European Pancreatic Club

Professor Henri Sarles, Director of the Unité de Recherches de Pathologie Digestive, Hôpital Sainte-Marguerite, Marseilles, presided at the second meeting of the European Pancreatic Club held in Marseilles on 28 and 29 April 1967.

CONTROL OF PANCREATIC SECRETION

A. A. Harper (Newcastle upon Tyne) During the ingestion of a meal the first mobilization of pancreatic enzymes in the acinar cells and adjustments of blood flow to supply the increased metabolic requirements of the activated gland are initiated by cephalic reflex pathways acting partly on the glandular cells and partly by vagal release of gastrin. The evanescent stimulus of ingestion is maintained and reinforced by the ingested food in the gastric storehouse. Distension of the stomach, soluble excipients in the food and the products of gastric digestion seem to be the stimulants in the gastric phase. The effects, which may persist for as long as any considerable portion of the meal remains in the stomach, are similar to those of the cephalic phase and are similarly mediated by vagal reflex pathways and hormonal release from the antral mucosa. Only when the gastric contents pass into the intestine is any considerable volume of water and bicarbonate secreted by acinar, centroacinar, and intercalated duct cells under the influence of secretin. Pancreozymin ensures the appropriate concentration of digestive enzymes in the juice by its ecbolic action on the pancreatic cells, and may also participate indirectly in maintaining an increased pancreatic blood flow.

PSYCHIC SECRETION OF THE PANCREAS IN MAN

H. Sarles, G. Prezelin, C. Figarella, C. Souville, and R. Dani (Marseilles) The success of psychic excitation in man is greatly facilitated by establishing complete trust between observer and subject. A special duodenal tube has been made which avoids contamination of the duodenum by gastric secretion. Pancreatic secretion begins two to four minutes after the stimulus of the sight and smell of food. It is not conditioned by the passage of gastric juice into the duodenum: (a) a solution of bromsulphthalein injected into the stomach does not pass into the duodenum; (b) the gastric response occurs almost always later than the response of the pancreas; (c) the gastric response and the pancreatic response are not parallel. Psychic secretion persists after cholecystectomy, it is diminished in pancreatic insufficiency. Appetite influences the response, which is higher after a prolonged fast or when food, which the subject is accustomed to take at that hour of day at which the test is carried out, is given. Anticholinergic drugs diminish or abolish the response. The four enzymes—amylase, lipase, trypsin, chymotrypsin—are excreted in parallel except when a psychic stimulus is given during prolonged secretin stimulation in which case lipase is dissociated from the other enzymes.

REGULATION OF EXOCRINE SECRETION OF THE PANCREAS

A. Svatos and V. Bartos (Prague) Excitation of the vagus nerve in the neck sends nervous impulses towards the duodenum where mediators liberate secretin and pancreozymin which stimulate not only the output of anylase, lipase, and trypsinogen but also collagenase and elastase. At the same time stimuli pass centrally in the cord and descend again to the pancreas to stimulate end organs which liberate inhibitors.

The pancreas infiltrated with Novocaine does not react to secretin. After nervous stimulation the concentration of secretin and pancreozymin increases in the urine. Therefore, secretin and the other hormones are not directly responsible for external pancreatic secretion but play an intermediary role.

VAGAL INNERVATION AND EXOCRINE SECRETION OF THE PANCREAS

J.-P. Govaerts and R. Kiekens (Brussels) In dogs furnished with a chronic fistula of the pancreatic duct, there is no variation in the output of enzymes after selective vagotomy in response to a test meal whereas total vagotomy leads to a delay in the production of exocrine pancreatic secretion.

RELATIONSHIP OF PANCREATIC BLOOD FLOW AND PANCREATIC SECRETION

T. E. Barlow, J. R. Greenwell, and T. Scratcherd (Newcastle upon Tyne) In the anaesthetized cat the first of a series of intravenous injections of secretin increases pancreatic blood flow in addition to stimulating secretion of juice. Subsequent injections produce a flow of juice but usually do not alter blood flow. Intravenous injections of pancreozymin, on the other hand, always increase blood flow in addition to stimulating enzyme output. Splanchnic nerve stimulation reduces blood flow and inhibits secretion. Small doses of adrenaline or noradrenaline produce a biphasic response. The first phase is a reduction in blood flow and inhibition of secretion which coincides with a rise in arterial blood pressure. This is followed by a second phase of increased blood flow which persists for many minutes.
A preceding injection of phenoxybenzamine prevents the first phase of vasoconstriction and increases arterial pressure. With certain doses of phenoxybenzamine the inhibition of secretion persists although the reduction in blood flow is abolished. The second phase of increased blood flow is abolished by previous administration of a combination of phenoxybenzamine and Alderlin.

