culty is to avoid injuring or tearing vessels essential to the nourishment of the colon. Koerte has collected 21 cases with 6 deaths. In 7 cases the difficulties were so great that the operation could not be completed; of these, 4 died. Boeckel reports 25 cases of total or partial excision, with 21 cured and 4 deaths. If the sac is excised, the space from which it has been removed should be packed with gauze and drained through the abdominal

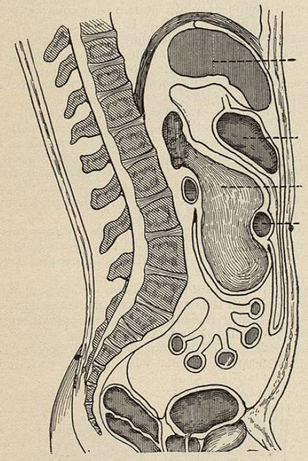

FIG. 3736.—Shows the Cyst Developed Between the Laminæ of the Transverse Mesocolon. The colon lies directly in front of the cyst. (From Kehr.) *a*, Liver; *b*, stomach; *c*, transverse colon; *d*, pancreatic cyst.

incision, or through a stab wound in the loin. It may be said that excision should be undertaken in favorable cases only, when adhesions are absent or are easily separated by blunt dissection, and when the blood-vessels involved in the sac wall are small and unimportant. It is certainly a much more grave operation than the simple incision and drainage of the sac.

TUMORS OF THE PANCREAS.—Tubercle, gumma, lymphoma, and sarcoma may occur in the pancreas, but they are very rare. Primary carcinoma of the pancreas is stated by Willigk and Lebert to occur in about six per cent. of all cases. It is more frequently found in the head than in the tail or body of the gland. The most common variety is scirrhus.

The *symptoms* are at first exceedingly indefinite. Later, fatty diarrhœa and vomiting occur, with tenderness on pressure over the gland. Jaundice is an early symptom, and is more persistent and less variable from day to day than when due to stone. The stools are persistently clay-colored. In obstruction from stone the color may vary. Diabetes is seldom present. An important diagnostic point, according to Courvoisier and Ecklin, is the condition of the gall-bladder. In stone the gall-bladder is usually small and shrunken, while in carcinoma it may be very much distended and palpable as a tumor. When stone and carcinoma exist together the difficulties in diagnosis are very great. An examination under an anæsthetic should be of great assistance. Emaciation is rapid and extreme. A palpable tumor is seldom found until the disease and its attendant emaciation are well advanced. The examination of the stomach contents, together with the comparatively good functionating power of that organ, should enable one to exclude carcinoma of the stomach. The tumor sometimes becomes adherent to the stomach, and in some cases the disease has perforated the stomach wall. Hæmatemesis might give evidence of this complication.

Treatment.—The treatment of carcinoma is most difficult and unsatisfactory. In the primary course of the disease the diagnosis is wellnigh impossible. If the disease is localized in the tail, its removal may in favorable cases be feasible; but extirpation of the whole gland, even if the patient recovered from the operation, would be followed by a fatal diabetes. Extirpation of the head of the gland presents technical difficulties that are almost insurmountable. There is the danger of injuring the vessels necessary for the nourishment of the colon, duodenum, and spleen; and if both of the pancreatic ducts are tied, diabetes and atrophy of the remaining gland tissue follow. There is also the difficulty of dealing with the common bile duct. Cholecystotomy may give relief from the icterus; and if there is great pressure on the duodenum, a gastro-enterostomy would relieve the obstructive symptoms, vomiting and inanition. Koerte reports ten cases of operation on solid tumors of the pancreas with six recoveries.

PANCREATIC CALCULI.—Pancreatic calculi may be single or multiple. They are composed of carbonate of lime and phosphates. In shape they may be round, oval, or angular, and in color an opaque white. Osler states that in one thousand autopsies at the Johns Hopkins Hospital there were two cases. In 1885 Johnston collected thirty-five cases in the literature. They had been found in the pancreatic ducts and in pancreatic cysts and abscesses.

As to their *etiology* but little is known. They may result from inspissation of the secretion or from an obstruction in the ducts, or be due to some undetermined action of bacteria. Probably, as in the liver, both slowing or obstruction in the outflow of the secretion and bacterial infection are etiological factors.

The results are found in the gland itself. They are: inflammatory indurations, cyst and abscess formation, a predisposition to the development of malignant disease, and obstruction to the common bile duct from pressure upon, or the blocking of, the ampulla of Vater at the duodenal opening.

A definite *diagnosis* is seldom possible. The pain could not be differentiated from gall-stone colic. Pain in the left hypochondrium is thought to be suggestive of pancreatic calculus. Pain, vomiting, fatty stools, diabetes, and the passage of carbonate of lime stones would render the diagnosis probable. Carbonate of lime calculi, however, are sometimes formed in the intestines.

