should be rejected. Salicylic acid is permanent in the air; is, when pure, free from odor of carbolic acid, but has a sweetish taste, with an acrid after-flavor. It dissolves in 450 parts of cold water and in 14 parts of boiling water; in 2.4 parts of cold alcohol, and very readily in boiling alcohol. Although salicylic acid is but feebly soluble in cold water, it dissolves freely in many saline solutions. Thus the pharmacopœial *solution of ammonium acetate* will dissolve twenty-five per cent. of salicylic acid; a twelve-and-a-half-per-cent. aqueous solution of potassium acetate will dissolve twelve and a half per cent. of the acid; a twelve-and-a-half-per cent. solution of potassium citrate in equal volumes of glycerin and water will dissolve six per cent. All of these solutions possess the sharp stinging taste of the uncombined acid. A serviceable and permanent solution of the acid, and one that instead of being sharp to the taste has a pure bitter flavor only, can be made as follows: Dissolve two parts of borax in twelve of glycerin by the aid of heat; add one part of salicylic acid, continue the heat, and stir until the acid dissolves. Almost all solutions of salicylic acid, either immediately or after a while, turn of a reddish or of a smoky color, resembling that of solutions of carbolic acid.

Salicylic acid is incompatible with strong oxidizing agents, like potassium permanganate, and with chlorine, bromine, iodine, ferric salts, carbonates, the most of which it decomposes, and spirit of nitrous ether. A soft or semi-liquid mass is formed with exalgin, antipyrin, phenacetin, urethane, and other synthetics, as well as with lead acetate and sodium phosphate. The salicylates give precipitates with strong solutions of most alkaloidal salts, as well as with strong acids. Lime water also yields a precipitate.

Salicylic acid, taken into the mouth, has not much taste, proper, but speedily and quite suddenly after the tasting a sharp stinging seizes the *throat*, often severe enough to bring tears to the eyes. Similarly, a little of the dry acid snuffed up the nostrils will sting quite strongly. The acid brings sharp pain to cuts and abrasions, but, swallowed, is much less irritant to the stomach than its effects on the throat would lead to suppose. Large doses, so taken, may upset digestion and cause a strong sensation of heat, and even actual burning pain, but no serious or lasting results follow. The acid is rapidly absorbed from the stomach into the circulation, presumably in saline combination, and thereupon exerts the peculiar influence characteristic of the salicylates (see *Salicylates*, below).

Salicylic acid was at first used as an internal medicine for the procurement of the therapeutic effects of the salicylates; but now, and very properly, salicylates themselves, because of their freedom from the locally irritant action of the uncombined acid, have superseded the acid for this purpose. The present medicinal application of the acid is for local purposes as a deodorant, detergent, or so-called antiseptic—purposes which salicylic acid fulfils by reason of its having a fairly potent germ-sterilizing faculty. (See Salicylic Acid in article *Germicides*.) For general local use, the solution of the acid in a glycerin solution of borax is convenient, this solution bearing any necessary dilution with either water or alcohol without precipitation. A dilution representing a two-per-cent. solution of acid is one very commonly employed. For other salicylic preparations for local use, see Salicylic Acid in article *Antiseptics*.