**THE RELATION BETWEEN CONCENTRATIONS OF BICARBONATE AND PROTEIN IN THE PANCREATIC JUICE IN THE DOG**

H. Worning and F. W. Henrikson (Copenhagen) According to the admixture theory of the production of the exocrine secretion of the pancreas, it is possible to express the relationship between the concentration of bicarbonate and concentration of protein mathematically. A straight line relationship exists, the point of intercept at the y axis being the concentration of bicarbonate in the distal pancreatic secretion. In pancreatic juice obtained from three dogs after injection of a normal meal, the actual concentration of protein and bicarbonate in the juice showed linear correlation. The intercepts at the y axis were nearly identical to the individual maximal concentration of bicarbonate in the pancreatic juice after stimulation with secretin. These observations are compatible with the admixture theory.

**ANALYSIS IN THE PERFUSED PANCREAS OF FACTORS REGULATING WATER AND ELECTROLYTE SECRETION**

R. M. Case and T. Scratcherd (Newcastle upon Tyne) The isolated cat pancreas, perfused with isomolar (290 m.osmoles/l) bicarbonate-Ringer solution, will secrete for many hours during secretin stimulation. Alterations in perfusate osmolality, by increase or decrease of perfusate NaCl, causes a linear decrease or increase respectively in secretion, over the range 150 to 620 m.osmoles/l. Increase in osmolality by addition of sucrose to the perfusate causes a more marked decrease in secretion, which ceases at 420 m.osmoles/l. Consistently, the osmolality of the secretion is almost identical with that of the perfusate, but the total electrolyte concentration of the secretion is a few millequivalents greater. Reduction in NaCl with compensatory addition of sucrose causes a fall in flow rate but the juice osmolality is maintained constant.

The volume rate of secretion is directly proportional to perfusate bicarbonate concentration, secretion ceasing if it is omitted. Though flow rate is also related to potassium concentration other ions seem less important. The perfused isolated cat pancreas is sensitive to the metabolic inhibitors ouabain, acetazolamide, and dinitrophenol.

**INTERACTION OF SECRETIN AND PANCREOZYMIN ON THE EXTERNAL PANCREATIC SECRETION IN DOGS**

F. W. Henrikson and H. Worning (Copenhagen) The pancreatic secretion of fluid, bicarbonate, and protein in four dogs with chronic Thomas type fistulas has been studied in response to secretin (IU/kg), pancreozymin (IU/kg), and combined secretin pancreozymin (IU/kg of each). The secretion rates of fluid, bicarbonate, and protein after combined, submaximal stimulation were highly reproducible, as indicated by the coefficients of variation 1-7% (fluid), 3-9% (bicarbonate), 5-1% (protein). The secretion rates of fluid and bicarbonate obtained after the combined stimulation with secretin and pancreozymin (IU/kg b.w. of each) were very close to those obtained after isolated stimulation with maximal doses of secretin. Secretin and pancreozymin have a synergistic effect on the pancreatic secretion of fluid and bicarbonate, while the effect on the protein secretion is additive.

**A STUDY OF THE ULTRASTRUCTURE AND HISTO-ENZYMEOLOGY OF THE DOG PANCREAS DURING CONTINUOUS STIMULATION BY SECRETIN AND AFTER REPEATED INJCTIONS OF PANCREOZYMIN**

A. Ribet, R. Fedou, J.-P. Pascal, and N. Sannou (Toulouse) Secretin was infused in a dose of 70 units/kg/hour over six to seven hours into seven anaesthetised dogs in which the pylorus and bile ducts had been ligated, and a cannula inserted into the canal of Wirsung. Repeated injections of pancreozymin (2-3 units/kg/hour) were also given, and in some instances 500 mg/hour of Diamox or atropine 1 mg/kg/hour.

The washing out of enzyme was established in 20 minutes, but was never complete. Lipolytic activity was never abolished, but remained at a constant level which varied in different animals. The correlation between volume and bicarbonate has been confirmed at the 70 U kg/hour dose, but a superimposed dose of secretin leads to an increased volume, though bicarbonate concentration falls. The sum of Cl and HCO₃ was constant at 154 ± 10 m-equiv/l. Diamox produced a decreased volume, but no significant fall in HCO₃. Atropine had little effect on volume and HCO₃ but lowered lipolytic activity.

