Page 1

_{nar}kland Memorial Hospital

November 21, 1963

MEDICAL GRAND ROUNDS

MASE 11: # 162 233

Prought to PMH in a comatos but after the intravenous and all neurological signs or ion to administration with a comatos recent alcoholic binge difference "ALCOHOL-INDUCED HYPOGLYCEMIA" per day concerned. Serum bilirubi BSP on the fourth hospital action of the fourth hospital

One year later effort or including to provide of provides of provides in the total and not eating during the same period of time she and age norrought to PMP include. Her blood glucose tas 35 mg yer cent and she again resounded promptly to latronether phonose administration. Three days of a 1200 calorie dist contrining only 50 grams of profile and 50 grams of carbohydrate followed by one day of comprete tasting and expressed trained in fasting blood plucose concentrations of 72 and 70 mg per cent. BSP test special raise 4% retention.

ASE 111: B. H. # 262 460

This 51 year old cm was brought to the EOR in a stuperbook which. Prior to becoming stuporous, he noted an episode of weakness, nervousness, and there is usness. He lost consciousness, fell to the floor biffing his head and nose. On the full He was found to have a blood glucose of 18 mg per cost and responded immediately the derevencus glucose. He gave a long history of alcoholists and noted in the past two public many attacks of weakness and nervousness at times progressing to unconsciousness. In the bookstrud during heavy drinking spreas when he had not defut for several days. Shysteral many attacks of weakness found. His BUN was 7 mg per cent but numerous fasting blood sugars ranged from 108 to 189. The blood sugar at 3 hours being over 187 mgg. His glucose noter and tests were diabetic, the blood sugar at 3 hours being 489 mg per cent and at 6 hours 262 mg per cent. One brother had diabetes. After 36 hours of a blood of a followed by 36 hours of tasting, his blood glucose was 102 mgs. Twenty-four hour is 30 meterold excretion was 7,4 and 7,7 mg. Liver, function studies were as follows:

T. P. with A/G = 8.7 with 5/2.7 Silirubin 0.5 mgS; BSP 16% retention; Profirement 11.5 sec.

Te remained asymptomatic throughout his hospital stay and was discharged with the diagnosis

CASE 1:

This 36 year old man was brought to in 1960 by his family hecause they were unable to arouse him. Although a heavy drinker for many years, he apparently was well the evening before admission despite the fact that he had consumed large amounts of alcohol, including bootleg whiskey, ate poorly and became drunk. The day of admission the patient developed a peculiar behavior characterized by loud irrational talking and increased physical activity. After about 3 hours of this unmanageable and at times hostile behavior he "fell asleep". However, later when it was not possible to arouse him he was brought to the EOR. After blood tests were drawn he was given 50 per cent alucose intravenously whereupon he responded by awakening and resuming his maniacal and combative behavior. FBS prior to glucose administration was 28 mg per cent. Physical examination was not remarkable except for 3F hepatomegaly. Despite intravenous glucose and vitamins within 24 hours he developed typical delerium tremens. BSP on the second hospital day showed 20 per cent retention. This fell to 2 per cent within a few days. BUN on admission was 8 mg per cent and rose to 14 mg% with refeeding. Workup failed to reveal any of the usual causes of organic hypoglycemia.

CASE 11:

This 40 year old **because** woman a known chronic alcoholic and binge drinker, was brought to **b** in a comatose condition. Initially she was thought to have had a stroke but after the intravenous administration of 50 cc of 50 per cent glucose she became alert and all neurological signs of a cerebrovascular accident disappeared. Her blood glucose prior to administration was 25 mg per cent. The only pertinent history was that of a recent alcoholic binge during which time she did not eat but drank about a fifth of whiskey per day. Physical examination was not remarkable insofar as evidence of liver disease was concerned. Serum bilirubin on admission was 1.9 mg per cent and fell to normal in 2 days. BSP on the fourth hospital day showed 19 per cent retention. This fell to 10 per cent by the 6th hospital day. Liver biopsy was normal. Fasting blood sugars were normal.

One year later after drinking large amounts of whiskey for 2-3 days and not eating during the same period of time she was again brought to intravenous glucose administration. Was 35 mg per cent and she again responded promptly to intravenous glucose administration. Three days of a 1200 calorie diet containing only 50 grams of protein and 50 grams of carbohydrate followed by one day of complete fasting and exercise resulted in fasting blood glucose concentrations of 72 and 70 mg per cent. BSP test showed only 4% retention. Serum bilirubin was 1.1 mg%. Workup for panhypopituitary or adrenal disease was negative.