SALICYLATES.—In saline combination, whether with metallic or ethereal bases, the local pungency of free salicylic acid disappears while yet the faculty for constitutional action remains. As already said, it is probable that the acid, when taken as an internal medicine, enters the circulation only after conversion into a salicylate, so that, as a matter of fact, what is commonly called the constitutional action of salicylic acid is, so far as we know, the action of a salicylate. The constitutional effects in question are as follows: After a full dose a non-pyrexial subject experiences, in about fifteen minutes, a moderate reddening of the face with a sense of fulness of the head, or perhaps even a pronounced headache, and a buzzing or roaring in the ears precisely similar to what occurs in cinchonism. Almost simultaneously free perspiration begins, and, according to dose, there is more or less tendency to a reduction of pulse rate, of respiration rate, and of body temperature. Tests for salicylic acid will reveal the presence of the substance in the urine, the saliva, and the sweat. The urine, furthermore, will be discolored, appearing brown by reflected and green by transmitted light, from the presence of indican or of pyrocatechin. It will also contain a something that will reduce copper salts in copper test solutions (Brunton), and will show an increased amount of urea and uric acid. In overdoses, salicylates readily irritate the kidneys, setting up albuminuria; may derange the cerebral faculties, causing hallucinations and delirium; and may dangerously or even fatally depress the functions of heart and lungs, determining collapse or death by failure of respiration. These several untoward effects occur very irregularly, and, according to Squibb, in "a very large proportion" of instances are determined, not by the salicylic acid, but by a *contaminating acid* very commonly present in market samples of salicylic acid, and hence in salicylates derived therefrom. The constitutional effects of salicylates, which are valuable in medicine, do not appear in experimentation with a subject in health. They consist, in general, in a reduction of fever temperatures, and, in particular, in an abatement of pains in fibrous tissues, notably the pains in acute articular rheumatism. The antipyretic power of salicylates is second to none, in all the three elements of quickness, degree, and duration of reduction of temperature. For a full antipyretic effect, however, considerable dosage is necessary—considerable enough to cause disagreeable sweating, *tinnitus aurium*, depression of pulse and respiration rate, and, every now and then, actual toxic symptoms. Other antipyretics, therefore, which act more kindly, are preferable, except in rheumatism. The antirheumatic faculty of salicylates is unapproached by any other known medicine, so that, as is well known, salicylates constitute a standard set of medicines for the treatment of acute rheumatism. Under salicylate medication the fever lessens, pains abate, and the disease runs a shorter as well as milder course. It is therefore particularly as remedies for rheumatism and, though not so surely, for gout that salicylates are prized in medicine.

The salicylates in *common medical use* for the purpose of salicylate medication are the salicylates, respectively, of *sodium*, *lithium*, and *methyl*. The salicylates, respectively, of *physostigmine*, *quinine*, and other alkaloids, are used for the sake of the medicinal action of the respective bases only.

Sodium Salicylate, $2NaC_7H_5O_3.H_2O$. The salt is official in the United States Pharmacopœia under the title *Sodii Salicylas*, Sodium Salicylate. It occurs as an amorphous powder, white, without odor, and having a sweetish, saline, and slightly alkaline taste. It is permanent in the air, dissolves readily in water, glycerin, and boiling alcohol. In cold alcohol it requires six parts for solution. It should be kept in well-stoppered bottles, protected from heat and light. Sodium salicylate is the most commonly used salicylate, and is a very important medicine. It is easily made *in solution* by mixing salicylic acid and a sodic carbonate in the presence of water, whereupon sodium salicylate results, and remains in solution, and carbon dioxide gas escapes in effervescence. From this solution the salt can be obtained by evaporation to dryness, carefully conducted. Extemporaneous preparation of the medicine *in solution* being easy, Squibb points out an advantage of such extemporaneous making of the salt in all cases in which the prescriber or the dispenser may not be certain of the purity of the market article. The point is that it is not possible to establish the purity of a given sample of *sodium salicylate* except by an elaborate chemical analysis, whereas a good sample of *salicylic acid* is immediately recognizable by the simple fact of its *crystalline condition*. Hence, in making one's own sodium salicylate from a selected well-crystallized sample of salicylic acid, purity is assured. And in the instance of this salt purity is important, since, as above said, there is probably good reason to lay many of the untoward effects of salicylates to the door of the contaminating acid of salicylic acid. Squibb recommends the following formula for the preparation of a solution of sodium salicylate of a strength convenient for use as a medicine: "Take of salicylic acid, well crystallized, 437 grains = 28.32 gm.; bicarbonate of sodium, 270 grains = 17.5 gm.; water, free from iron, a sufficient quantity. Put the acid into a vessel of the capacity of a pint, add 4 fluidounces = 120 c.c. of water, stir well together, and then add the bicarbonate of sodium in portions with stirring, until the whole is added and the effervescence is finished. Filter the solution, and wash the filter through with water until the filtered solution measures 6 fluidounces, or 180 c.c. This solution contains 10 grains (= 0.65 gm.) of the medicinal salicylate of sodium in each fluidrachm (= 3.75 c.c.). If made from good materials, the solution before filtration is of a pale, amber color, but as most ordinary filtering paper contains traces of iron, the filtered solution is often of a deeper tint." The proportions of the ingredients for this solution are estimated so that the solution shall be neutral, but, "owing to the varying proportions of hygrometric moisture in the materials," the neutrality may not always be absolute. According to Squibb, a well-made sample of sodium salicylate, prepared by use of a well-crystallized sample of acid, is always, when evaporated to dryness, *white*, and is free from all *odor of carbolic acid*, unless it has been shut up for a long while in a bottle. Even then, however, the odor should be but very faint—only perceptible on close examination, and should disappear upon exposure of the sample to air. *Solutions* of sodium salicylate of good quality should have none of the carbolic-acid smell.