A histochemical study of 15 enzymes was made at times of varying pancreatic activity. The excretory ducts were very rich in dehydrogenase activity; during secretin stimulation increased dehydrogenase activity was observed both in the ducts and acini. After pancreozymin, an increase in activity, especially of glucose-6-phosphate dehydrogenase, isocitric dehydrogenase, and succinic dehydrogenase, was observed in the region of the acinar cells. At the moment of excretion of pancreatic enzyme a universal fall in enzymatic activity is found in the acinar cells, but little change occurs in the duct system.

In response to secretin, electron microscopy revealed a dilatation of excretory pores, immature granules, a dense intra-ergastoplasmic material and an increased number of mitochondria in the centro-acinar cells. After pancreozymin, zymogen granules migrate to the apex of the cell; they are small and numerous vacuoles were observed related to the excretion of protein, together with more rare structures (myelin-like forms, structures resembling cytolysosomes, crystalline forms). Towards the end of excretion, empty excretory pores, the predominance of vast areas with free ribosomes...
replacing the area of rough membranes, and the abundance of these rarer structures already mentioned were seen.

ULTRASTRUCTURE OF THE EXOCRINE PANCREAS IN MAN AND ANIMALS AFTER STIMULATION WITH SECRETIN AND PANCREOZYMINE

G. LABO, G. GASBARRINI, AND L. BARBARA (Bologna) After secretin in the acinar cells the endoplasmic reticulum and mitochondria are modified, and prezymogen and zymogen granules are increased. After pancreozymin, the prezymogen and zymogen granules are fewer, while the acini and excretory ductules are filled with an electron-opaque substance.

After secretin and pancreozymin, all these features are observed, the excretory ductules being distended by opaque substance. Findings similar to those found in response to pancreozymin are found when sorbitol is infused into the duodenum.

EFFECT OF INSULIN ON THE RATE OF BIOSYNTHESIS OF SOME PANCREATIC ENZYMES

J.-C. PALLA, A. BEN ABDELJILIL, AND P. DESNUELLE (Marseille) Amylase (number of units per μg DNA-phosphorus) is about 10 times lower than normal in the pancreas of alloxan diabetic rats after one week, and about 20 times lower after two weeks. When diabetic animals receive daily injections of insulin, the level of amylase increases after one day and reaches normal or higher than normal values after three to five days. The rate of biosynthesis of the enzyme undergoes similar variations. It is very low in diabetic animals but becomes normal after treatment with insulin.

To see whether insulin is acting directly to induce amylase biosynthesis, or indirectly through its well-known effect on cell permeability, insulin was injected into normal rats fed on various diets. In rats ingesting much glucose, injected insulin is unable to raise the already high level of amylase further. In rats ingesting proteins exclusively, insulin has no effect on amylase despite the fact that the enzyme level is rather low in these circumstances. But it strikingly increases the level of chymotrypsinogen.

A tentative explanation of the results is that insulin controls the biosynthesis of amylase by favouring the entry of glucose into acinar cells, and the biosynthesis of chymotrypsinogen (and probably of other proteolytic enzymes as well) by favouring the entry of amino acids into the same cells.

EFFECTS OF LYSINE AND THREONINE DEFICIENCY ON THE EXOCRINE PANCREAS OF YOUNG GROWING RATS

J. CHRISTOPHE, A. VANDEMEERS, R. ROBBERECHT, AND J. RATHE (Brussels) Young rats made deficient in lysine and threonine stop growing immediately. After three weeks of protein malnutrition the mitotic index is very low in the pancreas and each acinar cell contains on an average 19% less RHA and 38% less protein. Hydrolase levels are much more affected than total proteins and a relative increase in the secretion of these enzymes is observed. In the case of amylase it has been demonstrated that variations of enzymatic activity correspond to modifications of the amount and not of the quality of the protein. From the total rate of protein synthesis in vivo, calculated after the intraperitoneal injection of leucine 1-14C, it appears that protein synthesis is increased (+100%) when compared to control values. These results apparently mean that the low protein content of the pancreas is due to accelerated secretion and not to inadequate synthesis or an instability. At the end of this kwashiorkor-like condition, the major modifications of enzyme concentration develop within eight hours. A single meal of a well-balanced diet leads already to prompt increases in the pancreas and to definite increases in the small intestine. The excess formation of hydrolase is due to the synthesis of new messenger RNA having a half life not longer than five to six hours. The total rate of protein synthesis, calculated from radioactive data, is doubled after three days of normal diet.