A stone might be removed from a cyst or abscess or from a dilated duct. If jaundice is present and the obstruction cannot be found and removed, cholecystotomy would be indicated. *George E. Armstrong.*

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PANCREATIN.—PANCREATINUM: "A mixture of the enzymes naturally existing in the pancreas of warm-blooded animals, usually obtained from the fresh pancreas of the hog (Sus scrofa Linné; class, Mammalia; order, Pachydermata). A yellowish, yellowish-white, or grayish amorphous powder, odorless, or having a faint, peculiar, not unpleasant odor, and a somewhat meat-like taste.

"Slowly and almost completely soluble in water, insoluble in alcohol.

"Pancreatin digests albuminoids, and converts starch into sugar; prolonged contact with mineral acids renders it inert.

"If there be added to 100 c.c. of tepid water contained in a flask, 0.28 gm. of pancreatin and 1.5 gm. of sodium bicarbonate, and afterward 400 c.c. of fresh cow's milk previously heated to 38° C. (100.4° F.), and if this mixture be maintained at the same temperature for thirty minutes, the milk should be so completely peptonized that if a small portion of it be transferred to a test tube and mixed with some nitric acid, no coagulation should occur.

"Peptonized milk, prepared in the manner just described, or even when the process is allowed to go on to the development of a very distinct bitter flavor, should not have an odor suggestive of rancidity."

The pancreas contains four distinct enzymes which are known by their action: the proteolytic—trypsin; the diastasic—amylopsin or diastase; the milk-curdling; and the fat-splitting. No one of these ferments has been isolated. The proteolytic enzyme converts proteids with equal or greater facility than pepsin, but it differs from pepsin in respect to the media in which it exerts its activity, and also in respect to the final products of its action. Trypsin bears no relation to an alkaline medium which corresponds to the dependence of pepsin upon acid; it acts with equal facility in a neutral or a faintly alkaline medium. Alkalies, more particularly sodium carbonate or bicarbonate, up to one per cent. of the digesting mass, are generally stated to be most favorable to the action of trypsin; the writer, however, has not found in digestion in vitro that sodium bicarbonate in 0.1 per cent. to 1 per cent. has given better results than parallel tests in which the alkali was omitted, while more than traces of free alkali were found unfavorable. Trypsin in antiseptic solutions (with thymol) containing as small an amount as 0.1 per cent. anhydrous sodium carbonate, has been found to undergo rapid deterioration at ordinary room temperature. While the pancreas juice obtained from living animals is alkaline, the pancreas gland, as soon as it may be conveniently treated upon removal from the recently killed animal, will be found to give an acid reaction. Aqueous infusions, glycerin or hydro-alcoholic extract, from such gland are invariably acid to litmus, and the acid present in these solutions does not in the slightest degree interfere with the pancreas enzymes in vitro; this acidity is reasonably to be attributed to nucleic acid, and undoubtedly the proteid is bound up in the cell with acid. The ash is invariably acid, containing phosphoric acid and potash, presumably acid phosphate. Minute percentages of mineral (0.03 per cent. HCl) and organic (0.25 per cent. acetic) acids do not interfere with the action of trypsin, but have been observed slightly to enhance it. Furthermore, the latent mother ferment, trypsinogen, is developed by the influence of the acid constituents of the gastric juice, and probably likewise of foodstuffs, for in the treatment of the gland itself it is found that the addition of minute amounts of organic acids yields the ferment in an active form from the trypsinogen. Trypsin, however, is very sensitive to more than traces of free mineral acid, 0.1 per cent. to 0.15 per cent. HCl destroying it immediately, and subsequent neutralization failing to revive it. So far, therefore, as may be gathered from these facts there is no evidence in support of the impression which has gained so much credence—that pancreatin depends upon an alkali for activity or in any way bears such a relation to an alkali as pepsin does to acid.

Trypsin converts native proteids into soluble and diffusible forms of albumoses and peptones which differ in no known way from those derived from peptic action, and causes by prolonged digestion a further cleavage of these proteids into simpler nitrogenous bodies—the amido-acids, leucin, tyrosin, etc., and hexone bases, ammonia, etc. Recent researches have led to the opinion that the development of these proteids into these crystalline bodies is essential to their complete utilization in nutrition.

Trypsin exhibits a special affinity for the digestion of certain native forms of proteids—fibrin, muscular tissue, both raw and cooked; these are promptly digested by the trypsin, whereas its action upon coagulated egg albumen is very slow in comparison with that of pepsin.

The products of peptic digestion (those intermediary between raw proteid and true peptone, syntonin and albumoses) are likewise, after neutralization, quickly converted into peptone by trypsin. Rapidity of action seems to be the natural function of trypsin. It exhibits a peculiar affinity for the casein of milk, as natively existing in milk, peptonizing this proteid with great celerity without the intervention of an alkali.

