1059 PHYSIOLOGY

Effect of bile-pancreatic secretions removal on protein synthesis following hormonal stimulation. R.Mongeau*, J.Dunnigan* and J.Morisset. G.I.Research Unit, Fac. Sci., Sherbrooke Univ., P.Q. Canada. It has been shown by Lyman that removal of pancreatic juice from the intestine was a stimulus for enzyme secretion. Experiments were then designed to determine the effect of this removal on pancreatic protein synthesis following a single shot of I.V. Pancreozymin (8U/Kg) and Secretin (10U/Kg). In the canulated rats, protein synthesis was reduced 24, 21 and 11%, 5, 10 and 15 minutes following stimulation; increases of 31, 60 and 36% were noticed after 30, 45 and 60 minutes. In the control intact animals, protein synthesis was reduced 30, 23 and 0.5%, 5, 10 and 15 minutes following stimulation; increase of 24% was observed after 30 minutes but preliminary data seem to indicate that at 45 and 60 minutes protein synthesis is back to control level. Secretory studies showed that in the canulated rats, the maximal enzyme output following stimulation occurred between 5 and 10 minutes while in the control group the enzyme left in the pancreas reached its lowest value at 30 minutes to get back to control level at 60 minutes. It seems that removal of pancreatic juice from the intestine would prolong the increase in protein synthesis observed 30 minutes after stimulation. NRC Canada Grant A-6369.

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[illegible] -Met) IN PANCREATIC [illegible] Mary M. Green.* [illegible] Ca. 94609 [illegible] reatic juice and [illegible] which pure bile or [illegible] by catheter. [illegible] ritoneally (i.p.) or [illegible] (TCA) precipi- [illegible] juice contained [illegible] peak activity in [illegible] in the precipi- [illegible] ^{75}Se activity occurred [illegible] after [illegible] tion, [illegible] virtually all activity was [illegible] TCA supernatant. The TCA-supernatants of pure bile [illegible] bile-pancreatic juice contained about equal fractions [illegible] injected dose, indicating that ^{75}Se activity in the [illegible] of bile-pancreatic juice came from bile. [illegible] ^{75}Se-Met was given intraduodenally the fraction of the [illegible] appearing in the TCA precipitate was larger than when [illegible] was given i.p. and peak activity was delayed. The [illegible] suggest that appreciable amounts of absorbed free [illegible] acids may be recycled via an enterohepatic circulation [illegible] rat. (Supported in part by NIH Grant AM-15446.)

1061 BIOCHEMISTRY

PARALLEL DISCHARGE OF SECRETORY PROTEINS FROM PANCREATIC LOBULES. George A. Scheele* and Alan M. Tartakoff* (SPON: L. J. Greene). Rockefeller University, New York, N.Y. 10021. We have used an in vitro system of guinea pig pancreatic lobules to study kinetics of discharge of proteins from exocrine cells. Pancreatic lobules remained morphologically intact for at least 5 hr and showed low levels of resting discharge (5% per hr). Stimulation with optimal doses of carbachol (10^{-5}M), caerulein (10^{-9}M) or pancreozymin (7 x 10^{-9}M) caused discharge of 65% and 90% of the secretory proteins in 2 hr and 5 hr, respectively. Enzyme activity was used to monitor the kinetics of discharge of amylase, lipase, RNase and the zymogens chymotrypsinogen and procarboxypeptidase B (after activation with trypsin). These proteins were discharged in parallel during resting and stimulated secretion for the period studied (5 hr). Secretion independent of enzyme activity was also followed by SDS-gel electrophoresis. Radioactively labeled proteins discharged by carbachol, caerulein, or 75 mM KCl had similar distribution profiles on gels. The majority of gel bands has been identified with known secretory enzymes and zymogens. Quantitative analysis of carbachol induced secretion carried out at sequential intervals over 3 hr showed parallel changes of radioactivity in gel bands. The evidence suggests that all secretory proteins are discharged in parallel. (Supported in part by USPHS, NIH Special Fellowship AM 49448.)