STUDY OF THE RELATION BETWEEN SECRETION AND BIOSYNTHESIS OF PANCREATIC ENZYMES

G. MARCHIS-MOUREN AND H. REGGIO (Marseille) The speed of biosynthesis of the proteins of exocrine pancreatic secretion has been measured in varying secretory states. Slices of pigeon pancreas 1 mm thick were incubated in Kreb's solution under oxygen at 30°C in a Dubonff metabolic agitator. Samples of the medium were taken at regular timed intervals and in these protein and enzymes were estimated. Up to 60 minutes the discharge of protein and amylase, lipase, and chymotrypsinogen bears a linear relationship to time.

Slices have been taken from both fasting and fed pigeons, to which a preliminary injection of carbamyl choline may have been given. The speed of the discharge of protein and enzymes is different. The slopes of the linear relationships of fed pigeons is three or five times greater than of fasting pigeons, while carbamyl choline injected 45 minutes before death diminishes excretion in both fasting and fed pigeons.

METABOLISM AND SECRETION OF RAT PANCREAS IN VITRO

H. BAUDUIN, J.-J. REUSE, AND J.-E. DUMONT (Brussels) The dependence of secretion on protein synthesis and on sources of energy was studied in vitro in rat pancreas. A Kreb's-Ringer Tris medium pH 7.4, 0.154 M enriched with 10 mM glucose and containing the mixture of essential amino acids enriched in glutamine and asparagine (Campagnes) was chosen. In these experimental conditions glycolysis can furnish not more than 10% of the adenosine triphosphate of the pancreatic cell; the mitochondria are therefore the main source of energy in the pancreas.

Carbamyl choline can evoke a liberation of chymotrypsinogen into the incubation fluid. The inhibition of protein synthesis by puromycin does not prevent the stimulation of secretion by carbamyl choline. Oligomycin inhibits the formation of mitochondrial ATP.
the presence of this inhibitor carbamyl choline continues to liberate pancreatic enzyme. Other substances which interfere with the formation of ATP (antimony, dinitrophenol, anoxia) increase the liberation of enzyme, an observation which suggests that ATP must be necessary to retain enzymes within the cell.

In optimal conditions of incubation the pancreas can release enzyme in response to physiological stimuli and this stimulation requires neither active synthesis of protein nor a normal formation of ATP in the parenchyma.

**ANGIOGRAPHIC EVALUATION OF THE EFFECT OF VASOACTIVE SUBSTANCES ON THE PANCREATIC CIRCULATION**

**ERIK BOJSEN (Lund)** Different opinions exist concerning the action of vasoactive drugs on the pancreatic circulation. Except for an estimation of the changes of the amount and content of pancreatic juice after vasoactive drug infusion, no objective method exists which measures a change of flow through the pancreatic vessels.

In order to find out whether angiography could give some information of the pancreatic blood flow, selective coeliac and superior mesenteric angiograms were performed before and after infusion of adrenalin and bradykinin into these vessels. Angiography is in itself an unphysiological method, but repeated injection of contrast medium will not substantially change the angiographic pattern.

The main purpose of the present investigation was, however, not to define the change in blood flow but to find a method which increases the vascular detail during pancreatic angiography in order to provide more exact information on pancreatic disease. Bradykinin caused a marked increase of flow through all vascular beds within the coeliac and superior mesenteric territories and thus also through the pancreatic arteries. The angiographic detail was poor after bradykinin as a consequence of the increased flow.

Adrenalin, on the other hand, caused a marked constriction of gastric, splenic and hepatic arteries, while the pancreatic vessels became wider and the contrast medium passed more rapidly through the pancreas. The doses injected into the coeliac or hepatic arteries ranged from 5 to 10 μg adrenalin, which definitely increased the information gained about the pancreas. One exception to this rule was in pancreatitis, where the pancreatic vessels were smaller and less well demonstrated compared with the control study. The test may prove useful in the differentiation of inflammatory and neoplastic disease of the pancreas.