Certain differences in the physical phenomena observed in tryptic and peptic digestion have led some to suppose that trypsin exerts a peculiar erosive action. The swelling of tissue, the gelatinous character which fibrin almost instantly assumes under pepsin acid digestion, is not to be accounted for by any peculiar action of the pepsin itself; it is due to the influence of the hydrochloric acid which combines with raw proteins to form syntonin—this being very penetrable by the enzyme. In fact, one is struck with the similarity in adaptation to digestion, between gelatinous starch and this swollen, gelatinous fibrin. Boiled albumen presents no visible difference in its digestion with trypsin or with pepsin, for the acid does not swell the coagulated albumen. Trypsin (like pepsin) acts only by effecting the solution of the surface exposed—by conversion into more soluble forms.

A peculiar effect of trypsin upon milk is the conversion of casein into a form which becomes coagulable at the boiling point. This partially peptonized casein has been termed "metacasein," which, upon more complete conversion, loses its coagulability. This behavior of milk has been suggested (Roberts) as a convenient means of testing the activity of pancreatin, simply by ascertaining under certain conditions the time at which this "onset" point of conversion occurs. This is an extremely interesting reaction, and significant of the peculiar nature of casein, which, unlike other forms of native proteid, is not coagulable by heat, probably owing to its peculiar combination with inorganic constituents, losing this characteristic, after a certain amount of digestion and again becoming non-coagulable like other peptonized proteids. By rendering milk slightly alkaline by the addition of sodium bicarbonate or potassium bicarbonate, this metacasein reaction is prevented, and the milk then at any period of peptonization may be heated to the boiling point without curdling.

The starch-converting ferment of pancreatin, commonly known both as amylopsin and as diastase, very rapidly liquefies starch paste, converting starch into maltose. Raw or uncooked starch is similarly converted, though less rapidly, the action being proportionate to the diffusion of the starch, to the surface presented to the digestive ferment, completely cooked gelatinous starch being with great facility brought into complete contact.

The products of pancreas digestion of starch are apparently identical with those of diastase from other sources—the achroo-dextrins, dextrins, and maltose. Amylopsin is extremely susceptible to the influence of chemical reagents. Its action is not enhanced in the slightest degree in alkaline media; indeed, it is greatly enfeebled by free alkali; it is also weakened by acids (mineral and organic) beyond a very slight percentage. Acids which tend to promote the development of trypsin exhibit no corresponding behavior on amylopsin. In vitro, in neutral media, or as found in its normal association with the acids of the pancreas gland or in extracts or

infusions therefrom, amylopsin exerts enormous energy in the conversion of starch. It no doubt exists preformed in the pancreas gland, and there is ground for the belief that it differs in its constitution from the proteolytic enzymes.

The fat-splitting and emulsifying agent of pancreatin (steapsin or lipase) is the most delicate of the enzymes; it is rapidly destroyed by all acids, except the fatty, and by strong alcohol. Steapsin rapidly liberates the fatty acids, and this can be very readily observed by the addition of a few drops of a neutral solution of pancreatin to a neutral solution of butter in ether, to which a little litmus has been added. The nature of the ferment, its susceptibility, and the so far insuperable difficulty of separating it in any degree from the other ferments of the gland, complicate its study and have precluded the establishment of accurate, conclusive data concerning it.

The coagulating ferment behaves in a manner similar to that of the rennet. When added in a sufficient quantity to pure milk at a temperature of 100° F., the characteristic milk curd is almost instantly formed. This casein curd, however, is not permanent, and cannot be separated so freely as that obtained by the action of rennet; if the milk be maintained at an ordinary temperature the trypsin will rapidly attack the casein, and by stirring the mass, solution can be readily effected.

The milk-curdling ferment often escapes detection owing to the rapid peptonizing action of trypsin upon the casein.

Although pancreatin is officially defined as "a mixture of the enzymes naturally existing in the pancreas," no official test is given for other than the proteolytic ferment, and this is determined by its action on milk under conditions which are approximate to those commonly employed in the preparation of peptonized milk. The provision against the development of rancidity in peptonized milk is especially important, for pancreatin, which produces this result, is distinctly objectionable,—it yields a milk which is unfit for food, especially for the sick.

The term "pancreatine" in the past has been applied to indefinite preparations of the pancreas and more often identified with the emulsifying ferment—the function of the gland which was first observed and thought to be its chief and important characteristic. The official adoption of this title, however, now makes it applicable only to a product which contains all the pancreas enzymes. This of course is in distinct opposition to scientific nomenclature of the enzymes, for the term might best be applied to some one particular ferment, in conformity with the use of pepsin for the proteolytic ferment of the stomach.

"Pancreatine" was originally applied to the starch-converting agent of the pancreas juice by Bouchardat and Sandras, to the ferment obtained by them from infusion of pancreas with water and precipitated with alcohol.