Sodium salicylate is used almost exclusively as an internal medicine, being commonly held to be lacking in the germ-sterilizing faculty which gives salicylic acid, as such, its applicability as a local antiseptic. For the purposes of internal salicylate medication, as set forth above, the salt is thoroughly effective, and, if made from a well-crystallized and therefore fairly pure sample of salicylic acid, rarely produces untoward effects in reasonable doses. So large a quantity as 5 gm. (about seventy-seven grains) has been given at a single dose in rheumatism without producing serious derangement, but the ordinary dosage for an antipyretic or antirheumatic effect does not exceed 1.3 gm. (20 grains) repeated every two hours, for three or four doses, or until a distinct impression is produced, followed by doses of half the quantity every hour or two thereafter, so long as the influence of the medicine may be required. The medicine is readily enough taken in simple aqueous solution, but if the faint, mawkish taste of the salt be objectionable, the addition of twenty per cent. of glycerin and the flavoring with a drop or two of oil of gaultheria will render the mixture perfectly palatable.

Lithium Salicylate, $2LiC_7H_5O_3.H_2O$. The salt is official in the United States Pharmacopœia under the title *Lithii Salicylas*, Lithium Salicylate. It occurs as a whitish powder which deliquesces on exposure to the air. It dissolves freely in water and alcohol, and resembles the sodium salt in taste. It should be kept in well-stoppered bottles. The effects of this salt are similar to those of sodium salicylate, with the possible superaddition of medicinal virtues, in rheumatic or gouty cases, derived from the basic element. The dose is similar to that of the sodic salt.

Methyl Salicylate, $CH_3C_7H_5O_3$. This salicylate is an ethereal body which constitutes nine-tenths of the substance of oil of wintergreen and practically the whole of the volatile oil of betula, both of which oils are themselves official medicines. Under the title, however, *Methyl Salicylas*, Methyl Salicylate, the United States Pharmacopœia recognizes the salicylate as made in the laboratory by distilling salicylic acid or a salicylate with methylic alcohol and sulphuric acid. Methyl salicylate is a colorless or slightly yellowish liquid, with the characteristic odor and taste of oil of wintergreen. It dissolves freely in alcohol. It should be kept in well-stoppered bottles protected from light. Methyl salicylate acts like the salicylates generally, with the usual pungent qualities of the volatile oils. In large doses—half an ounce or more—it is dangerously and even fatally poisonous, causing intense irritation of the stomach and intestines with constitutional symptoms of the salicylic influence. In doses of from five to fifteen minims it makes a very efficient salicylic medicine for rheumatism, and is, with many, the favorite salicylate. It may be administered in emulsion or in capsules.

Sodium Dithio-salicylate. Dithio-salicylic acid is a product of reaction between salicylic acid and sulphur chloride, under the influence of heat. The sodium salt of this product is a grayish-white, very hygroscopic powder, freely soluble in water. It has been proposed as a substitute for ordinary salicylates, on the score of being equally, if not more, potent as an antirheumatic remedy, while it is less apt to disturb the stomach. About 0.2 gm. (gr. iij.) may be given two or three times a day, or oftener, according to indications. It is not official in the United States Pharmacopœia.

Iodo-salicylic Acid is a modification of salicylic acid that has been used as a substitute for the ordinary acid in acute rheumatism. It occurs as a white powder slightly soluble in water, but freely so in alcohol, ether, and the fixed oils. It may be given in quantities of from 1 to 3 gm. (gr. xv. to gr. xlvi.) a day.

Cresotic Acid, Cresotinic Acid.—This is an homologue of salicylic acid to which it is allied in physical, chemical, and physiological properties. Its formula is C_6H_3-$OHCH_3COOH$. There are three isomeric acids, the ortho-, meta-, and paracresotic acids. They are always present in salicylic acid of commerce. In 1890 (*Phar. Jour. and Trans.*, November 22d) Professors Charteris and Dunstan, of Glasgow, pointed out that the ill effects that often followed the employment of salicylic acid were due to the presence of ortho- and paracresotic acids. These statements were described more in detail in a second paper in the *British Medical Journal*, March 25th, 1901.