**ARTERIOPORTOGRAPHY IN CHRONIC PANCREATITIS**

**C. HERNANDEZ (Paris)** Serial coeliac and superior mesenteric arteriography has been practised to avoid double femoral puncture, the sole source of morbidity (0-5% in 1,700 arteriographies at l'Hôpital Bichat). This technique avoids the superimposition of the arterial and parenchymatous phases, dissociates the spleno-portal and mesenteric-portal streams and does not impair appreciably the quality of the arteriolar pictures of the coeliac and mesenteric arcades. The iodinated injection is followed by "xylocaine serum" which proves the quality of arteriolar image but most of all facilitates the interpretation of the returning spleno-mesenteric-portal axes.

The study comprised 120 patients. In the majority changes lay in the larger arterial trunks at some distance from the lesion, and are interpreted as due to peripancreatitis. Changes in immediate relation to the pancreas are less often encountered, for the arteries are less well seen in chronic pancreatitis than in other pancreatic lesions.

1 A slender walled circular narrowing of the coeliac trunk or, in this order of frequency, of the proximal segments of the splenic, common hepatic, coronary, gastric, and gastroduodenal arteries, found in 20% of chronic pancreatitis, it is not pathognomonic though it is not found in cancer of the pancreas.

2 A regular, tapering cone-shaped narrowing, in order of frequency of the splenic, common hepatic, and gastroduodenal arteries, was found in 35% of cases; the look in cancer is much more irregular, eccentric and often is complete.

3 A cylindrical, muff-like symmetrical narrowing, which may extend over an appreciable length of artery, was found in 65% of cases of chronic pancreatitis. In cancer the picture is much more irregular with a nibbled or notched appearance leading to asymmetrical block.

4 Poor vascularity was frequently observed but its incidence cannot be estimated since its appreciation is largely objective. This appearance is in marked contrast to the persisting arteriolar picture, even hypervascularization, seen in cancer.

No arterial abnormality was found in 8% of confirmed cases of chronic pancreatitis. There is no correlation between the arterial lesion and the severity of pancreatitis; it is not possible to forecast either the extent or localization of the disease. Pseudocysts may be revealed by this technique.

Finally the effect of chronic pancreatitis on the splenic, mesenteric, and portal veins may be demonstrated either as simple compression, a thrombosed segment of splenic vein, or in the end massive splenic or portal thrombosis with associated portal hypertension.

**VALUE OF SELECTIVE ANGIOGRAPHY AND PERCUTANEOUS TRANSHEPATIC CHOLANGIOGRAPHY IN PLANNING OPERATIONS ON THE DISEASED PANCREAS**

**S. BAYINDER, E. WAGNER, AND K. SCHULTIS (Giessen)** In two years, 30 patients with pancreatic disease have been studied by arteriography. A comparison has been made of the results of this technique, peritoneoscopy and transhepatic cholangiography. This last has proved most useful in the diagnosis of obstructive jaundice secondary to pancreatic disease.

**FRONTAL TOMOGRAPHY OF THE PANCREAS WITH PNEUMO- AND RETROPERITONEUM COMPARED WITH AXIAL TRANSVERSE TOMOGRAPHY AND SELECTIVE ARTERIOGRAPHY**

**C. GUEN AND H. PIETRI (Marseilles)** Frontal tomography undertaken with pneumoperitoneum and retropneumo-
The peritoneum is acceptable to patients and free from risk (no accidents in 180 cases). When the pancreas is normal the body and tail of the pancreas are always visualized; in one in five cases the head is well seen; when the head is ill defined, recourse is made to hypotonic duodenal insufflation.

In the pathological pancreas abnormalities of the upper and lower surfaces are well defined; in contrast the anterior and posterior surfaces are better studied by axial stratigraphy. Calcification of the pancreas is well seen, as are enlarged glands of the hila of spleen and liver, and, in the case of cancer, invasion of neighbouring organs.

Selective abdominal arteriography, which is more tedious for the patient, gives characteristic indirect evidence of cysts and pseudocysts. The vascular outline obtained by this technique is proving more and more useful to the surgeon when planning his operation.

The scope and interpretation of pancreatic scanning


Pancreatic scanning with $^{131}$I selenomethionine is the only current technique which can adequately visualize the whole organ. $^{131}$I selenocystine has not proved to be so valuable. The greater part of the dose taken up by the pancreas is incorporated and excreted as digestive enzymes. Uptake is maximal throughout the gland at 30 to 60 minutes after injection. Thereafter activity is concentrated towards the centre of the gland, presumably towards the central duct and then the head of the pancreas. Timing is thus crucial in interpreting the scan. Selenomethionine scan is always followed by a liver scan using colloidal gold ($^{197}$Au). The use of secretin and pancreozymin and morphine has been abandoned. The best stimulus to uptake is a functioning gastrointestinal tract and a secreting organ.