The pancreatic enzymes, certainly the proteolytic, amylolytic, and curdling, are freely soluble in water, and are readily extracted from the gland by infusion, by dilute glycerin, by hydro-alcoholic menstrua. It is not possible, however, to prepare a liquid extract of the gland which will retain for any lengthy period all the several, chief enzymic properties of the pancreas. Whatever the reaction of the mingled ferment solution may be whether due to the fresh gland acid constituents or to added acid or alkali, the diastase especially loses its activity. This will either be due to unfavorable reaction or to the influence of the trypsin, should the conditions be favorable for its action. The pancreatic liquors (originally suggested by Roberts) have not been found by any means so effective and agreeable and convenient for general purposes, especially for the peptonization of food, as the extract in a dry form. The activity of pancreatin, whether in a dry or a liquid form, simple or in combination with other agents, is readily tested by applying it to the digestion of proteids in an alkaline medium (a procedure which differentiates tryptic action from that of pepsin); and its effect upon starch may be tested by the very simple method which establishes the presence of diastase,—by its action on starch mucilage at 100° F. The proteolytic ferment may be tested upon fibrin or milk, using the United States Pharmacopœia test. Negative reaction in any respect with these tests is absolute evidence of the absence of the ferment which is thus to be indicated.

Pancreatin is so susceptible to change and enfeeblement that it should not be prescribed in solution with soluble chemical agents—mineral acids or alkalies. Pepsin-acid solutions are particularly incompatible with pancreatin; even that degree of acid which is suitable for the preservation of the pepsin weakens the activity of the pancreatin, and this is increased by the influence of the pepsin, under the commercial conditions to which a pharmaceutical product must be submitted, and for which it must be suitable by a reasonable degree of permanency. Alkaline agents are indicated and freely prescribed with pancreatin, and this is best accomplished in dry mixtures—tablets, capsules, powders, etc. While in certain conditions, for instance, in the peptonizing process, the salts of the alkalies (sodium bicarbonate, etc.) fulfil a useful purpose, alkaline solutions of pancreatin do not retain their activity at ordinary temperature; they are suitable only for immediate use.

The liquid preparations of the pancreas gland, therefore, should as a rule be prescribed alone, separate from the remedies to be used in association. In the dry form, however, complete freedom of combination of any remedy indicated is afforded, for the dry enzymes are very stable.

The whole relation of the enzymes of the different digestive glands mixed in artificial solutions may perhaps best be summed up by this fact: that the ferment for which the reaction of the solution is most favorable will exert an injurious action upon the other enzymes; in other words, the *active* enzyme-proteid will convert the other enzyme-proteids which are in the unfavorable environment.

Therefore, from a pharmaceutical standpoint, we have to keep strictly to the ascertainment of conditions which are favorable to the extraction and production of these enzymes in a form of reasonable stability, and to the avoidance of incompatibles, these being simply agents which are positively known to injure the ferment in vitro; and to the adoption of certain definite standards of activity, and the development of proper methods for utilizing their digestive properties either in laboratory operations or in the artificial digestion of peptonized food for the sick. It must be ever considered that these data do not by any means offer a clear picture of, or arbitrary conclusion as to, the relation of the enzymes in the whole digestive scheme, where the enzymes in natural association are mingled under exceedingly complex conditions; first as to the influence of the constituents of the juices on the several enzymes thereof; secondly as to the influence of each secretion in its entirety upon the other, and as to the influence of the food constituents in their native form and as converted by gradual and successive digestive changes.

The study of the enzymes in vitro and of the entire digestive secretions warrants the conclusion that the ferments bear a different relation to, and influence upon, each other when mixed together simply with water and with reactions obtained by acids or alkalies, than they do in their physiological interaction. For instance, pancreatin will continue to act in an alkaline medium in the presence of food, and pepsin will continue to act for a long time in the presence of acid albumin, while aqueous solutions of these ferments of the same degree respectively of alkalinity and acidity by simple exposure to ordinary conditions of temperature are rapidly deteriorated.

Pawlow, after his recent elaborate and original studies of the digestive secretions, calls especial attention to the importance of his experiments concerning the "interaction of the digestive juices." He says: "Hence the chemical agencies of digestion form an alliance of a complicated nature in which the individual members are linked together mutually to relieve and support each other"; and he insists that it is indispensable in physiological inquiry to bring into view the "whole train of normal occurrences"; that "to constantly remember that all parts of the organism work together sheds a bright light over the special field under review."

No official method is given for pancreatin. It is commonly obtained by mechanical and chemical means—by the precipitation of an infusion, or a mixture of the pancreas gland with water freed as much as possible from the fat and connective tissue by mechanical means, this mixed with alcohol in excess, and the precipitate collected, expressed, and dried. Pancreatin is also prepared from the animal pancreas by freeing the gland in so far as possible from connective tissue and fat by careful trimming, reducing to pulp, passing through a sieve, desiccating and powdering, and further purifying by extraction with suitable solvents of fat, coloring matter, etc.

A liquid diastasic extract of the gland may be obtained by treating the pancreas as soon as possible after removal from the animal, the gland meanwhile kept refrigerated, in which state the trypsinogen remains unchanged; rapid extraction and clarification yield the amylopsin in an exceedingly active form, and by repeated filtration an agreeable, efficient pharmaceutical product is finally obtained.

