Pain Appreciation.—If pain be regarded as a reaction, evidently two factors, at least, are involved in its appreciation. The character or intensity of the inducing agency and the individual's susceptibility. Since each individual's own experience is the only guide to the physician's estimation of the intensity of the painful feel ing, much judgment and sympathy are needed correctly to gauge the patient's susceptibility. Pain to many is but an incident. They are either anæsthetic or stoical, either really feeling little or able to control their expressions of pain; others, again, are hyperæsthetic or exaggerational; either they really are extremely susceptible or they possess little or no control over their feelings. At all events the grade of the patient's own feeling is the true measure of the pain for themselves, but it may not be a useful guide in the diagnosis of a disease proc-

It has become popular, since the studies of Lombroso and his school, to generalize regarding pain susceptibilities among individuals in certain occupations or professions, or among the peoples of a country. Thus the Teutons are reputed to be relatively non-susceptible; that thieves, prostitutes, and the like are anæsthetic Such generalizations are founded on the most flimsy evidence and are based purely on half-truths at best. Moreover, the question of control over one's expressions of pain is rarely taken into account by many of these stu-

Pain that is acute and severe in character usually causes a well-known picture of contracted muscles dilated pupils, cold wet hands and feet, a picture closely ng and indeed inducing at times the well-known act of fainting.

Pain Location.-For the most part the feeling of pain is referred to the diseased area, and when lesions are found to be superficial and within reach it is easy at once to distinguish their true nature and to locate them correctly, and then to apply the proper treatment. When no superficial lesion is found, the question arises whether the pain sensation is in direct relation to an adjacent organ or whether it is a referred sensation from a more

Of the facts which help to a correct judgment the grade of pain intensity is one of the most important. Those pains which are less intense and more illy defined are more liable to be referred pains from a more remote area.

By the researches of Dana and Head* the mapping of areas of referred sensations has become an almost definite matter. Head has shown that a diseased viscus very frequently, if not always, sends sensory impulses to the spinal cord, which impulses are felt as irregular pains, usually dull, at times very acute, in the skin area supplied by the sensory nerve of the spinal-cord segment related to the viscus segment. By means of the work of this author and others many of the earlier charts illustrating referred pains are being revised, and more definite conclusions are now possible, although as yet many of the ascertained facts have more importance in neurologi-Smith Ely Jelliffe. cal than in general diagnosis.+

PALISADE WORMS. See Nematoda.

PALM BEACH, FLORIDA.—This popular and fashionable winter resort is situated in Southern Florida on the east coast, in latitude 26° 57', about two hundred and eighty miles south of Jacksonville. It lies upon a narrow strip of land between Lake Worth and the Atlantic Ocean. The vegetation at this latitude is naturally tropical and luxuriant, and art has added to the natural beauty by parks, gardens, and paths running through groves of palms and tropical trees. Flowers abound, and such tropical fruits as the banana, pineapple, guava, tamarind, and mango are found here. Indeed, nature and art have combined to render this spot peculiarly attractive and fascinating. The accommodations are luxurious and

* Head and Campbell, "Brain," vol. 23, 1900, p. 353. † Pain: James Mackenzie, M.D., "Brain," Autumn, 1902, p. 368.

consequently expensive. There are two large hotels affording every comfort, and several smaller and less expensive ones. There are also numerous fine private resilences. Many means of recreation are offered the visitor: bicycling through the many beautiful paths; fishing,

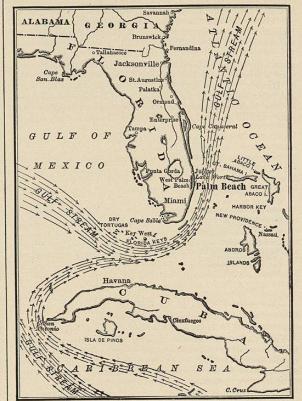


FIG. 3728.

rowing, sailing, shooting, surf bathing, swimming in a large salt-water pool, and golf upon the fine and extensive links. Hot salt-water baths are to be had in some of the hotels. Palm Beach is easily and comfortably reached direct by railway from Jacksonville. One is referred to the article upon Florida in this Handbook for an extended consideration of the climate of Florida, including this region. In this article will be found the climatic data for Jupiter, which is only seventeen miles north of Palm Beach, and which therefore has essentially the same climate as that of Palm Beach. The average mean temperature (Fahrenheit) for the months of December to March inclusive is: December, 67.2°; January, 63.4°; February, 66.7°; March, 68.8°. The maximum temperature for the same months is: December, 82°; January, 80°; February, 84.7°; March, 85.5°. Minimum, December, 41°; January, 38.5°; February, 39.8°; March, 44.8°. The average relative humidity is 82 per cent. The average number of clear and fair days is: December, 23.9; January, 24; February, 22.1; March, 27.1. The average precipitation is: December, 2.88 inches; January, 3.43; February, 2.72; March, 2.59.

The distinguishing characteristics of the winter climate of Palm Beach are warmth, sunshine, equability, and moisture. It is a warm, moist, marine climate Such a climate is well suited for elderly and feeble persons, convalescents of a certain kind; for persons affected with neurasthenia or with chronic bronchitis, and for the valetudinarian in general, but not for those who are affected with pulmonary tuberculosis. For one who desires to escape the inclemency and strain of a northern winter and live an outdoor existence in the midst of at-

tractive surroundings, and who, moreover, is able to pay for luxurious accommodations, Palm Beach can unquali fiedly be recommended. Further, it is easily and comfortably reached from the North. Good medical service is at hand, which is a matter of the first importance in a health resort. The season extends from December to March.

Sixty-seven miles south of Palm Beach is Miami, the terminus of the East Coast Railway and the port of departure for Nassau, Havana, and Key West. town of about three thousand inhabitants. "The Royal Palm." a large and luxurious hotel, is situated here in the midst of a large tropical park. The climate is essentially the same as at Palm Beach, and much the same sort of outdoor life and amusements are afforded the visitor here as at the former place. Edward O. Otis

PALMYRA MINERAL SPRINGS .- Jefferson County, Wisconsin

Post-Office.—Palmyra Springs. Hotels and sani-

Access.—Viâ Chicago, Milwaukee and St. Paul Railroad to Palmyra, 118 miles north of Chicago and 20 miles west of Waukesha. The sanitarium stage meets trains.