The normal pancreas assumes three main shapes. Its position is variable. A major use of this technique is to detect space-occupying lesions in or adjacent to the pancreas. Non-functioning tumours appear as filling defects, but in one case of the Zollinger-Ellison syndrome, an undifferentiated tumour in the tail of the pancreas was associated with enhanced uptake. Aneurysms of the aorta and coeliac axis branches adjacent to the pancreas are also associated with filling defects and distortions of normal relationships. In acute pancreatitis there is general absence of uptake, a feature noted too in some elderly and diabetic subjects. Reproducibility of scans is good and patients scanned six-12 months later show very similar patterns.

Lymphangiography in chronic pancreatitis

J.-C. Sarles (Marseilles) J.-C. Sarles has added seven further cases to the four previously studied by lymphangiography, in all 10 men and one woman. Two features are characteristic of chronic pancreatitis: (1) a striking delay in the proximal movement of Lipiodol; (2) a striking obstruction, but never complete, at the origin of the thoracic duct with distal lymphatic stasis.

It has been stated that the complete arrest of the opaque medium is present in cancer of the pancreas. In a single case of cancer of the head of the pancreas, lymphangiography showed a picture identical to that found in chronic pancreatitis. It is not possible to distinguish chronic pancreatitis from a malignant lesion by lymphangiography.

The place of axial transverse statigraphy in the diagnosis of pancreatic disease

P. Bret (Lyons) Thirteen years' experience and more than a thousand examinations confirm that this technique can without danger support a diagnosis in 80% of patients with pancreatic disease.

It is not yet possible to compare the results of arteriography but it can be said that is more valuable in diagnosing tumours of the islets of Langerhans.

Ultrastructure of the rat exocrine pancreas after long-term intake of ethanol

N. Darle, R. Ekholm, and Y. Edlund (Gothenberg)

Male Sprague-Dawley rats, kept on a standard diet, were given 20-40% ethanol as a substitute for drinking water over periods ranging from three to 12 months. The pancreatic tissue was fixed by infusion of glutaraldehyde into the abdominal aorta of the anaesthetized animal.

Both by light and electron microscopy the pancreatic tissue kept its normal appearance surprisingly well. One, definite and characteristic change was observed, the presence of lipid droplets in the acinar cells. By electron microscopy these droplets appeared as discrete, rounded globules, varying in size between 0.3 and 1.5 μ, and mainly contained in the basal portions of the cells. This change was quite obvious by electron microscopy after three months and by light microscopy after six months' ethanol intake, and became more pronounced the longer the experiment continued.

A study of the effect of ethanol and dietary fat on the pancreas of the rat

C. Figarella, F. Tasso, J. Clop, H. Sarles, and Picard (Marseilles) The enzymatic content of the pancreas of the Wistar CF rat (120 g) was studied under the influence of diets deficient in protein (7 g per 100 g), with normal fats (17 g per 100 g) or rich in fat (37 g per 100 g) with or without alcohol in addition.

1 Enzymes increase in parallel with weight in control rats studied for 110 days, while amylase and lipase diminish in protein-deficient rats, without appreciable change in chymotrypsinogen and trypsinogen, no matter what the fat ration.

2 With a diet of 7% casein, replacement of water by 20% by weight of ethanol, no matter what fat was taken, led to a significant fall in the pancreatic content of all four enzymes.

Early changes, observed by ultramicroscopy, are the development of phospholipid inclusions and by a diminution in zymogen granules, with a transient hypertrophy of the Golgi apparatus and mitochondrial...
changes. Alcohol seems to be the determining factor in these changes. The cytopathological appearances permit an approach to the more general problem of the participation of the different membranous and cellular components in forming lipid inclusions.

THE POSSIBLE ROLE OF PHOSPHOLIPASE A IN ACUTE PANCREATITIS

W. CREUTZFELDT AND H. SCHMIDT (Göttingen) Lysolecithin, injected into the pancreatic duct of rats, resulted in severe pancreatic necrosis. The same effect was seen with a mixture of phospholipase A and small amounts of bile acids. In this case thin-layer chromatography showed a high concentration of lysolecithin in the necrotic pancreas of the rat. Nearly 50% of the extracted phospholipid phosphorus was found as lysolecithin, whereas lecithin and cephalin were markedly reduced.