Pancreatin as a remedy in intestinal indigestion is usually administered in two- to five-grain doses, about three and a half hours after meals and at bedtime, in capsules or tablet form. It is also given with soda bicarbonate (ten grains) an hour or so before breakfast or at bedtime, taken in a glassful of water as hot as can be conveniently sipped, say, 115°–130° F., this particularly in catarrhal conditions and in biliousness. Pancreatic extract with oxgall, ipecac, and bismuth has gained repute in disorders of intestinal digestion. The elixir or essence of amylopsin is much used as a remedy in salivary or intestinal indigestion; in the former case it is given immediately before food, or mixed at table with farinaceous food. Inasmuch as the full pitch of gastric acidity does not appear until about half an hour after eating, this diastase certainly has the same physiological conditions for its activity as that normally mingled with the food in the saliva. The diastasic essence is given at the completion of stomach digestion to promote intestinal starch digestion.

In the artificial reinforcement by pancreatic ferments, the essential consideration is obviously to protect them from action *in gastro*; and clinical experience, with the various expedients used, has shown that the pancreatic ferments exert distinctly beneficial action.

The pancreatic ferments are peculiarly and happily fitted for the preparation of partially or completely digested foods for the sick; under their influence and by very simple means and methods, the chief and complete foods of almost every variety are readily peptonized in the household. These foods may be so prepared as to convey the ferments in an active form, thus promoting further digestion, or the digestive agent may be destroyed at any desired stage by raising the temperature of the food to 160° F., or, more simply, to the boiling point.

Special products and devices, such as peptonizing tubes, are much used; milk, either cold or by the warm process, is thus adapted to the varying requirements. The peptonized milk gruel deserves more extensive use, as the simultaneously converted farinaceous foods—wheat, arrowroot, etc.—increase the nutritive value and convey a very agreeable taste, masking that of the milk. Porridge of oatmeal, wheat, etc., is easily made more digestible by adding, at the proper temperature, a small quantity of the diastasic essence to a portion as served at the table; for the aged and for infants this is an efficient method. (See also article on *Dietetics*.)

Trypsin as a surgical solvent is peculiarly serviceable in cases in which acid is undesirable or alkali necessary; in such situations, and where fluid cannot readily be kept in contact, the trypsin powder is preferable, adhering as it does to moist surfaces, and being thus exceedingly active; in nasal diseases, in diseases of the throat, urethra, etc., the trypsin powder is successfully applied. By its use in diphtheria, great relief is often afforded to the distressing local manifestations, in addition of course to the specific constitutional treatment. The pancreatic extract has been used with marked success as a solvent in abscess cavities of the liver, hip-joint disease, etc.

Trypsin is used as the essential agent in the preparation of an artificial human or humanized milk from cow's milk, for the reason that cow's milk proteids, under the regulated influence of the enzyme, become practically identical in solubility with the proteids of human milk; in consequence of this change a cow's milk mixture with percentage composition adjusted to the standard of human milk becomes notably thinner, of a grayish-yellow color, and acquires a marked resemblance to human milk in physical and physiological characteristics and deportment with all reagents. This milk so converted by trypsin gives minute, diffusible coagula with gastric juice, and with acid of normal gastric percentage; it corresponds in digestibility in vitro to human milk with pepsin and acid, and is not coagulated by rennet. The enzyme itself, as the physiological factor in the process, is instantly destroyed by simply heating the milk to 160° F. or by boiling it after the enzymic action has been utilized; the enzyme thus becomes so much inert proteid, so minute in amount as to be a negligible quantity in the food and quite incapable of in any way influencing the digestibility of the milk.

This use of the enzyme in infant feeding is based on the unquestionable postulate, confirmed by all data, chemical, physiological, and clinical, that the radical difference in digestibility and deportment between cow's and human is milk attributable to the nature of their respective proteids—largely casein in cow's milk, and soluble, non-coagulable peptone-like proteids in human milk; it is also based upon comparative analyses and observations of this humanized milk and many specimens of average, normal human milk. Theoretical objections based upon presumed defects in this method, as presenting a food unnaturally digestible or conveying a digestive agent, are obviously erroneous in view of the foregoing facts. The enzyme may, however, be so used as to secure a degree of digestibility beyond the normal where this is required, by simply prolonging the subjection of the casein to the proteolytic agent or the enzyme administered in the food, by chilling the milk instead of pasteurizing or sterilizing it when the desired degree of digestion is accomplished. In fact, this is like the use of the enzyme as a means of aiding the digestion of mother's milk itself by giving pancreatin in a few one-grain doses immediately after nursing.

Benjamin T. Fairchild.

PANCREON is a combination of pancreatin with tannic acid, said by Gockel to possess the tryptic, amylolytic, and emulsifying powers of pancreatin, but to be unaffected by the gastric juice. Out of 100 gm. of albumin subjected to the action of 1 gm. of pancreon for fifteen minutes at 40° C. (104° F.) in a weak alkaline medium, 85 gm. were digested. The dose of pancreon is 0.3–0.5 gm. (gr. v.–viij.) three times a day.