The only preparation of this acid that has been employed for therapeutic purposes is the paracresotate of sodium. It posseess antipyretic and antirheumatic properties similar to those possessed by salicylate of soda, but in a lesser degree. The dose is from five to twenty grains three or four times a day; it is free from toxic action, and may be administered more freely if necessary.

Edward Curtis.

SALICYLIC ALDEHYDE, salicylous acid, ortho-oxybenzaldehyde, artificial oil of spiræa, $C_6H_4.OH.COH$, is obtained by heating phenol and sodium hydroxide with chloroform. A colorless fluid with the odor of meadowsweet, it is readily soluble in alcohol and chloroform, but in water is soluble only enough to impart its odor. In dose of 0.1–0.5 gm. (gr. iss.–viiss.), it is employed as a diuretic and intestinal antiseptic.

W. A. Bastedo.

SALICYLIDEN-PHENETIDIN. See *Malakin*.

SALICYLO-ACETIC ACID. See *Aspirin*.

SALICYL-QUININE. See *Saloquinine*.

SALICYL-QUININE SALICYLATE. See *Rheumatin*.

SALICYL-RESORCIN-KETONE, tri-oxy-benzophenone, is a compound which in the intestine sets free salicylic acid and resorcin. It is used externally in skin diseases, and internally as an intestinal antiseptic. Dose, 3–4 gm. (gr. xlv.–lx.).

W. A. Bastedo.

SALICYL-SULPHONIC ACID.—$C_6H_3(OH)(SO_3H)$-$COOH$. A white crystalline body, very soluble in water and alcohol. It is formed by the action of sulphuric anhydride on salicylic acid.

This compound was recommended as a test for albumin by G. Roch (*Pharm. Centralblatt*, September, 1889) and by Dr. John A. Macwilliam (*British Medical Journal*, April 18th, 1891), working independently of each other. It acts upon all forms of proteid bodies. When the proteid present is a native albumin, a derived albumin, a globulin, or fibrin, the precipitate is not dissolved upon boiling, but becomes decidedly flocculent. When the proteid is an albumose or peptone, the precipitate dissolves upon heating, to reappear on the cooling of the fluid. The peptone and albumose may be distinguished by saturating the solution with ammonium sulphate; the albumose is at once precipitated, while the peptone remains in solution. The peptone may then be detected by adding the salicyl-sulphonic test.

Compared with other tests, the delicacy of the salicyl-sulphonic test varies, according as a cloudiness immediately (two or three seconds) appears, or follows after one-half to one minute. In the latter case it is one of the most delicate tests we possess, revealing the presence of 1 part of albumin in 12,500 of water; in the former, it is placed by Dr. Macwilliam between the cold nitric acid test and the acetic acid and heat test.

Dr. Roch recommended that a few crystals of the acid should be shaken with the urine, or that 5 c.c. of a twenty-per-cent. solution should be added to 10 c.c. of the urine to be tested. Dr. Macwilliam is more exact in his manipulations. He recommends that a small amount of urine, about twenty minims, be placed in a small test tube, and that to this a drop or two of a *saturated* aqueous solution of the reagent be added. The urine must not be alkaline, and, if necessary, it should be acidulated. On adding the reagent the tube should be shaken quickly, to mix the contents, and the fluid should be examined at once. The occurrence of an opalescence or cloudiness immediately or within a few seconds indicates the presence of proteids. The development of the reaction after an interval of a minute or two shows the presence of proteids in minute quantities, which are probably insignificant from a clinical point of view. The fluid is then to be heated, when the ordinary albumin is coagulated and formed into a flocculent mass. *Beaumont Small.*

SALIFEBRIN, salicylanilid, is a proprietary combination of acetanilid and salicylic acid. *W. A. Bastedo.*

SALIFORMIN, urotropin salicylate. See *Urotropin.*

SALIGALLOL, the di-salicylate of pyrogallic acid, is a resinous substance, soluble in chloroform or acetone. Kromayer finds that it has but a weak pyrogallol action, but is of value for the preparation of an excellent skin varnish which may serve as a vehicle for other medicaments. "Solutio saligalloli" is a sixty-six-per-cent. solution of saligallol in acetone. *W. A. Bastedo.*

SALINE SOLUTION, NORMAL. See *Hypodermoclysis.*

SALINS-MOÛTIERS. See *Brides-les-Bains.*

SALIPYRIN.—A compound containing 57.7 parts of antipyrin and 42.3 parts of salicylic acid. It is prepared by adding to a boiling aqueous solution of antipyrin a proper molecular proportion of the acid. It forms as a white, coarsely crystalline powder, odorless, with a not unpleasant sweetish taste. It is almost insoluble in water, about one part in two hundred, sparingly soluble in ether, but readily soluble in alcohol. It is decomposed by acids and alkalies.

