consequence of augmented caloric intake.

23. Mallov, S. Effects of chronic ethanol intoxication on liver lipid content of rats. Proc. Soc. Exp. Biol. Med. 88:246, 1955.

Fed rats diet adequate for maintenance of good growth and normal liver lipid values in control animals. Twenty-two per cent of carbohydrate calories isocalorically substituted for by ethanol. Approximately threefold increase in liver triglyceride in 30 days. Large supplements of choline or B_{12} prevent increase in liver triglyceride. Supports concept that alcohol increases requirement of certain nutritional factors.

24. Lieber, C.S., Jones, D.P., and De Carli, L.M. Effect of prolonged ethanol intake: production of fatty liver despite adequate diets. J. Clin. Invest. 44:1009, 1965.

Adequate diet for growth and providing normal liver lipids in control rats. Thirty-six per cent of carbohydrate calories replaced by ethanol. Liver triglycerides increased eightfold in 24 days. Basic diet contains adequate choline and methionine for optimal growth of rats. Did not determine if fat accumulation prevented by extra choline. In view of Mallov's findings, present study may be another example of alcohol increasing choline requirement. Does not prove alcohol produced fatty liver independent of induced nutritional deficiency.

Consumption of moderate amounts of alcohol, either in addition to or as isocaloric substitution for carbohydrate in an otherwise adequate diet produced fatty liver, histologically, in 5 human subjects with a previous history of alcoholic fatty liver, but whose hepatic morphology and liver tests were normal at the time these studies were instituted. No attempt to see if choline would prevent development of the fatty changes.

Conclusions

Chronic alcohol intake can induce fatty liver in rats and in man. This effect has not yet been disociated from ethanol-induced choline or other nutritional deficiency.

25. Lieber, C.S., and Spritz, N. Ethanol-induced fatty liver on fat-free and fat-containing diets: role of dietary, adipose, and endogenously synthesized fatty acids. J. Clin. Invest. 44:1069, 1965 (Abstract).

Fatty liver following prolonged ethanol intake contains e[illegible]usly synthesized, and when available, dietary FA. Elimination of dietary [illegible] reduces alcohol steatosis significantly.

Effect of Ethanol on Plasma Lipids in Man

26. Lieber, C.S., Leevy, C.M., Stein, S.W., George, W.S., Cherrick, G.R., Abelmann, W.H., and Davidson, C.S. Effect of ethanol on plasma free fatty acids in man. J. Lab. Clin. Med. 59:826, 1962.

Plasma FFA fall 30% then return to control levels during ethanol administration of 50 to 60 minutes.

27. Jones, D.P., Losowsky, M.S., Davidson, C.S., and Lieber, C.S. Effects of ethanol on plasma lipids in man. J. Lab. Clin. Med. 62:675, 1963.

Ethanol administered for 6 to 8 hours accompanied by 74% rise in serum TG; 50% fall in FFA. Phospholipids, cholesterol and cholesterol esters do not change. More prolonged ethanol ingestion produces increased serum TG and phospholipids. FFA data not reported.

28. Jones, D.P., Perman, E.S., and Lieber, C.S. Decreased circulating free fatty acid turnover after ethanol ingestion in man. J. Clin. Invest. 43:1241, 1964 (Abstract).

FFA decrease of 42-61% during 2 hour period of ethanol ingestion associated with decreased turnover of FFA of 37-58%, and attributed to decreased influx of FFA into vascular compartment from adipose tissue.

29. Bouchier, I.A.D., and Dawson, A.M. The effect of infusions of ethanol on the plasma free fatty acids in man. Clin. Sci. 26:47, 1964.

Confirm fall in FFA during ethanol infusion of 2 to 48% - followed by a rise after infusion stopped of 2 to 75%. Rise can be prevented by administration of blocking agents of β receptors to adrenaline. Conclude ethanol causes mobilization of FFA from adipose tissue and that this is mediated by adrenaline.

30. Schapiro, R.H., Scheig, R.L., Drummey, G.D., Mendelson, J.H., and Isselbacher, K.J. The effects of prolonged ethanol ingestion on the transport and metabolism of lipids in man. New Eng. J. Med. 272:610, 1965.

During prolonged alcohol intake, serum TG and FFA levels fluctuate; in general, height of each is related to blood alcohol concentration. Serum FFA assume composition similar to that of adipose tissue.

31. Nestel, P.J., and Hirsch, E.Z. Mechanism of alcohol-induced hypertriglyceridemia. J. Lab. Clin. Med. 66:357, 1965.

Alcohol fed for 6 hours increased rate of incorporation of FFA into triglyceride and to a rise in plasma TG concentration.

Alcoholic Fatty Liver

32. Keefer, C.S., and Fries, E.D. The fatty liver - its diagnosis and clinical course. Trans. Assoc. Am. Phys. 57:283, 1942.

In the chronic alcoholic, severe hepatic insufficiency may ensue during the stage of fatty liver and before any fibrosis has occurred.

33. Ballard, H., Bernstein, M., and Farror, J.T. Fatty liver presenting as obstructive jaundice. Am. J. Med. 30:196, 1961.

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Hyperlipemic Syndromes

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Nine ounces of 40 per cent ethanol fed daily for 6, 6, 14 and 18 months were not deleterious for 4 cirrhotics on good diet.

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Miscellaneous

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