W. A. Bastedo.

PAPAW JUICE.—*Papaya. Carica.* The milk juice obtained from the nearly ripe fruit of *Carica Papaya* L. (fam. *Papayaceæ*).

This interesting plant is the well-known melon tree of tropical America, now widely introduced into other tropical countries. All of its parts contain a latex or milk juice, which is more abundant and more milky in the nearly ripe fruit than elsewhere. This milk juice possesses a bitterish and very acrid taste, is irritant to mucous membrane or to the abraded skin, and has considerable detergent power. It possesses the property of peptonizing albuminous substances, after the manner of trypsin, and of softening an additional portion which is not truly peptonized. By reason of its possessing this property, it has been largely used in its own home for application to tough meat to render it more palatable and

digestible, a fact which has led to its examination by chemists and physicians with a view of determining its availability for use as a digestant. Its digestant principle has eluded isolation, as have all similar substances. It has been found possible, however, to concentrate the activity in a peculiar extract called caricin (Moncorvo), papain (Wurtz), or papayotin (Peckolt), which is extracted with water, the solution filtered and the filtrate precipitated with alcohol, and perhaps again dissolved and reprecipitated for somewhat further concentration. The fresh juice, which consists largely of water, yields also considerable resin, divisible into two portions, nearly five per cent. of a kind of caoutchouc, a little fat, malic acid, leucin, tyrosin, and other unimportant matters. The leaves, from which the papain can also be obtained, yield the crystalline alkaloid *carpaine* ($C_{14}H_{28}NO_2$), which is most abundant in the young leaves, constituting about one-fourth of one per cent. of their weight when dried. The seeds, which are pungent and which are used for their tænicidal properties, contain a resin which shares the pungency, though the latter is said to be due to a volatile principle allied to the volatile oil of mustard.

Action and Uses.—Since about the year 1880, great attention has been given in Europe and America to attempts to employ papain as a digestant. Reports as to the energy, and even as to the manner of its action, vary most widely, even when presented by careful experimenters, and the conviction is forced that the market preparations employed by them must have differed in character. It appears very likely that some of these preparations were mixtures of different digestive ferments, the results being such as might be expected from an admixture to the papain of pancreatin or pepsin. Much of the information which has been supplied to physicians, and which has found its way into professional journals and books, has been smuggled under the guise of scientific literature from interested commercial sources.

It has been definitely established that as a digestant papaya is wholly proteolytic. It disintegrates, softens, and liquefies albumen in the form of white of egg, musculin, fibrin, and casein, and considerable of the product is peptonized. This action takes place in an alkaline or neutral medium. Davis (1893) and Hobein (1894) have shown that it is inactive in an acid medium, the papain employed by the second-named authority having been prepared by himself from papaya. Fairchild, using specimens the identity and purity of which were authenticated by himself, has fully confirmed this conclusion. Nevertheless, some eminent authorities claim that there is a slight activity in acid media. Dr. Lafayette B. Mendel, who takes this view and who has made special researches in this direction, has furnished us with the following account of the products of papain digestion:

"The products of the reaction of papain with proteids consist in large part of proteoses. Peptones—*i.e.*, compounds not precipitable with ammonium sulphate, but still giving the biuret reaction—are also formed. The papain proteoses resemble the related products obtained by gastric digestion. Regarding the occurrence of further products of proteolysis, such as leucin, tyrosin, tryptophan, and other characteristic derivatives of tryptic digestion the evidence is somewhat uncertain. Underhill and the writer have usually failed to find leucin, tyrosin, and tryptophan in appreciable quantities, at least under conditions in which they are readily formed in large quantities by other tryptic enzymes. Emmerling has succeeded in isolating small quantities of these substances from the products formed after very prolonged digestion, although even under such conditions proteoses predominate. Papain accordingly resembles trypsin in dissolving proteids in media of various reactions, thus differing from pepsin; its resemblance to the latter lies in the similarity of the products formed by the two enzymes. Harlay has made comparable observations with the enzyme of the related *Carica hastifolia*. Kurajeff has found that commercial preparations of papain induce the formation of peculiar proteid precipitates in solutions of proteoses such as the widely used 'Wittepepton.' The reaction corresponds with that described for rennin as 'plastein formation,' by Danilewski and his co-workers. The importance of this proteid-clotting or precipitating function of enzymes can only be conjectured at present. Thus it may play a rôle in proteid synthesis and regeneration; and the significance of such an enzyme in plants at once becomes apparent. On milk papain preparations exercise a clotting or curdling action. Whether these properties are all due to the same enzyme, or whether more than one unorganized ferment is present in the plant, are questions which have not yet been settled."