Palmyra is a pretty little town of 1,000 inhabitants, nestling in the foothills of the famous Kettle Range of Wisconsin. The location is 850 feet above tide-water, and it combines many of the features sought after by the summer seeker for health or recreation. This entire section is favored with a salubrious climate, and is altogether free from malaria. The soil is dry, sandy, and porous, overlying glacial deposits of gravel, which affords the best natural facilities for through drainage. The scenery here is noted for its tranquil beauty and loveliness. In his attractive brochure on "Summer in the Northwest" Mr. W. J. Anderson informs us that the beautiful little Spring Lake, or Palmyra Lake, as it is generally called. "may be classed as one of the gems of Wisconsin. Its bottom is covered with mosses, ferns, and other aquatic plants, which in mid-summer bloom and blossom as a garden. It is fed by numerous mineral springs in the vicinity, and affords an enticing prospect for the angler or the lover of boating." Seven miles distant is the Scuppernong trout pond, which is said to contain millions of trout of all varieties and sizes. Many other beautiful lakes are within easy driving distance, over excellent roads. The Palmyra Springs Sanitarium is delightfully situated on the margin of Palmyra Lake, of which it commands a charming view. This is a substantially built brick structure, four stories in height, containing spacious halls, wide verandas, and all the modern accessories for the health and comfort of its occupants. There are facilities for the administration of electricity in its various forms, massage, etc. The baths embrace salt, shower, shampoo, Turkish, Russian, and natural mineralwater baths, the rooms being spacious and luxuriously furnished. All kinds of facilities for indoor and outdoor diversions are at the option of the guests. Directly opposite the sanitarium is a forty-acre forest of native oaks the "Sanitarium Grove." It's winding walks and shaded nooks add no little to the attractiveness of the place. At a distance of one mile and a half from the sanitarium is the great Geyser Spring. It is thirty-eight feet in depth and fifty feet across the surface, and supplies ten million gallons of water per day. The water is soft, pure, and palatable, and is believed to possess remedial value. The mineral springs at Palmyra are very numerous. A cluster of half a dozen in the spring park, which could all be covered by a canvas forty feet square, are quite dissimilar in taste, of varying temperature, and of different analysis. One spring is slightly thermal, having a temperature of 72° F.; another, ten feet distant, is a little cooler (62.5° f'.); while others vary in temperature from 50° to 52° F. Back of the sanitarium, and four hundred feet from it, is another group, known as Magnesian Springs. They are remarkably pure and free from organic matter. Following are analyses of three of the springs, No. 1 being by Prof. W. S. Haines, of Rush cooler (62.5° F.); while others vary in temperature from

Medical College, Chicago, and Nos. 2 and 3 by Prof. Bode, of Milwaukee:

Spring No. 1.—One United States gallon contains: Sodium sulphate, gr. 0.94; potassium sulphate, gr. 0.23; calcium bicarbonate, gr. 15.70; magnesium bicarbonate, gr. 10.94; magnesium chloride, gr. 0.18; iron bicarbonate, gr. 0.5; calcium phosphate, a trace; alumina, a trace; silica, gr. 0.70; organic matter, a trace. Total, 28.74 grains.

Spring No. 2 .- One United States gallon contains: Sodium chloride, gr. 0.21; sodium sulphate, gr. 0.64; sodium bicarbonate, gr. 0.16; calcium sulphate, gr. 0.30; calcium bicarbonate, gr. 9.86; magnesium bicarbonate, gr. 7.91; iron bicarbonate, gr. 0.6; alumina, gr. 0.19; silica, gr. 0.61; organic matter, gr. 0.35. Total, 20.29 grains.

Spring No. 3.—One United States gallon contains: Sodium chloride, gr. 0.43; sodium sulphate, gr. 0.40; sodium bicarbonate, gr. 0.18; calcium sulphate, gr. 0.80; calcium bicarbonate, gr. 12.84; magnesium bicarbonate, gr. 10.14; alumina, gr. 0.22; silica, gr. 0.90. Total, 25.91 grains.

These waters all possess mild diuretic and antacid properties. The water of Spring No. 3, being entirely free from organic matter, is well adapted for carbonating and bottling. The numerous topographical, climatic and other advantages of Palmyra render it a suitable resort for a large variety of ills and ailments. The spring waters exert a beneficial influence, especially in rheumatism and dyspepsia, although their use is also extended to functional hepatic disorders, the early stages of Bright's disease, and to eczema, pityriasis, and other skin troubles. James K. Crook.

PANACEA SPRINGS .- Halifax County, North Caro-

POST-OFFICE. - Littleton.

Access.—These springs are situated three and a half niles from the town of Littleton, at an altitude of 380 feet above the sea-level.

The location is in a beautiful valley surrounded by picturesque hills covered with rocks of immense size, and still clothed in their primeval forest growth of gigantic oaks. The meteorological conditions which prevail here are of a salutary character, there being neither long droughts nor excessive rains. The springs are fifteen or twenty in number and flow about five hundred gallons of water per hour. The following analysis was made some years ago by Dr. H. B. Battle, of the State Experiment Station. The bases and acids only are given: One United States gallon contains: Iron, gr. 2.18; alumina, gr. 0.32; calcium, gr. 1.11; magnesium, gr. 0.20; manganese, gr. 0.01; potassium, gr. 0.70; sodium, gr. 2.23; hydrochloric acid, gr. 0.82; suphuric acid, gr. 0.42; phosphoric acid, gr. 0.53; silica, gr. 1.18. Total, 9.70 grains. (Carbonic acid, large amount; not determined.)

It is evident that the acids and bases would unite in the form of carbonates, chlorides, sulphates, and phosphates.* The waters are very useful in chronic diarrhea and the debility which usually accompanies the disease. They are highly recommended in the debilitated states attending uterine and ovarian diseases and in restoring anæmic and puny children. James K. Crook.

PANARITIUM ANALGICUM. See Morvan's Disease

PANCREAS, ANATOMY AND PHYSIOLOGY OF .-1. Gross Anatomy.—The pancreas is an elongated gland of a reddish-yellow color. The size is somewhat variable in different individuals, but the gland is usually from

^{*} According to E. E. Smith, M.D., Ph.D., of New York, to whom we

five to six inches in length, from half an inch to an inch in thickness, and weighs from two and a half to three and a half connect (60 to 90 gm)

and a half ounces (60 to 90 gm.).

The pancreas, like the liver, is moulded in shape by the organs with which it is in relationship, so that it is irregularly prismatic in shape, especially in its middle

portion or body.