CASE III:

This 51 year old was brought to the EOR in a stuporous state. Prior to becoming stuporous, he noted an episode of weakness, nervousness, and tremulousness. He lost consciousness, fell to the floor hitting his head and nose. On the EOR he was found to have a blood glucose of 18 mg per cent and responded immediately to intravenous glucose. He gave a long history of alcoholism and noted in the past two years many attacks of weakness and nervousness at times progressing to unconsciousness. These occurred during heavy drinking sprees when he had not eaten for several days. Physical examination revealed no evidence of pituitary or adrenal disease. Only an enlarged ($3F \downarrow CM$) non-tender liver was found. His BUN was 7 mg per cent and numerous fasting blood sugars ranged from 108 to 189 mg per cent, most values being over 120 mg%. His glucose tolerance tests were diabetic, the blood sugar at 3 hours being 400 mg per cent and at 6 hours 262 mg per cent. One brother had diabetes. After 36 hours of a Conn diet followed by 36 hours of fasting, his blood glucose was 102 mg%. Twenty-four hour 17-0H steroid excretion was 7.4 and 7.7 mg. Liver function studies were as follows:

T. P. with A/G = 8.7 with 5/3.7; Bilirubin 0.5 mg%; BSP 16% retention; Prothrombin 11.5 sec.

^{He} remained asymptomatic throughout his hospital stay and was discharged with the diagnosis ^{Of} diabetes mellitus and ethanol-induced hypoglycemia.

ALCOHOL HYPOGLYCEMIA - CLINICAL PICTURE

- Brown and Harvey. Spontaneous hypoglycemia in "smoke" drinkers. J.A.M.A. 117:12, 1941.
- Tucker and Porter. Hypoglycemia following alcohol intoxication. Am. J. Med. Sci. 204:559, 1942.
- 3. Cumins, L. H. Hypoglycemia and convulsions in children following alcohol ingestion. J. Pediat. 58:23, 1961.
- 4. Neame, P. B. and Joubert, S. M. Postalcoholic hypoglycemia and toxic hepatitis. Lancet 2:893, 1961.
- 5. Taylor, J. S. Hypoglycemia in chronic alcoholism. Brit. Med. J. 1:648, 1955.
- Freinkel, N., D. L. Singer, R. A. Arky, S. J. Belicher, J. B. Anderson and C. K. Silbert. Alcohol Hypoglycemia. I. Carbohydrate metabolism of patients with clinical alcohol hypoglycemia and the experimental reproduction of the syndrome with pure ethanol. J. Clin. Invest. 42:1112, 1963.

METABOLISM OF ALCOHOL

- Westerfield, W. W. The intermediary metabolism of alcohol. Am. J. Clin. Nutrit. 9:426, 1961.
- 8. Westerfield, W. W. and M. P. Schulman. Metabolism and caloric value of alcohol. J.A.M.A. 170:197, 1959.
- 9. Seligson, D., H. H. Stone and P. Nemir, Jr. The metabolism of ethanol in man. Surg. Forum. 9:85, 1959.
- Lunquist, F., N. Tygstrup, K. Winkler, K. Mellegaard and S. Munck-Petersen. Ethanol metabolism and production of free acetate in the human liver. J. Clin. Invest. 41:955, 1962.
- II. Smith, M. E. and H. W. Newman. The rate of ethanol metabolism in fed and fasting animals. J. Biol. Chem. 234:1544, 1959.

METABOLIC EFFECTS OF ETHANOL METABOLISM

- 12, Klingman, G. I. and Goodall. Urinary epinephrine and levarterenol excretion during acute and sublethal intoxication in dogs. J. Pharmacol. exp. ther. 121:313, 1957.
- 13. Figueroa, R. B. and A. P. Klotz. Alterations of alcohol dehydrogenase and other hepatic enzymes following oral alcohol intoxication. Am. J. Clin. Nutrit. 11:235, 1962.
- Kalant, H., R. D. Hawkins, and C. Czaja. Effect of acute alcohol intoxication on steroid output of rat adrenals in vitro. Am. J. Physiol. 204:849, 1963.

- 15. Reboucas, G. and Isselbacher, K. J. Studies on the pathogenesis of ethanolinduced fatty liver. I. Synthesis and oxidation of fatty acids by the liver. J. Clin. Invest. 40:1355, 1961.
- 16. Lieber, C. S. and R. Schmid. The effect of ethanol on fatty metabolism: stimulation of fatty acid synthesis in vitro. J. Clin. Invest. 40:394, 1961.
- 17. Raiha, N. C. and E. Oura. Effect of ethanol oxidation on levels of pyridine nucleotides in liver and yeast. Proc. Soc. Exp. Biol. and Med. 109:4, 1962.
- 18. Forsander, O. A. and Raiha, C. R. Metabolites produced in the liver during alcohol metabolism. Alcoholism 47:29, 1957.
- 19. Horning, M. C., E. A. Williams, H. M. Maling and B. B. Brodie. Depot fat as a source of increased liver triglycerides after ethanol. Biochem. & Biophys. Res. Comm. 3:635, 1960.
- 20. B. B. Brodie, W. M. Butler, Jr., M. G. Horning, R. P. Maickel, and H. M. Maling. <u>Alcohol-induced</u> triglyceride deposition in liver through derangement of fat transport. Am. J. Clin. Nutrit. 9:432, 1961.
- 21. Westerfeld, W. W., E. Stotz, R. L. Berg. The coupled oxidation-reduction of alcohol and pyruvate in vivo. J. Biol. Chem. 149:237, 1943.
- 22. Lieber, C. S., D. P. Jones, M. S. Losowsky and C. Davidson. Interrelationship of uric acid and ethanol metabolism in man. J. Clin. Invest. 41:1863. 1962.
- 23. Lieber, C. W. and C. S. Davidson. Some metabolic effects of ethyl alcohol. Am. J. Med. 33:319, 1962.
- 24. Rosenfeld, G. Inhibitory influence of ethanol on serotonin metabolism. Proc. Soc. Exp. Biol. & Med. 103:144, 1960.
- 25. Tygstrup, N. and F. Lundquist. The effect of ethanol on galactose elimination in man. J. Lab. & Clin. Med. 59:102, 1962.