Riedel, who in 1894 made a very elaborate series of experiments to determine the most favorable conditions for the activity of papain, concluded that the most favorable temperature was about that of the body; that one part of papain to one hundred of albumin was the most favorable proportion; that the more concentrated the papain solution the greater the activity, and that the capacity of papain for digesting egg albumen was about one hundred times its own weight. The answer to the last question depends naturally upon the degree of concentration of the papain; yet it has been found impossible to carry this concentration more than a little way. The activity of a definite portion of the dried papaw juice itself is much greater than that of the papain extracted from it; a single instance is recorded in which such a juice, very carefully prepared, digested one thousand times its own weight. The difficulty is that this action is extremely variable; so much so that it is not at all probable that commercial dried papaw juice could ever be brought to a uniform standard of strength.

As a general statement, it may be said that a good average sample of papain is capable of digesting from fifty to one hundred times its own weight of albumen, under favorable conditions. It is also very noteworthy that it loses its power rapidly upon being kept. If kept with ordinary care in well-stoppered vials it will ordinarily have but little value at the end of a year.

As to whether papain possesses any diastasic action in the conversion of starch, we have also discordant reports, but are obliged to conclude that it has none. As to its milk-curdling power, it certainly possesses a small and variable degree; but this is of a peculiar character, the process and the coagulum differing distinctly from those resulting from the use of rennet.

Papaya is a powerful irritant to denuded tissues and to mucous membrane. So powerful is this action that if a large amount be taken into the stomach in concentrated form it acts as an irritant, or even as a caustic emetico-cathartic poison. Applied to a raw surface it acts as an escharotic, and is very apt to be followed by putrefactive processes. Papain, prepared as above described, is less active in this direction, though still irritant. Desjardins states that the irritant property is almost completely destroyed by boiling, which also produces a new substance, having a powerful lumbricidal action, similar to that of the seeds.

The principal native use of papaya has been stated above. Owing to its locally stimulant action, it has also been used as a cosmetic, to remove pimples and similar roughnesses from the skin, and to produce a smooth, healthy surface. Its irritant properties have been utilized in the form of caustic applications to cancerous and other morbid tissues, but the practice cannot be considered good. Its dissolving action upon albuminous substances has been utilized by applying it to diphtheritic membranes. For this purpose a five-per-cent. solution, preferably made alkaline with 0.5 per cent. of bicarbonate of soda or potash, is applied at short intervals with a brush, or in the form of a spray. The results appear to be highly irregular and uncertain. A similar solution, but twice as strong, is applied to warts, corns, and other cutaneous indurations. Almost its entire use in Europe and America is for internal administration as a digestant, either alone or combined with other ferments. Owing to its irritant effect it should be administered when the

stomach is full of food, and dilution with milk-sugar or other neutral substance is desirable. Opinions differ widely as to the dose, but the best evidence is in favor of the use of a considerably larger dose than that of official pepsin. Where there is an irritable condition of stomach or bowels, the dose should be reduced, and the drug should not be used in case of an ulcerated condition of those organs.

Allied Drugs.—The juice of the fruit and leaves of the pineapple has similar properties and uses, already referred to under *Bromeliaceæ*. *Henry H. Rusby.*

PARA-ACET-AMIDO-PHENOL ETHYL CARBONATE, a tasteless, white, crystalline powder, insoluble in water and readily soluble in alcohol, is administered in dosage of 0.5 gm. (gr. viij.) as an antipyretic, analgesic, and hypnotic. *W. A. Bastedo.*

PARA-CHLORALOSE. See *Chloralose.*

PARACHOLIA.—The term used by Pick to designate the hypothetical secretion-anomaly by which the bile leaves its accustomed channels and passes into the blood, giving rise to icterus. By a number of recent writers icterus is regarded as due to a diseased condition of the liver cells, the process being analogous to the secretion of albumin in diseased conditions of the kidney cells. Normal liver cells should secrete bile into the bile vessels, and urea and sugar into the blood capillaries. According to Minkowski it is, therefore, not without analogy that the liver cells in diseased conditions should give off the bile into the blood-vessels. Such a process is designated by him as *parapedesis*. Liebermeister and Pick also explain many forms of icterus as due to functional disturbances of the liver cells, either with or without evident anatomical changes, the former designating such a disturbance as *diffusion* or *akathectic icterus*, the latter as *paracholia*. Pick believes that the pathogenesis of the obscure forms of icterus may be explained by this hypothesis. He accordingly distinguishes three classes: *nervous paracholia*, *toxic paracholia*, and *infectious paracholia* (*Wiener klin. Wochen.*, 1894). *Aldred Scott Warthin.*

PARADISE SPRING.—Cumberland County, Maine. Post-Office.—Brunswick. Hotels and inns.

This spring is located about one mile from the centre of the village of Brunswick and five hundred feet from the Androscoggin River. It is reached by way of the Maine Central Railroad to Brunswick, and thence by Jordan Avenue. The country about the place is level—a sandy plain, covered by pines extending to beautiful Casco Bay, three miles distant. Concerning the meteorological conditions prevailing about Brunswick, we are indebted to Prof. Leslie A. Lee, of Bowdoin College, for the following description: "The climate of Brunswick is peculiarly agreeable. Fair weather predominates, the annual number of cloudy days averaging not more than eighty-six in a long period of years. The prevailing winds are from the southwest during the summer and from the northwest during the winter. On this account the air is much drier than would be expected from the proximity of the village to the sea, and fogs rarely occur."