The pancreas lies in the loop of the duodenum and is hence deeply placed in the abdomen, stretching across the posterior abdominal wall nearly transversely at the level of the first and second lumbar vertebræ, and is almost concealed by the stomach which lies in front of it. Regionally the pancreas lies almost completely in the epigastrium, but the tip of the free end or tail, which comes into contact with the inner surface of the spleen, lies in the left hypochondrium.

For the description of relationships, it is usual to consider the gland as consisting of head, neck, body, and tail, although these parts are not very clearly marked off naturally from one another.

The larger rounded right extremity of the gland forms the head, which accurately fits into and fills the concave

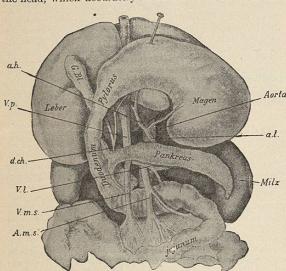


Fig. 3729.—Diagrammatic Picture Showing the Relations of the Pancreas to the Stomach, Duodenum, and Blood-vessels. (After Koerte.) a.h., Arteria hepatica; V.p., vena portæ; d.ch., ductus choledochus; a.l., splenic artery (art. lienalis); V.l., splenic vein; V.m.s., superior mesenteric vein; A.m.s., superior mesenteric artery; G.Bl., gall-bladder: Leber, liver; Magen, stomach; Milz, spleen.

side of the sharp curve formed by the second and succeeding parts of the duodenum. The neck is a portion about an inch in length which curves upward, forward, and to the left, from the anterior portion of the head, to unite it to the body and tail at about a right angle. In this angle are placed the superior mesenteric vessels, which lie in front of the head and are covered, as they pass upward toward the cœliac axis and portal vein, by the neck, which lies in front of these main trunks. The body and tail, which together measure from four to five inches, cannot really be differentiated from each other, the tail being merely the extremity of the body which turns upward toward the spleen.

The inferior vena cava, left renal vein, and aorta lie behind the head of the gland, and the origin of the superior mesenteric artery, the crura of the diaphragm, the splenic vein, left kidney, and suprarenal gland are the chief posterior relations of the body. In front, the pancreas is separated from the overlying pylorus and stomach by the lesser omental sac, and the lower portion of the head of the gland is crossed by the transverse colon and its mesocolon. The transverse mesocolon is attached posteriorly to the lower border of the gland and splits here

into two layers, one being reflected upward, over what is known as the anterior surface of the body of the pancreas, while the other passes back over the narrow inferior surface and is then reflected downward, so leaving the posterior surface of the body free from peritoneal investment.

The pancreas is richly supplied with blood from three different sources, which freely anastomose with one another, viz.: 1. By the superior pancreatico-duodenal artery, a branch of the gastro-duodenal and hence of the hepatic artery, which curves round between the head of the pancreas and the duodenum. 2. By the inferior pancreatico-duodenal, a branch of the superior mesenteric, which courses round the head of the pancreas in the direction opposite to that of the superior pancreatico-duodenal and finally communicates with it. 3. By the splenic artery, which in its wavy and tortuous course toward the spleen, grooving the upper border of the pancreas, gives off to that gland many small twigs called the pancreatica parva, in addition to a larger branch near its termination, the pancreatica magna, which penetrates the gland and passes back from left to right parallel and close to the chief pancreatic duct.

The main pancreatic duct or canal of Wirsung runs deeply embedded in the substance of the gland, somewhat nearer the lower than the upper border, from left to right throughout the length of the gland. It is easily distinguished by its white glistening appearance, and the best guide for finding it is the artery which, as above described, runs parallel and close to it. It commences by the union of many small ducts from the lobules of the tail, and, being joined by ducts from the lobules on all sides, increases in size until near its termination at the duodenum, where it measures about one-tenth of an inch. It follows the course of the gland described above, bending downward, backward, and to the right, as it courses through the neck, and passing toward the posterior part of the head where it enters, in common with the bile duct, into the second part of the duodenum, between three and four inches below the

pylorus, upon a slightly raised papilla.

A second duct, called the accessory duct or duct of Santorini, is found in the majority of bodies. This duct is usually much smaller and runs from near the orifice of the main duct to open separately about an inch nearer the pylorus; but in exceptional cases it may be large and take on the functions of a main duct, the extremity of Wirsung's duct being then much smaller than usual. The presence of two ducts arises from the development of the gland as two separate outgrowths from the

The smaller of these two outgrowths arises close to the common bile duct, and its original duct forms at a later period the proximal end of Wirsung's canal. The other larger growth arises nearer the pylorus, and the accessory duct of Santorini is formed from the proximal end of its duct. At about the sixth week of development the two ducts fuse, and, the upper duct afterward developing less rapidly, the main pancreatic duct comes to be formed of the central end of the lower duct and the peripheral parts of both the others.

2. Minute Anatomy.—The pancreas is a compound racemose gland which, in its general arrangement and in the appearance of its cells, closely resembles a serous salivary gland. It may be distinguished, however, by the longer, tubular, and somewhat convoluted alveoli, which are often cut in oblique or longitudinal section and then present the appearance of long columns of cells lining the central ducts. This appearance is never evident in salivary gland sections, because their alveoli are not elongated. The ducts also serve to differentiate the pancreas from the salivary glands, for they are much less numerous in the former and the cells lining them do not show any of that longitudinal striation which is present in the cells of the ducts of the salivary glands.

The ultimate branches of the ducts which pass to the individual alveoli are very narrow and are lined by flattened cells.

The alveoli in the loaded condition of the gland are compactly filled by the charged cells so that no distinct lumen is visible, but after active secretion the cells shrink considerably in size and the lumen becomes obvious

By special methods of treatment, such as injection under pressure backward from the main duct, or perhaps better by the Golgi method of staining with silver chromate, it can be shown that intercellular canaliculi exist which branch off from the lumen of the alveolus and pass between the constituent cells. The Golgi method, when the result is good, further demonstrates intracellular canaliculi which penetrate into the cells themselves and drain off the secretion from their interior.

The secreting cells present characteristically different appearances according to whether the gland has been resting and has hence become charged with secretion, or whether it has been recently active and as a result is exhausted of those materials which contribute the solids of the secretion. These materials are deposited in a granular form during the period of rest, and are hence visible under the microscope, and give by their amount an indication of the condition of the gland.