MECHANISM OF ETHANOL-INDUCED HYPOGLYCEMIA

- 26. J. B. Field, H. E. Williams and G. E. Mortimore. Studies on the mechanism of ethanol-induced hypoglycemia. J.Clin. Invest. 42:497, 1963.
- 27. Freinkel, et al. See: Ref. A-6 J. Clin. Invest. 42:1112, 1963.
- 28. A. Lochner and L. L. Madison. The quantitative role of the liver and peripheral tissues in ethanol induced hypoglycemia. Clin. Res. 11:40, 1963.
- 29. A. Lochner and L. L. Madison. The mechanism of ethanol-induced hypoglycemia. Proc. 23rd Ann. Meeting Am. Diab. Assoc. pg 38, June 15, 1963.
- 30. W. C. Clark, J. E. Wilson and H. R. Hulpieu. Production of hypoglycemia by solox and by ethanol. Quart. J. Stud. on Alcohol 22:365, 1961.

HYPOGLYCEMIA IN DIABETICS

10

IV.

LIVER DISEASE AND DIABETES MELLITUS

- 31. Zimmerman, H. J., L. J. Thomas and E. H. Scherr. Fasting blood sugar in hepatic disease with reference to infrequency of hypoglycemia. A.M.A. Arch. Int. Med. 91:577, 1953.
- 32. Mellinkoff, S. M. and P. A. Tumulty. Hepatic Hypoglycemia. Its occurrence in congestive heart failure. N.E.J.M. 247:745, 1952.
- 33. Skillern, P. G. and E. H. Rynearson. Medical Aspects of Hypoglycemia. J. Clin. Endo. and Metab. 13:587, 1953.
- 34. Howard, J. E. Differential diagnosis and therapy of spontaneous hypoglycemia. V. A. TB 10-108, April 30, 1955.

11. ADDISON'S DISEASE AND DIABETES MELLITUS

- 35. Beaven, D. W., D. H. Nelson, A. E. Renold and G. W. Thorn. Diabetes Mellitus and Addison's Disease. A report of eight cases and a review of 55 cases in the literature. N.E.J.M. 261:443, 1959.
- 36. Gittler, R. D., S. S. Fajans, and J. W. Conn. Coexistence of Addison's Disease and Diabetes Mellitus: Report of three cases with a discussion of metabolic interrelationships. J. Clin. Endo. and Metab. 19:797, 1959.
- 37. Wehrmacher, W. H. Addison's Disease with Diabetes Mellitus. Arch. Int. Med. 108:114, 1961.

III. PANHYPOPITUITARY DISEASE AND DIABETES MELLITUS

- 38. Harvey, J. C. and de Kleck, J. Houssay phenomenon in man. Am. J. Med. 19:327, 1955.
- 39. Kemp, J. A. Amelioration of diabetes mellitus due to pituitary necrosis. Arch. Int. Med. 98:814, 1957.
- 40. Georas, C. S., G. F. Meissmer, J. A. Dillon and D. G. Calenda. Amelioration of Diabetes Mellitus after pituitary infraction. N.E.J.M. 263: 374, 1960.
- PANCREATIC INSULINOMA AND DIABETES MELLITUS
 - Gittler, R. D., G. Zucker, R. Eisinger and N. Stoller. Amelioration of Diabetes Mellitus by an insulinoma. N.E.J.M. 258:932, 1958.
 - Breidahl, H. D., J. T. Priestley, and E. H. Rynearson. Clinical aspects of hyperinsulinism. J.A.M.A. 160:198, 1956.
 - 43. Scholz, D. A., W. H. ReMine and J. T. Priestley. Hyperinsulinism: Review of 95 cases of functioning pancreatic islet cell tumors. Staff Meet. Mayo Clin. 35:545, 1960.

44. Markowitz, A. M., C. A. Slanetz, Jr., and V. K. Frantz. Functioning islet cell tumors of the pancreas: 25-year follow-up. Ann. Surg. 154:877, 1961.

HYPOGLYCEMIA-PRODUCING TUMORS AND DIABETES MELLITUS.

- 45. G. W. Thorn. Case Records of M.G.H. Weekly Clinicopathological Exercises. Case 34 - 1963 N.E.J.M. 268:1129, 1963.
- 46. L. Lowbeer. Hypoglycemia-producing extrapancreatic neoplasms: A Review. Am. J. Clin. Path. 35:233, 1961.
- 47. Tranquada, R. E., A. B. Bender and P. M. Beigelman. Hypoglycemia associated with carcinoma of the cecum and syndrome of testicular feminization. N.E.J.M. 266:1302, 1962.

page 7