An identical distribution of phospholipids was found in the necrotic part of the pancreas from a patient who died from acute pancreatitis. In the normal part of the same pancreas the distribution of phospholipids was nearly normal. In a mixture of human bile and pancreatic fluid lecithin is converted quantitatively to lysolecithin. The intrapancreatic activation of phospholipase A as a decisive factor in the pathogenesis of acute pancreatitis was discussed.

THE SIGNIFICANCE OF THE HAEMIN PIGMENT OF NEMIR AND DRABKIN IN THE PATHOGENESIS OF ACUTE PANCREATITIS

H. SCHMIDT AND W. CREUTZFELDT (Göttingen) The toxic effect on the pancreas of the abnormal haemin pigment, described by Nemir and Drabkin, was studied in rat experiments. Sterile mixtures of rat blood and trypsin which contained the abnormal haemin pigment (incubated for 24 hours) produced when injected into the pancreatic duct only moderate parenchymal necrosis. The same effect was seen with fresh mixtures of blood and trypsin, which contained no abnormal haemin. Severe haemorrhagic pancreatitis was obtained only when blood-trypsin mixtures which showed bacterial contamination were injected.

Our experiments do not confirm the hypothesis that the possible formation of the abnormal haemin pigment plays an important role in the pathogenesis of acute pancreatitis.

PANCREATIC LYMPH CIRCULATION AS A FACTOR IN THE TRANSPORT OF LABELLED ALBUMIN AND RED BLOOD CELLS FROM THE PANCREAS OF THE DOG

M. PAPP (Budapest) The concentration of 10 ml of albumin labelled with \(^{131}\)I infused into the duct of Santorini of the pancreas at a pressure of 30 to 50 cm water was found to be significantly higher in the lymph of the thoracic duct than in the plasma of the pancreatic vein, both in normal dogs and in dogs with bile-induced pancreatitis. In both the plasma contained more of the labelled albumin transported in the first three hours from the pancreas than did the lymph. Experiments carried out under similar conditions with \(^{51}\)Cr-labelled erythrocytes of the normal dog failed to produce evidence of appreciable transport.

PANCREATIC ENZYMES CIRCULATING IN THE BLOOD DURING PANCREATIC INJURY ASSESSED BY IMMUNOLOGICAL TECHNIQUES

E. VAREL (Paris) Even in acute haemorrhagic pancreatitis in which pancreatic digestion liberates enzymes in the abdomen, it has not proved possible to demonstrate unequivocally enzymes circulating in the blood. The proteolytic inhibitor in plasma is much too strong for enzymatic activity to be demonstrated.

An immunological technique has been developed which reveals the presence of alpha chymotrypsin and trypsin in peripheral blood. This method could be adapted to diagnostic use.

CAPILLARY MICROSCOPY IN ACUTE PANCREATITIS

F. X. SAILER, G. SCHONBACH, AND L. AMANN (Giessen) The injection of bile into the pancreatic ducts of rabbits leads to acute pancreatitis. A film was presented of the intravital capillary microscopy changes which occur in developing pancreatic lesions.

METOCLOPRAMIDE AND EXOCRINE PANCREATIC SECRETION

A. DELCOURT AND P. WETTENDORFF (Brussels) Metoclopramide given intramuscularly or intravenously in a dose of 10 mg facilitates the passage of a tube in the duodenum. The routine use of this drug in practice depends on whether it has an effect on pancreatic secretion stimulated by secretin and pancreozymin.

The pancreas of dogs provided with a cannula in the pancreatic duct is stimulated by a continuous infusion of these duodenal enzymes. Varying doses of from 1 to 10 mg/kg of metoclopramide were given after a 'washout' and stabilization of the secretory response.

In doses of less than 10 mg/kg body weight no effect was observed, but at this dose there was a transient inhibition of enzyme discharged.

At dose levels used in man, the hormonal stimulation of pancreatic secretion is not modified.

MAXIMAL BICARBONATE SECRETION IN MAN

K. G. WORMSLEY (Manchester) Using increasing doses of secretin given by intravenous infusion, maximal bicarbonate output has been assessed in normal subjects and patients with disease of the upper alimentary tract. We have found that normal subjects and patients with disease of the stomach and gall bladder secrete more bicarbonate than they can secrete acid, while patients with duodenal ulcer and acute and chronic pancreatitis secrete more acid than they can secrete bicarbonate.