Even in the fully charged condition of the gland

Even in the fully charged condition of the gland the granular deposit never quite fills the cell, a clear finely striated outer zone always being left, which takes stain readily and hence appears deeply colored in prepared sections as compared with the central granular

In the fully charged cell about three-fourths of the cell substance lying toward the lumen is completely obscured by a thick granular deposit which hides the nucleus and the outlines of the cells so that the lines of division are invisible in fresh sections.

The first effect of secretion is an increase in volume of the cells, probably due to water and salts being taken up from the surrounding lymph; but this is quickly followed by a diminution in size, accompanying which there is a rapid diminution in the amount of granular deposit present in the cells. The granules become fewer in number in the central part of the cells toward the lumen, where they are still present, and the outer granule-free zone becomes greatly increased in width and comes to occupy nearly the whole cell. These changes are shown in hardened and stained sections by the greater amount of cell which becomes deeply stained.

As a result of the gradual clearance of the granules from the protoplasm the cell nucleus and its outlines become more clearly visible. These granules seen in the cells do not consist of deposits of the enzymes found in the secretion of the glands, which are described below, but probably of other substances which form precursors of these, the so-called zymogens.

The zymogens are inactive until they have been changed into the free enzymes, as is shown by the fact that neutral extracts of the fresh gland are almost inactive, but become active when treated by dilute acetic acid (one per cent.), or a dilute solution of sodium carbonate (two per cent.) in presence of oxygen.

Recent research has further demonstrated that the fresh pancreatic juice as it flows from the gland duct contains a large percentage of its zymolytic material in the inactive form of zymogens and that it is only in the intestine itself that the change into active enzyme is completed (vide infra). In addition to the nucleus a body called the paranucleus can be demonstrated histologically in the pancreatic cells. This structure surrounds the nucleus of the cell and is shown by its property of staining more readily than the rest of the cell protoplasm. It is supposed to arise from the nucleus by a process of extrusion, and the view has been advanced that the zymogen granules are manufactured in this part of the cell.

3. Secretion.—The rate of secretion of the pancreatic juice varies with the state of digestion, being most rapid during the earlier periods after a heavy meal and then gradually diminishing. During prolonged inanition the flow practically ceases. It commences toward the end

of the next following meal and attains a maximum rate within the first two hours; it then falls off rapidly up to the end of the fifth hour. A secondary increase in the rate then occurs which attains its maximum at about the tenth hour, but is never so high as the first maximum; after this the flow once more falls off and practically comes to a standstill in the eighteenth hour after the meal. The richness of the secretion in ferments is inversely proportional to the rate of flow, the more rapidly secreted fluid being more diluted with water.

These variations in the rate of secretion are probably in part under the reflex control of the nervous system and in part are due to chemical stimulation of the pancreatic cells, by a substance secreted by the cells of the duodenal mucous membance and carried in the blood to

Regarding the reflex nervous influence upon the secretion, it is probable that the *afferent* channels are connected up to the medulla from the mucous membrane of the stomach and duodenum; at any rate it is an experimental fact that chemical or electrical stimulation of these surfaces causes a flow of pancreatic juice. The chief *afferent* nerve affecting the pancreatic secretion is

This fact is rendered somewhat difficult to demonstrate, in the first place by the important disturbances of the cardiac mechanism, and other organs, which follow stimulation of the vagus, and secondly by the fact that the vagus contains both excitatory and inhibitory fibres for the pancreas, and hence the net effect of stimulating the nerve upon the pancreas varies according to the relative excitability of the two kinds of fibres. At times a stoppage of secretion results and at other times an increase in the rate of flow. Until this had been demonstrated many contradictory experimental results regarding the action of the vagus in this respect had been published by different observers.

Pawlow and his pupils first clearly demonstrated that the vagus can act as an excitatory nerve for the pancreatic secretion. These observers got rid of the disturbing influence upon the heart by severing the vagus three or four days before placing the cannula in the duct of pancreas to observe the rate of secretion and stimulating the peripheral end of the vagus. The cardiac fibres are the first to degenerate and become completely inexcitable at a period when the excitatory fibres of the pancreas are still active. Apparently the inhibitory fibres to the gland cells also suffer early degeneration, for in all cases a positive result of increased secretion was obtained. Similar results were obtained by stimulation of the thoracic vagus below the place of exit of the cardiac fibres from that nerve. Popielski later discovered that the action of the vagus depended upon the rate of secretion which was already going on at the moment when the vagus was called into activity. This observer utilized the discovery of Dolinski, that application of acid solutions to the duodenal mucous membrane causes a copious flow of pancreatic juices (vide infra), to study the effects of stimulation of the peripheral end of the vagus during active secretion, and found that a stoppage secretion was the invariable result.

It is probable, then, from these experiments that the vagus contains secreto-inhibitory fibres for the pancreas, in addition to secreto-motor fibres as shown by Pawlow.

The action of injection of fluids of acid reaction into the duodenum in provoking an outflow of pancreatic juice is a subject which at the present time is exciting a good deal of attention, and although the matter is still sub judice, many interesting results have already been obtained

Popielski found that the effect was still obtained even when both vagi and sympathetics were divided. He further found that the effect was obtained when the stomach was separated from the intestine above the level of the pylorus, but not when the section of stomach from intestine was carried out below the pylorus, and from these experiments he came to the conclusion that the action was due to a local nervous mechanism, the nerve

cells for which lay in the intestinal wall close to the

pylorus.

More recently still Bayliss and Starling have discovered that an exceedingly copious flow of pancreatic juice is evoked when an extract of mucous membrane of the duodenum is made with a dilute acid, and then neutralized, filtered, and intravenously rejected. This effect follows, according to these observers, even when all nerves to the pancreas have been carefully severed. The result is obtained only by using extracts of the mucous membrane of the duodenum or of the upper end of the jejunum and is not given by exactly similar extracts from other parts of the intestine. The substance giving this effect is not an enzyme or a proteid body, since it is not destroyed by boiling in acid solution. The name of secretin has been given to the body by its discoverers, but it has not yet been isolated.

