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TREATMENT OF ACUTE PANCREATITIS WITH HEXAMETHONIUM BROMIDE

BY

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In 1889 Fitz described three types of acute pancreatitis—haemorrhagic, gangrenous, and suppurative—based on the gross pathology of the gland. McWhorter (1932) collected 64 cases and classified them as follows: (1) acute or subacute pancreatitis in which there was no haemorrhage but in which the gland was enlarged, oedematous, and very hard; (2) the haemorrhagic, in which haemorrhages were present but there was no evidence of gangrene or suppuration; (3) cases with gross necrosis or gangrene but no suppuration; and (4) cases with suppuration or definite abscess formation.

A classification on an aetiological basis suggested by McWhorter (1932) and Jones (1943) adds little to our knowledge.

A. Infectious Origin.—(1) By extension along the lymphatics; (2) by extension from the blood stream; (3) by extension along the pancreatic ducts, from the duodenum or from the bile ducts; (4) by direct extension from infected foci; (5) following activation of bacteria in the normal gland; (6) by bacterial permeability from adjacent diseased viscera.

B. Non-infectious Origin.—(1) Mechanical, including stasis in the ducts. (2) Chemical, and originating in activated ferments resulting from (a) bile; (b) duodenal contents; (c) degenerated duct contents; (d) autolysis. (3) Degenerative changes in the pancreas: (a) secondary to benign or malignant tumours; (b) resulting from vascular degeneration or haemorrhage; (c) toxic changes following systemic disease. (4) Trauma.

C. A Combination of Two or More of the Above Factors.

The disease most commonly occurs in the fifth and sixth decades in obese males. Bisgard and Baker (1940) pointed out the frequent association of cholelithiasis. The disease may affect the whole gland or may be limited to the head, the body, or the tail. The extent of necrosis depends upon the violence of the biochemical explosion. If small areas alone are involved they may be absorbed or converted into fibrous tissue; but, if large, the necrotic areas soon slough or suppurate.

Ian Aird (1949) states that "a complicated network of theory has been woven around pancreatitis in order to relate it to gall-bladder disease but without any conclusive or all-embracing theory." We believe that pancreatitis is due to a vascular accident and that the findings of biliary pathology are coincidental.

One of us was impressed with the similarity in pathology of thrombosis and embolism in other organs, and treated with systemic heparin two cases of acute pancreatitis confirmed by exploratory laparotomy. The results were satisfactory, but led to a continuous ooze of blood from the suture line in each case. Although pain was relieved the loss of blood from the suture lines was sufficient to require intravenous blood transfusion. We concluded that the systemic heparin may have been responsible for the recovery of these two cases, which we classified, according to McWhorter's criteria, as gangrenous lesions of part of the head.

The following two cases were treated with hexamethonium drugs, and had a very smooth convalescence.

Case 1

An obese male aged 64 had been in good health until the morning of May 5, 1952, when he was seized with a sudden agonizing abdominal pain. It was located around the umbilicus and the left flank.

On examination he was found to be very shocked, and was frequently vomiting small amounts of bile-stained fluid. His face was livid and beaded with sweat, and the extremities were cold and damp. The abdomen was uniformly rigid, with maximum tenderness around the umbilicus. No other abnormal physical signs were discovered. A provisional diagnosis of pancreatitis was made. This was confirmed by exploratory laparotomy. The relevant findings were an injected peritoneum and a hard oedematous dusky-red pancreas with darker patches in the head. The proximal 3-4 in. (7.5-10 cm.) of the small gut was distended and scattered and traced with lymphatic vessels. The omentum revealed fat necrosis. The biliary tract was normal on palpation. The abdomen was closed without drainage.

The day following exploratory laparotomy the patient remained in great pain, and for this reason a bilateral posterior splanchnic block was performed with 1/2,000 amethocaine. The relief from pain was dramatic and the improvement in the clinical condition most marked. Pain began to return after complete control for approximately six hours. It seemed reasonable to believe that ganglion-blocking agents, such as hexamethonium, would similarly relieve pain, and that administration of this drug would have none of the difficulties or dangers of repeated splanchnic blocks. Oral hexamethonium bromide, 250 mg., was given via the indwelling Ryle's tube twice a day, and the activity of the drug was observed by blood-pressure readings, carried out by the nursing staff. Pain disappeared after six hours, and the next day it was possible to assess the patient as convalescent. Treatment with hexamethonium was continued for five days, the patient being discharged, cured, on the tenth day. He remained well up to the time of submitting this report.

Case 2

This patient was a man aged 52. His history was complicated by a previous perforation of a peptic ulcer six years previously. Three years before his present illness he was subjected to gastrectomy, this being followed by a complete remission of his indigestion.

On the day of admission (August 9, 1952) he was seized with violent upper abdominal pain, mainly localized to the right hypochondrium. He frequently vomited small amounts with each severe attack of pain, which appeared to be colicky in type. The abdomen was explored and a considerable quantity of free sero-sanguineous fluid was found. The great omentum was studded with islets of fat necrosis and several feet of the small intestine was injected, distended, and traced with lymphatic vessels. The pancreas was hard, oedematous, and of a deep-red colour over the whole visible surface of the gland. The biliary tract felt normal on palpation. The abdomen was closed without drainage.

Hexamethonium, 250 mg., was given as soon as the patient was conscious, and this was continued twice a day for the next seven days, four-hourly blood-pressure readings

again being carried out by the nursing staff. The following day he was pain-free, and convalescence was smooth and uneventful. He was discharged fit and well 12 days after operation.