1062 PHYSIOLOGY

SELECTIVE ENZYME SECRETION ELICITED IN SITU BY A NEWLY PURIFIED DUODENAL PEPTIDE. J.W. Adelson* and S.S. Rothman. Dept. Physiol., Univ. California, San Francisco, Ca. 94122

A newly purified basic polypeptide extracted from hog duodenum was administered i.v. to anesthetized rabbits at 3.7-5 µg/kg bw. Pancreatic fluid was collected from the cannulated duct for consecutive 20 min periods. In animals which exhibited high lipase outputs [>4µmoles substrate split·min^{-1}/collection period ("units")] no significant changes in either lipase or chymotrypsinogen (ChTg) output were observed; overall protein output increased by about 30%. In animals exhibiting a low lipase output (<4 "units"), peptide administration resulted in a dramatic increase in ChTg output within 40 min (saline control:2.7±.31 SEM, peptide:10.1±2.3;p<0.001). In contrast overall protein output was increased by only 60% and lipase was not significantly increased (control:1.6±.2, peptide:1.9±.2). The peptide appeared to rapidly alter the specific enzyme composition of pancreatic fluid at low enzyme outputs. Neither CCK-PZ nor cholinergic agents cause similiar effects. Because of the rapidity of the effect, in all likelihood it was due to selective transport of enzymes rather than to alterations in enzyme synthesis by the acinar cell. The selective transport of digestive enzymes due to a factor of duodenal origin is difficult to reconcile with the view that these proteins are secreted en masse. (Supported in part by USPHS, NIH grant AMDD 15762).

1063 PHYSIOLOGY

HORMONAL CONTROL OF INTESTINAL ALKALINE PHOSPHATASE SECRETION. W.P. Dyck, G.A. Martin* and C.R. Ratliff*. Scott and White Clinic, Temple, Tex. 76501

A rise in intestinal alkaline phosphatase activity in the bowel lumen and thoracic duct lymph has been shown after the introduction of fatty acids into the duodenum. The possibility that ingested fat might exert its effect on intestinal alkaline phosphatase through the release of cholecystokinin (CCK) prompted the present study in which alkaline phosphatase secretion into duodenal juice was examined in 38 subjects following intravenous stimulation with Secretin (Sn) and CCK. Mean output of alkaline phosphatase rose from 4.8 ± 1.2 (SEM) to 14.4 ± 2.8 units/10 min. immediately following Sn stimulation and a further increase to 33.2 ± 9.5 units/10 min. was observed following CCK injection. Cholecystectomized subjects exhibited similar responses to those without previous surgery. Isoenzyme differentiation studies, based on different susceptibilities to inhibition by urea and L-phenylalanine, indicate an intestinal origin of the enzyme. These data suggest that Sn and CCK may exert a direct effect on the release of alkaline phosphatase from the brush border membrane of the intestinal epithelial cell.

1064 PHYSIOLOGY

INHIBITION OF CHOLERA TOXIN BY FECES AND SERA OF VARIOUS ANIMALS by K. M. S. Aziz* and P. W. Hochachka. Cholera Research Laboratory, Institute of Public Health, G. P. O. Box 128, Dacca-2, Bangladesh and Department of Zoology, University of British Columbia, Vancouver 8, B. C., Canada.

Feces or supernatants obtained from feces suspended in normal saline, of cow, horse, guinea pig, goat or sheep either did not inhibit the action of cholera toxin or the inhibition was barely detectable. Dog feces, however, showed some inhibition of cholera toxin.

Sera obtained from cow, horse, guinea pig, goat, sheep, dog, fish or fowl did not contain any significant inhibitor of cholera toxin. Sera obtained from snake (cobra), mice and rat contained significant inhibitor of cholera toxin. Rat serum was the most potent inhibitor.

Sera from adult or infant conventional rats or from germ free rats of various strains were all potent inhibitors of cholera toxin. 0.01 ml of sera, from either of the two strains of conventional rats or from Fischer or Sprague strains of germ free rats, neutralized 0.5 mg of NIH lot 001 toxin. Sprague-Dawley germ free rat serum was the most potent inhibitor, 0.05 ml of this serum inhibited the action of 26 mg of NIH lot 001 toxin. (Supported in part by NIH Agreement 08-002-1 and Cholera Research Laboratory.)