From the foregoing description it is obvious that secre-tin is quite distinct from the peculiar enzyme termed enterokinase, which has recently been shown by Delezenne, to exist in extracts of intestinal mucous membrane or in the succus entericus. This enzyme can be obtained from any part of the intestinal mucous membrane, and, like all enzymes, can be destroyed by boiling solutions

It acts upon the pro-ferments present in the pancreatic juice, and converts them into the active ferments. Fresh pancreatic juice collected by means of a cannula inserted into the pancreatic duct is practically inert when tested by its action upon fibrin; but when a solution of enterokinase, or, in other words, succus entericus, or an extract of intestinal mucous membrane, is also added to the mixture the fibrin is then rapidly attacked and dis-

Bayliss and Starling regard the secretion elicited by the action of acid upon the mucous membrane of the duodenum as being due to a chemical stimulation of the pancreatic cells by secretin taken up by the blood from the columnar cells of the duodenum and carried to the pancreatic cells, and not to any nervous action either central or local. According to these authors the main regulation of pancreatic secretion takes place by chemical means through the medium of the blood stream, which acts as a carrier of the stimulating chemical prod-

Thus, upon this view, the cells of the mucous membrane of the duodenum during a period of rest, corresponding to the period when the stomach is empty, store up a precursor of secretin which may be termed pro-On the passage of acid chyme from the stomach into the duodenum, the cells discharge secretin into the blood stream, and this body being carried to the pancreatic cells induces secretion of alkaline pancreatic

The pancreatic juice so secreted is almost inert, so far as action upon proteid is concerned, until it has become mixed with the *succus entericus* in the intestine. Here the action of Delezenne's enterokinase plays a complemental part, changing the pro-ferment into active ferment, for Bayliss and Starling find that the activity of the secretion produced by the injection of solutions of secretin into the blood stream is greatly increased by the addition of extracts of intestinal mucous membrane

It is obvious that the amount of pancreatic flow can thus be nicely regulated to the amount of digestion performed, for the stimulus to secretion will be proportionate to the quantity of acid gastric chyme thrown into the duodenum to cause evolution of secretin from the duodenal cells, and again the stimulus to secretion will be automatically removed when the quantity of alkaline pancreatic juice secreted is sufficient to neutralize the acid which gives the stimulus.

It is a discovery of high importance to our knowledge of pancreatic secretion that a material can be extracted from the duodenal mucous membrane, and peculiar to it alone, which is capable of evoking a copious flow of pancreatic juice, but a few words may judiciously be offered in criticism of the view of the authors that the process is

a purely chemical one, and that this method is the most mportant and naturally occurring one by which pancre-

atic secretion is regulated. In the first place, the experiments of Pawlow and Popielski, quoted above, undoubtedly prove that the pan creas possesses a nervous mechanism which is capable of regulating its secretion both in the direction of excitation and in that of inhibition, and this even while a strong application of acid is being made to the duodenum. also obvious that no such treatment of the cells of the duodenal mucous membrane with acids can normally occur in the process of digestion as takes place when they are extracted in a test tube with acid. In fact, at the height of pancreatic secretion, the reaction of the contents of the duodenum is normally alkaline, or they possess an acidity due to dissolved carbonic acid only, for the acid of the gastric juice is neutralized at once by the mixture of pancreatic juice and bile into which it is received. Hence there never can be any free acid in the duodenal cells, which must be still less acid than the contents of the intestine, so that any flow of secretin from these cells into the blood which may occur cannot be caused by an acid reaction.

Again, it is exceedingly difficult to prove that secretin acts directly on the gland cells and not through the central nervous system, even admitting that this substance is normally secreted into the blood stream. For it is experimentally impossible to prove that all the non-medullated nerves passing to the pancreas have been severed; a convincing proof of the peripheral action of secretin can in fact be given only by showing a secretory effect of this substance when perfused through an excised pancreas, and this has not yet been given.

In whatever way this peculiar substance found in the cells of the duodenal mucous membrane may eventually be shown to act, there is no doubt, however, that its discovery has awakened a new line of thought as to the mode of secretion of pancreatic juice and probably of other secretions, for there is no reason why the pancreas should be peculiar in this respect. We have also here another beautiful example of that interdependence of one organ in the body upon another, and of the usefulness of the products of the metabolism of one cell for the life work of another, situated in a different part of the body, and apparently not even remotely connected with it.

4. CHEMISTRY OF THE PANCREATIC JUICE.—It is impossible in the present state of development of the experimental technique for obtaining pancreatic juice to give any reliable figures as to the quantitative composition of that fluid. The irritation set up by the necessary operations for the collection of the secretion causes the flow, within a few hours, of a paralytic secretion, which is many times more diluted and consequently poorer in organic constituents than that which flows within the first few hours. For this reason it is also impossible to obtain any information experimentally as to the average quantity secreted in the twenty-four hours, and as the tables of total quantities and quantitative composition are quite illusory they are not here quoted.* The secretion obtained immediately after the production of a temporary fistula of the pancreatic duct is a clear, viscid fluid of strongly alkaline reaction, equivalent to 0.2-0.4 per cent. of NaOH, due to the presence of carbonates and phosphates of sodium. It undergoes spontaneous coagulation in the cold, and being very rich in coagulable proteids (eight to ten per cent.), which cannot be distinguished from serum globulin and serum albumin, it undergoes heat coagulation and sets to a solid white mass when heated to 75° C. If kept in a water bath at a temperature of 40° C., its own coagulable proteids undergo digestion by the trypsin present (vide infra) into albumoses and peptones, and the secretion is then no longer coagulable by heat. Alcohol precipitates both the proteid and the enzymes.

The inorganic salts present are practically identical with those of blood serum.

White blood corpuscles showing sluggish amæboid movements are present in the fresh secretion.

Traces of leucin have been detected in the fresh se cretion, but tyrosin is absent. The most important constituents of the pancreatic juice from the point of view of the physiological chemist are the enzymes to which it owes its powerful digestive action upon all three classes of foodstuffs.

There are four enzymes known to be present. These possess in each case all the general reactions which are characteristic of this class of bodies, and hence need not here be detailed (see article on *Enzymes*), and accordingly only the peculiarities of each will be recorded.

No complete separation of these enzymes has as yet been accomplished, that is to say, no one has succeeded in obtaining from the mixture present in the pancreatic inice solutions which contain one enzyme only. Hence the belief that each specific action of the pancreatic juice upon a foodstuff is due to a separate enzyme rests upon the partial proofs, first, that there is no known example of a single enzyme which acts upon two different varieties of foodstuff, and, secondly, that in certain cases, according to the method of extraction used, extracts can be prepared from the gland which are relatively rich in one enzyme and poor in another, although this has not been done for all four. For example, from the pancreatic tissue, after completely drying by alcohol, the diastatic enzyme can be extracted by anhydrous glycerin, while the proteolytic enzyme does not pass into solution.