We have also studied the electrolyte composition of duodenal juice in human subjects and have been unable to confirm the relationship between flow rate, bicarbonate and chloride suggested by Lagerlöf and by Dreiling and
Janowitz. On the basis of our analysis of the electrolyte content, we have been able to suggest limits of normal and abnormal duodenal juice composition.

PURIFICATION AND CHARACTERIZATION OF A NEW PROTEINASE FROM THE PANCREAS

W. Gross, W. Bernard, T. U. Hausamen, and W. Rick (Düsseldorf) While in fresh pancreas with specific substrates active trypsin or chymotrypsin cannot be demonstrated, a proteolytic enzyme active against casein or haemoglobin with an pH optimum of 7-5 is found. Using gel filtration, the enzyme was partially purified. None of the substrates specific for trypsin, chymotrypsin, elastase, collagenase, or the esteroproteolytic enzyme (G Jessing) is split by the enzyme. Ca++ and cystine have no effect. Soybean and pancreatic trypsin inhibitors, ovomucoid, Trasylol, (α)-aminocaproic acid, hydrocinnamic acid, and SH-reagents do not inhibit the activity of the enzyme. It is concluded that the enzyme is not identical with one of the known pancreatic enzymes.

TRYPTIC AND CHYMOTRYPIC INHIBITORY CAPACITY OF SERUM AND SEROUS EFFUSIONS IN PANCREATIC DISEASE

J. Warter, P. Metais, and J. Bieth (Strasbourg) The trypsin inhibitory capacity (TIC) and chymotryptic inhibitory capacity (CIC) of serum are measured as the amounts of trypsin and chymotrypsin added in excess in the presence of serum assayed against benzoylarginine-para·nitroanilide (BAPNA) and succinylphenylalanine-para·nitroanilide (SUPHEPA).

In 100 normal subjects the mean TIC is 4-90 ± 0-70 units and the mean CIC is 0-31 ± 0-07 units.

In calcified pancreas the inhibitory levels are normal. Slight increases (never exceeding 180% of normal) have been found in chronic pancreatitis. Relapsing acute pancreatitis and pseudocysts are associated almost always with a great elevation of TIC (up to 260% of normal). A rise in TIC is always found in neoplasms of the pancreas; although this was less in cancer of the body, it exceeds normal sometimes by 200% in cancer of the head of the pancreas, with obstructive jaundice.

CIC and TIC run almost always in parallel in pancreatic disease.

The presence of inhibitors in ascitic fluid and pleural effusions of pancreatic origin confirm the protective role of these inhibitors against proteases. Even in the presence of amylase and lipase, no free proteases have been found and it appears that proteases are inhibited by excess inhibitor. In the contents of pseudocysts also amylase and lipase may be present but no proteolytic activity.

A similar increase in TIC and CIC can be found in pathological states not arising in the pancreas associated with changes in α globulins (acute and chronic hepatitis, the active phases of chronic polyarthritis, and acute articular rheumatism).

TECHNICAL AND PHYSIOPATHOLOGICAL STUDY OF AUTOGRAPHS AND HOMOGRAPHS OF THE PANCREAS

J. F. Grenier, M. Gillet, A. Klein, J. Kachelhoffer, L. Michel, and A. G. Weiss (Strasbourg) Thirteen autographs and 27 homographs of the duodenum and pancreas were performed on 40 pancreatome·tized dogs. Imuran and cortisone were used as immuno-suppressive drugs. The longest survival of autotransplants was 26 days with a mean of 11 days; the longest surviving homotransplant survived 23 days with a mean of six days.

Variations in blood sugar and quantitative analysis of external pancreatic secretion give information of the functional value of these grafts and their survival.

HEREDITARY PANCREATITIS

W. Veeger (Gröningen) Three established and three probable cases of relapsing chronic pancreatitis have been found in three generations of a kindred and three proved cases in another family. They presented as the patients of Gross and Comfort but had no dibasic aminoaciduria.

Male twins suffering from relapsing chronic pancreatitis were studied. Both had pancreatic calculi, one had increased lysinuria. The twin without aminoaciduria presented with diabetes which was treated with tolbutamide. An increased excretion of coproporphyrin and uroporphyrin but not porphobilinogen was a feature. Several years later he developed chronic pancreatitis. It is possible that a latent form of hepatic porphyria is, like aminoaciduria, a feature of chronic pancreatitis.