Scattered throughout the town are large areas of pine forests, which give a resinous and balmy quality to the air. The average annual temperature is 44.40° F., rising to an average of 65.11° F. in the summer, and falling to a mean of 22.63° F. in the winter. The temperature of the spring water is about 45° in summer and 43° F. in winter. The outflow of water is abundant, being estimated at twelve thousand gallons per day. The following analysis was made by Prof. Henry Carmichael, of Bowdoin College: Reaction neutral. One United States gallon contains: Silica, gr. 0.38; iron oxide, a marked trace; calcium sulphate, gr. 0.06; calcium carbonate, gr. 0.07; magnesium carbonate, gr. 0.06; sodium chloride, gr. 0.02; sodium carbonate, gr. 0.36; potassium chloride, gr. 0.04. Total, 0.99 grain.

A more recent analysis by State Assayer Franklin C. Robinson shows a somewhat larger proportion of solids, viz., 1.05 grains per United States gallon of inorganic salts. The water is remarkably free from organic matter, containing, according to Robinson's analysis, but 0.07 of a grain per United States gallon. This organic matter was found by examination to be of vegetable origin, only a minute trace of nitrogenous material being detected. The water is excellent for table use, and has been supplied to the students of Bowdoin College for some time past. It is used commercially.

James K. Crook.

PARAFFIN INJECTIONS. See *Reparative Surgery.*

PARAFFIN-XYLOL is a solution of 1 gm. of paraffin in 10 c.c. of xylol, and is used as an antiseptic varnish for the hands in surgical operations.

W. A. Bastedo.

PARAFORM—paraformaldehyde, triformol, trioxymethylene ($HCOH)_3$—is a polymer of formaldehyde occurring as a white, insoluble, crystalline powder. It tends to decompose slowly with the production of formaldehyde gas, and, when acted upon by heat, as in some of the formaldehyde generators, may evolve the gas rapidly and in large quantities. On account of its slow and steady evolution of formaldehyde, it is used by physicians as an intestinal antiseptic and by dentists for disinfecting cavities. The dose is 0.5–1 gm. (gr. viij.–xv.). Unna prescribes: ℞ Paraform 2 gm. (gr. xxx.), ether 2 c.c. (ɱ xxx.), and flexible collodion 15 c.c. (ʒ ss.) as the best application for pityriasis versicolor, erythrasma, and other saprophytic skin diseases. Mense uses a three-per-cent. paraform collodion as a slow caustic for warts and other small cutaneous growths.

Paraform enters into the composition of eka-iodoform.

W. A. Bastedo.

PARAISO HOT SPRINGS.—Monterey County, California. Post-Office.—Paraiso Springs. New Cottages.

Access.—Take 8:15 A.M. Southern Pacific train from the corner of Third and Townsend streets, San Francisco, reaching Soledad station at 1:43 P.M. Thence by stage a drive of one hour and a half to the springs.

"Paraiso Springs," says Mr. E. S. Harrison in his history of Monterey County, "were the property of the Mission Soledad, which lies about five miles northeast of the springs. The title of the present owner was obtained from the Church of Rome, to which a patent was granted by the Mexican Government in 1778. In the records of the Mission Soledad the healing and invigorating qualities of these waters are duly set forth. The springs are situated in a picturesque alcove of the Santa Lucia Mountains on the western border of the Salinas Valley, about one hundred and fifty miles south of San Francisco. The altitude of the location, being nearly one thousand feet above the valley, renders the atmosphere dry, bracing, and invigorating. Below the resort, and for miles beyond, the eye scans the fertile valley, traversed by the grand Salinas River and Arroyo Seco, and the far-away Gabilan Mountains, forming a picture of great charm and glory. The commodious hotel and cottages combine all the luxury and comforts that can be found anywhere. On the premises are several valuable springs flowing about two thousand gallons of water per hour, and consisting of sulphur, soda, and iron waters. The temperature of the springs varies from 100° to 118° F. We give below the analyses of the waters of the two principal springs, the Paraiso Sulphur Spring and the Great Paraiso Hot Soda Spring.

The Paraiso Sulphur Spring.—According to the analysis made by Dr. Anderson in 1889, one United States gallon contains: Sodium chloride, gr. 2.76; sodium carbonate, gr. 1.15; sodium sulphate, gr. 37.10; potassium sulphate, gr. 0.83; magnesium carbonate, gr. 6.09; magnesium sulphate, gr. 2.19; calcium carbonate, gr. 0.89; calcium sulphate, gr. 4.40; ferrous oxide, gr. 0.73; silica, gr. 2.55; organic matter, gr. 7.35. Total, 66.04 grains. Gases: carbonic-acid gas, 2.04 cubic inches;