It is hence extremely probable that four distinct substances or their precursors are present in the gland cells and secretion which have been named as follows: (1) Amylopsin, a diastatic enzyme; (2) steapsin, or pialyn, a steatolytic or fat-splitting enzyme; (3) trypsin, a proteolytic enzyme; and (4) an unnamed enzyme which has the property of curdling milk.

It has been clearly demonstrated that trypsin is present in the gland cells, and also to a large extent in the fresh secretion before it is acted upon by the succus entericus in an inactive form, which is known as trypsinogen. It is at present unsettled whether steapsin and amylopsin possess similar precursors.

There are two views as to the action of the complementary enzyme called enterokinase of the succus enter One view is that this first attaches itself to the proteid, and renders it in a catalytic fashion more easily attackable by the pancreatic enzyme. The other and more probable view is that the enterokinase acts upon the trypsinogen and sets free trypsin which then attacks

Amylopsin.—This can be extracted from the fresh gland by most extractives, such as chloroform water, twenty-five-per-cent. alcohol, to which a trace of acetic acid has been added, fifty-per-cent. glycerin, saturated solution of sodium chloride, saturated boric-acid solution.

Its action upon starches is very rapid, and closely resembles that of other diastatic enzymes. The action is hydrolytic, and leads to the formation of a mixture of achroödextrins and maltose. One part of amylopsin (impure) is capable of hydrolyzing over forty thousand times its weight of starch (see article on Digestion).

The action is at a maximum at a temperature of 30°-45° C., decreasing gradually as the temperature is lowered down to 10° C., at which it is stopped, as long as the temperature is kept at that level, but recomm warming. The temperature of destruction is about 60°

Amylopsin acts best with a neutral reaction or in presence of an excessively minute trace of acid, the optimum according to Melzer coinciding with 0.01 per cent. of hydrochloric acid. By greater amounts of acid than this, not only is the activity lessened, but the ferment is itself rapidly destroyed; it is less susceptible to the fixed alkalies withstanding the action of one per cent. of sodium carbonate, but is rapidly destroyed by free alkalies.

Steapsin.-This enzyme is exceedingly unstable, and hence great care is required in obtaining active extracts

the enzyme is lost in the process of extraction, and hence, as shown by Rachford, the fresh pancreatic juice is always more active than any extract of the gland, and should be used in experimenting upon the action of this enzyme. It was formerly believed that this ferment acted only upon a small fraction of the fat of the food, because the action of extracts of pancreas upon fats was so slow and incomplete: but this arises from the great loss of activity in the process of extraction, and it is now known that the steapsin has sufficient power to split up the entire fats (Rachford), and it is probable that fats are taken up in solution (see article on Digestion).

That the action is truly enzymic is shown, first, by its toppage on boiling; and, secondly, by its taking place when bacteria are excluded by the presence of antiseptics.

If extracts of the gland containing steapsin are desired, the fresh gland must be taken and extracted with a very dilute (1 to 1,000) solution of sodium carbonate, or a ninety-per-cent. solution of glycerin, containing 1 per mille of sodium carbonate.

Such solutions, or the fresh pancreatic juice, act upon neutral fats, hydrolyzing them, and forming free fatty acids and glycerin. A similar hydrolyzing action has been noted upon other synthetically prepared esters.

The action is increased by the presence of bile (Rachford). The effect here is probably a physical one, the bile salts or bile acids dissolving the fatty acids which are a product of the hydrolysis, and so allowing fresh portions of neutral fat to be attacked.

The optimum temperature is 38° C., and at this temperature the action is twice as rapid as it is at 18° C.

Trypsin.—This enzyme acts upon proteids more powerfully and completely than any other known to us, forming in succession alkali-albumin, deutero-albumose, peptone, and a large number of amido-acids. Primary albumoses do not seem to be formed, or, if they are formed, they at once pass into more completely hydrolyzed forms, and the action is both more rapid and complete than is that of pepsin. The ferment can be extracted by any of the usual extractives from the gland. It is insoluble in strong alcohol or glycerin, and the latter of these two reagents has been utilized for its differentiation from

According to Sir William Roberts its activity goes on increasing with the temperature up to 60° C., and it is destroyed at a temperature of 75° to 80° C. These figures do not agree with those of Biernacki, who found it to be destroyed at a temperature of 50° C. when in solution in five-tenths per cent. sodium carbonate, and when in neutral solution at a temperature of 45° C.

Trypsin acts best in an alkaline medium, the usual optimum given being that of a one-per-cent. solution of sodium carbonate. It, however, can act in a neutral solution or even in the pre ence of a faintly acid reaction, provided no free inorganic acid is present. A small amount of hydrochloric acid, combined with proteid, does not stop its action, but much acid, even when combined with proteid, has a destructive effect.

The Milk-Curdling Ferment.—The presence of a milkcurdling enzyme in the pancreas was first discovered by Kühne, and has since been confirmed by other observers.

More recently the subject has been re-investigated by Halliburton and Brodie, who found that the coagulum produced by this enzyme differs considerably from that btained by the action of the rennin of the gastric juice. Thus, instead of a jelly-like coagulum which is obtained in the water bath at a temperature of 35°-40° C., a finely granular precipitate is obtained by the action of pancre atic juice or pancreatic extracts, which does not at this temperature interfere with the fluidity of the mixture. But on cooling to the temperature of the room a coherent curd is formed; if this be now heated to body temperature t again becomes fluid, and on cooling a second time it again sets to a clot, and this process can be repeated indefinitely. Further, the coagulation by means of the pancreatic enzyme differs from that by rennin in that it is not prevented by excess of ammonium oxalate, and from the gland substance. In any case, a good deal of | hence does not require the presence of calcium salts.

^{*}See Schäfer: "Textbook of Physiology," vol. i., p. 366 et seq.

The use of this pancreatic enzyme is difficult to understand, since any milk taken by the mouth would be coagulated in the stomach by the rennin there present. A similar difficulty exists regarding the purpose of rennin in the gastric secretion of fishes and other animals from whose food milk is absent, as also regarding the presence of milk-curdling ferments in the juices of certain plants.

whose food milk is absent, as also regarding the presence of milk-curdling ferments in the juices of certain plants. A possible explanation is that such ferments may have a less obvious action upon other forms of proteid, a fact which yet remains to be discovered. Benjamin Moore.