Discussion

The treatment of acute pancreatitis has previously been based on its frequent association with cholelithiasis. It is our opinion that the findings of biliary calculi are coincidental, and that the pathological changes in the gland can be explained wholly in terms of a vascular catastrophe. The more serious or fulminating lesion can be explained by thrombosis or embolism of a main pancreatic vessel. Certainly the appearance of the gland at operation is supportive evidence, but the picture is clouded by the biochemical action, which releases a sanguineous or sero-sanguineous fluid rich in pancreatic ferments. If small areas only are involved they may be absorbed, converted into fibrous tissue, or calcified. It is impossible to reverse a pathological process which has involved sloughing or abscess formation, and this parallel may be seen in the upper or lower limb when embolism or thrombosis occurs in a main vessel. Survival of an organ depends on the location of the thrombosis or embolism, the state of the collateral vessels, and the presence or absence of vasospasm.

It is reasonable to suppose the same vascular phenomena take place in the pancreas, but the exact nature of the process must remain a matter of conjecture.

Andrew Dale (1952) reported optimistic results from the treatment of acute pancreatitis with splanchnic blocks. Our own experience of a single case before this publication supports his findings, but the mode of action is not understood. Ganglion-blocking drugs seem to produce an excellent result. The disease is robbed of its terrorizing pain. It, of course, cannot affect the established gangrenous or suppurative process in a gland which must be subjected to drainage.

In our experience exploratory laparotomy is indicated even if there appears to be no doubt about the diagnosis, as an assessment of the degree of destruction of the gland is then possible, and in the case of gangrenous, sloughing, or suppurative lesions drainage of the gland is indicated. Associated cholelithiasis should be ignored unless the pathology can be directly related to "inflammatory changes" in the pancreas. The inflammatory changes bear a striking resemblance to thrombosis or emboli of the main vessels to other intra-abdominal organs and the upper and lower limbs. Gangrene, sloughing, and suppuration follow gross disturbances of the blood supply, and the severity of the symptoms may be related to the extent of the infarction.

We feel, however, that types 1 and 2 of Fitz's classification might well be treated with drugs of the methonium group. In the cases reported hexamethonium was chosen arbitrarily. Each member of the methonium group varies in effect from ganglion to ganglion, and it may well be that some other member of the group would have a more pronounced action on the splanchnic ganglion. Paton (1951) suggests that tetramethonium may have this action.

In our two cases the relief of pain and the improvement in the general clinical condition were contrary to previous experience. We feel that a vascular catastrophe is the causative factor in acute pancreatitis, and further investigation along these lines may lead to a better understanding of the disease and simplify the treatment.

ADDENDUM.—Since submitting this paper for publication two further cases have been treated with equally successful results. *Case 3*, a man aged 62, admitted with severe abdominal pain, general collapse, and urinary diastase of 75. Diagnosis was confirmed by exploratory laparotomy, and he was treated with hexamethonium bromide. He was discharged on the tenth post-operative day and has remained free of symptoms for five months. *Case 4* was that of a man of 72 with typical acute abdominal pain. The urinary diastase was 68. Exploratory laparotomy confirmed the diagnosis, and treatment with hexamethonium relieved him of his pain. He was discharged from hospital on the twelfth day and has remained free from symptoms for four months.

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LOCAL EFFECTS OF CERTAIN MEDICAMENTS ON THE TEETH

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It is a common experience for dental surgeons to be confronted by small children, aged from 2 years upwards, suffering from gross caries of their deciduous dentition. This condition may arise from a variety of causes, and it is often difficult to decide what is the principal factor in a particular case. If, however, a child known to have normal dental structures suddenly develops rapid decay affecting particularly the labial and buccal surfaces of his teeth, the possibility of chemical damage must be considered. It has been observed that such damage often occurs after the protracted use of some of the commonly used iron tonics.

Certain of these iron tonics are very acid. Representative samples, tested with a Cambridge pH meter, gave the following hydrogen-ion concentrations:

	Undiluted pH	Diluted to 50% with water	
		pH	pH
Syr. ferr. phosph. co.	1.5	..	1.9
Mist. ferr. sulph. pro infant., N.F.	1.67	..	2.28
Elix. ferr. glucon., R.F.H.	3.52	..	3.8
Mist. ferr. et ammon. cit., N.F.	6.66	..	7.7
"Colliron"	8.56	..	8.87

The deleterious effect of acids on the teeth is well known. McClelland (1926) showed that teeth left in a solution of pH 4.5 for twelve hours suffered some degree of decalcification, and Stafne and Lovstedt (1947) reported many cases of dental damage following the prolonged and regular sipping of pure lemon juice (pH about 2.5). Hardwick (1950) has demonstrated that the amount of enamel decalcification that occurs when a tooth is immersed in an acid solution does not depend entirely on the pH of the solution but also on the nature of the acid. For example, N/100 lactic acid, with a pH of 2.9, in some circumstances produced etching of the enamel, whereas N/100 hydrochloric acid (pH 2.0) did not.

A laboratory test to ascertain the effect on the teeth of certain stock iron tonics was carried out. Sound teeth were suspended for a week in the various liquids at blood temperature with part of the crown immersed beneath the surface. In this case the resultant degree of damage to the teeth was proportional to the acidity of the solution. Syr. ferr. phosph. co. caused the most damage, the exposed enamel flaking freely away from the cusps of the tooth. Mist. ferr. sulph. produced severe etching and decalcification of the enamel, which could be scraped off the surface with a finger-nail. Elix. ferr. glucon. produced very slight etching, with milky-white decalcified areas. No macroscopical effect was observed on the teeth immersed in mist. ferr. et ammon. cit. or colliron.