PANCREAS, DISEASES OF THE .- The great importance of diseases of the pancreas was not generally recognized by the medical profession until within comparatively recent times, but that pathological alterations of the organ not uncommonly exist was known to all of the older pathologists. That changes in the pancreas sometimes occur in individuals who have diabetes mellitus was first recognized by Cowley in 1788, but prominence was not given to the matter until 1877 when Lancereaux's work was published, and the relation between the two conditions has been recently definitely proven by the experimental work of von Mering and Minkowski. Spiess in 1866 recognized hemorrhage into the pancreas as being a frequent cause of sudden death, and Zenker some years later accentuated this relation; but its great importance was first fully recognized by Draper, who particularly directed attention to it in 1886. In 1889 Draper's fellow-townsman, Fitz, in a most admirable paper, opened up a new field to the clinician in bringing together a great mass of isolated facts concerning pancreatitis, and coordinating them in such a masterly manner that since this time inflammations of the organ have been brough within the list of those diseases which may be diagnosti cated. Several years before the appearance of the article by Fitz, Senn, of Chicago, very thoroughly reviewed the subject of pancreatic cysts. In the article that follows the writer wishes particularly to express his indebtedness to the various papers upon this subject written by Fitz, to the chapter on these diseases in Osler's "Practice of Medicine," and to the recent monograph upon the subject by Koerte.

FATTY AND HYALINE CHANGES IN THE PANCREAS, AND AMYLOID INFILTRATION.

FATTY CHANGES.—The fatty alterations that occur in the pancreas may be divided into (a) fatty degeneration, and (b) fatty infiltration.

(a) In many acute diseases, especially in those accompanied by high temperature, fatty degeneration occurs in the pancreatic cells. Happily, the condition is one that passes away with its cause, and is not generally supposed to give rise to serious or permanent change in the organ. There is no symptomatology of the condition.

(b) Fatty Infiltration.—This condition is frequently observed in obese individuals, and is not generally believed to produce any serious interference with the functions of the organ, though cases of diabetes have been reported in which this lesion was present in the pancreatic tissues to a marked degree. In these instances it is likely, as in a case recently observed by the writer, that the fatty changes were secondary to interstitial pancreatitis and that they were not responsible for the diabetic condition.

HYALINE DEGENERATION.—In a very interesting paper Opie has recently called attention to the fact that diabetes sometimes occurs in which the only alteration found post mortem is hyaline degeneration of the islands of Langerhans in the pancreas. Whether or not there is any connection between the two conditions cannot as yet be stated with certainty.

AMYLOID INFILTRATION.—Amyloid infiltration of the coats of the blood-vessels of the pancreas occurs in those conditions in which this material is being produced in the body. So far as is known it does not give rise to any serious alterations of the pancreatic functions.

PANCREATIC HEMORRHAGE.

Pancreatic hemorrhage is a condition that occurs to a slight degree in quite a number of different affections, but the term is here limited to those sudden and profuse extravasations of blood into the organ that are commonly

known as pancreatic apoplexy.

Etiology.—In the vast majority of instances those suffering from severe pancreatic hemorrhage have passed middle life, and the disease appears particularly to affect corpulent individuals. In many instances those who have had the disease have been addicted to the continuous use of alcohol. It commonly occurs also in those who have previously suffered more or less with "indigestion," and in many cases there appear to have been previous mild attacks. It is more common in males than in females. In some instances it has followed injury. As to the exact nature of the condition of the blood-vessels that predisposes to this disease we are still in great ignorance, careful microscopic studies being much needed to elucidate this rather obscure morbid state. It has been assumed by some that syphilitic disease of the blood-vessels is the most common cause of the malady, but adequate proof of this has not as yet been brought forward. That minute hemorrhages occasionally occur in the pancreas as the result of chronic induration of the organ there can be no question, and extravasations of a similar kind are occasionally found in connection with obstructive diseases of the circulation—such as are produced by organic heart lesions, emphysema, and tumors pressing pon the inferior vena cava. Recently Chiari has shown that minute hemorrhages are sometimes produced in the pancreas by what appears to be post-mortem digestion portions of the organ.

Morbid Anatomy.—In cases of severe hemorrhage into the pancreas the entire organ may be blood-stained, and be either of an almost black, dark purple, or brownishred hue. In by no means all instances, however, does the gland as a whole present this appearance, as all degrees of hemorrhage are met with from the complete infiltration of the organ to single, minute ecchymotic spots situated in some part of the substance of the gland. In the affected region the pancreas is usually distinctly in creased in size, though in some instances it appears to be normal in bulk. The organ may be of normal consistence, distinctly softened, or quite friable. It is of interest to note that in no instance has any one succeeded in finding the blood-vessel from which the hemorrhage came. Under the microscope the tissues of the pancreas may present a practically normal appearance, though, especially in obese individuals, more or less fatty infiltration is generally present. Blood in various stages of disintegration is found both within the interstitial tissues of the organ, and within its parenchyma in the diseased regions. In some instances the tissues of the pancreas present evidences of extensive necrotic change, as was bserved by the writer in one instance in which the nuclei of all of the cells in the affected areas entirely failed to take basic stains. It not uncommonly happens that the hemorrhage does not remain confined to the pancreas, but extends into the surrounding retroperitoneal tissues, even so far as the left kidney, and it occasionally forces

its way into the fat of the omentum and mesocolon. Symptoms.—The disease comes on in almost all instances with extraordinary suddenness, the individual having usually been in perfect health previously, though in rare cases the condition is preceded by slight prodromal pains in the upper part of the abdomen. In most instances the pains are confined to the region of the pancreas, but in some cases they may be diffused throughout the abdomen, and have been sometimes mistaken for colic in the beginning. Following the pain there are usually nausea and vomiting of a most persistent kind, and occasionally there is an urgent desire to defecate. Along with these symptoms a profound depression of the vital powers invariably occurs; the pulse is small, feeble, and exceedingly rapid. There is pronounced and oftentimes urgent dyspnœa, the patient tosses from one side of the bed to

the other, is bathed in cold perspiration, the countenance exhibits great anxiety, and there is every symptom of impending dissolution. In a comparatively short time the abdomen not uncommonly becomes swollen, and tenderness develops in the epigastric region. The temperature is either normal or subnormal. Constipation is quite frequent. If the hemorrhage is at all extensive the patient rapidly grows worse, and death usually occurs within a few hours. There can be no question that recovery sometimes follows the milder forms of the disease.

Diagnosis.—Pancreatic apoplexy is distinguished by the sudden onset, with excruciating pains in the epigastric region, nausea and vomiting, and rapid collapse. It is differentiated from intestinal obstruction by the sudden onset, and by the extreme urgency of the symptoms. In biliary colic the history, the absence of excessive vomiting, and symptoms of collapse serve to distinguish between the two conditions. In gastric and duodenal ulcer perforation is preceded by frequent attacks of severe pain in the epigastric region, tenderness over the site of the ulcer, and the vomiting of blood. Moreover, ulcer generally occurs in anamic young women.

Prognosis.—In all cases of severe hemorrhage death follows in a very short time, the patient not, as a rule, surviving longer than two or three hours. On the other hand, when the amount of blood effused is small, recovery may occur, though in these cases the condition very quickly becomes one of pancreatitis. Patients have survived even very severe hemorrhages, as is conclusively shown by the fact that recovery has occurred in several instances in which the diagnosis was made by an exploratory incision.

Treatment.—The nature of the lesions in this disease makes it, of course, impossible for drugs in any way to influence the local condition, and the treatment is therefore necessarily entirely of a symptomatic kind. Morphine should be given to relieve the pain, and the collapse should be treated in the usual way by the application of warmth, and by the hypodermatic injection of strychnine and atropine. For the reason that death in this condition cannot be produced merely by the loss of blood, but is brought about by the pressure exerted upon the surrounding nerve structures, it has been suggested that free incisions around the pancreas might relieve this condition, and thus be the means of saving the patient's life.

Acute Pancreatitis.

There are at least three more or less separate and distinct varieties of acute inflammation of the pancreas: (a) the acute hemorrhagic, (b) the acute suppurative, and (c) gangrenous pancreatitis, each of which demands separate consideration.

(a) Acute Hemorrhagic Pancreatitis.—By the term acute hemorrhagic pancreatitis is meant that condition of the pancreas in which the hemorrhagic lesion is accompanied by evidences of so-called inflammation. This condition cannot be clearly separated from that of simple pancreatic hemorrhage, the latter merging insensibly into the former.

Etiology.—This disease is much more commonly observed in persons past middle life than in the young, but instances have been reported in which the malady occurred in children, the sufferer in one instance being only nine months old. It is more common in males than in females, though the number of recorded instances of the disease is not as yet sufficiently great to determine its relative frequency in the two sexes with certainty. It occurs more commonly in obese individuals than in those who are lean. In quite a large percentage of the recorded cases the subjects have been alcoholics. Like pancreatic apoplexy this condition has been frequently observed to occur in individuals who had previously suffered for a greater or less length of time with derangements of the digestion, and in some cases there has been a clear history of previous attacks of the malady. It is also noteworthy that many of those who have had the disease had pre-

viously suffered for a period of years with unmistakable symptoms of gall-stones and inflammatory states of the gall-bladder. In view of the fact that in conditions of this kind bacteria are always present in the gall-bladder and ducts, the investigations of Hlava, Williams, and Flexner, who produced experimental inflammations of the pancreas by the injection of various bacteria, seem to be of special significance.

Morbia Anatomy.—In acute hemorrhagic pancreatis

the pancreas presents much the same macroscopic appearances that it exhibits in pancreatic apoplexy. The organ, wholly or in part, is almost black, of a purple hue, or of a dark red color, and in the affected regions is considerably swollen. The tissues of the gland are in some instances softened and quite friable. The amount of hemorrhage varies in different instances. It may be confined to the head, body, or tail of the organ, or may be diffused throughout its entire extent. Not uncommonly the hemorrhage extends into the retroperitoneal tissues, and is frequently found present in the omentum, mesentery, and mesocolon. The spleen may be enlarged. Within the pancreas itself there are not uncommonly ound small areas of a dull whitish opaque appearance that are made up of fat which has undergone a peculiar chemical alteration. This change in the fat is known as fat necrosis, and is dependent upon the fat-splitting ferments elaborated in the gland. Williams describes the appearance as follows: "Frozen sections of the white necrotic nodules showed them to be made up of coarse granules and masses, globules and crystals, and a small amount of masses of brown pigment. Many of the opaque masses were about the size and shape of fat cells, and evidently represented altered fat cells The surrounding tissues were mildly congested; a few small extravasations were noted; the fat cells appeared normal. Sections of the same embedded in celloidin, and stained with hæmatoxylin or carmine, give similar results." It is noteworthy that tetroxide of osmium is not reduced by the structures composing these necrotic tissues. It has been shown by Langerhans that the areas of fat necrosis are made up of a substance that results from the combination of lime with certain fatty acids. Osler speaks of a case in which death was the result of Bright's disease, and in which the lobules of the pancreas were entirely isolated by areas of fat necrosis with extensive deposition of lime salts. In hemorrhagic pancreatitis it very frequently happens that areas of fat necrosis are found in the fatty tissues of the omentum, mesentery and mesocolon, and in the adipose tissues situated behind the gland. It should be remarked, however, that minute areas of fat necrosis are sometimes found in the living human being where there is no disease of the organ, and Chiari has shown that post mortem there are often found in the pancreatic tissues minute alterations that appear to be the result of auto-digestion -alterations which bear a close relation to the necrosis that occurs in the fatty structures. Balser, who first accurately described the condition in man, has also shown that it not uncommonly occurs in the fatty tissues around the pancreas in healthy swine. This observation has been recently confirmed in this country by Williams, who has also shown that it occasionally occurs in the abdominal adipose tissues of the cat. It is very interesting to note that experimental fat necrosis in connection with hemorrhage into the pancreas has been produced artificially by a large number of investigators, among whom are to be a large limited of livestigators, and light with a temperature of the especially mentioned Hlava, Langerhans, Hilderbrand, Dettmer, Williams, Flexner, Rosenbach, and Opic. These investigators have shown that the condition may be induced in dogs and other animals by the injection, into the pancreas or its ducts, of bacteria, acids or alkalies, by ligation of the organ, by simply injuring it or by injuring it and at the same time infecting it with bacteria, and by the introduction of sections of fresh pancreas into adipose tissue. Symptoms.—The initial symptoms that usher in an

Symptoms.—The initial symptoms that usher in an attack of acute hemorrhagic pancreatitis are those of pancreatic hemorrhage. There is a sudden onset with ex-