It possesses antipyretic and antirheumatic properties, and was introduced as a substitute for the salicylates in the treatment of rheumatic affections. It is probably as serviceable as salicylic acid or antipyrin, but is equally inefficient in preventing relapses, and does not seem to offer any special advantage over other remedies for rheumatism. The amount to be given is one drachm and a half, in divided doses, during the day; the first dose being thirty grains and the subsequent doses about fifteen grains each.

As an antipyretic it is not very satisfactory; it requires to be given in doses of thirty grains, to be repeated every hour if necessary. As an analgesic it has proved of value in sciatica, in the pains of myelitis, in neuralgia, and in nervous disease accompanied by pain.

The results of its employment show it to be a harmless and useful drug, but not very reliable. It has not superseded either of its component parts. Profuse perspiration and gastric disturbances frequently follow its employment. *Beaumont Small.*

SALITANNOL, $C_{14}H_{10}O_7$, is a condensation product of salicylic and gallic acids, forming a white, amorphous powder. It is insoluble in water, ether, chloroform, and benzol, slightly soluble in alcohol, and readily soluble in solutions of the caustic alkalies. It is employed surgically as an antiseptic. *W. A. Bastedo.*

SALITHYMOL, $C_6H_3.CH_3.C_3H_7.O.COC_6H_4OH$, is a combination of thymol and salicylic acid somewhat similar to salol. It is obtained by acting with phosphorus trichloride on equimolecular quantities of the sodium compounds of salicylic acid and thymol, and then crystallizing from alcohol. Salithymol is a white crystalline powder of mild sugary taste, very soluble in alcohol and ether, and nearly insoluble in water. Its uses are those of salol, but it is claimed to be preferable, as it sets free thymol in the intestine, while salol liberates phenol. The dose is 0.3–1 gm. (gr. v.–xv.). *W. A. Bastedo.*

SALIVA.—The saliva is formed by the admixture of the secretions of the three pairs of chief salivary glands, viz., the parotid, submaxillary, and sublingual, and of the small buccal glands.

The mechanical and chemical functions of the saliva in connection with deglutition and digestion have already been considered in the articles upon these subjects, and hence the secretion and chemical composition of the fluid only need be taken up in this article.

Secretion.—The three paired salivary glands form typical examples of racemose, tubulo-saccular secreting glands. Each gland possesses a main duct by which the secretion is carried to the mouth. Within the gland this duct divides and subdivides in a racemose fashion, giving rise finally to a large number of minute ductules lined by a single layer of columnar cells. Each ductule, as it passes toward the secreting cells, divides, and the cells lining the secondary ductules so formed become flattened in shape; then each secondary ductule widens to form a tube of secreting cells, which usually possesses branches also lined with similar secreting cells, which may again branch and be lined with secreting cells in similar fashion. Thus a racemose clump of secreting tubules is formed around the end of each ductule. These secreting tubules are termed *alveoli* or *acini*, and are lined by polyhedral cells which surround in a single layer a minute central cavity or *lumen*, into which the secretion is poured when the gland becomes active. This layer of secreting cells is sheathed externally by a thin basement membrane, and lying upon this is a network of fine capillary blood-vessels for the nutrition of the secreting cells. The lymph exuding from this capillary plexus bathes the secreting cells after it has passed through the fine basement membrane, and the cells taking up the lymph, even during periods of rest, transform its constituents into definite chemical substances which are stored up in the cells in such a manner as to be visible under the microscope as minute granules.

When the gland becomes active as a result of stimulation in the natural fashion, two important changes, which have been shown to be independent of each other in their innervation, occur: in the first place, the vaso-dilator fibres supplying the walls of the blood-vessels of the gland are stimulated, so giving rise to an increased blood supply, and hence to an increased flow of water and salts to the secreting cells to serve as a vehicle for carrying off those cell products which have accumulated in the cell during the period of intermission in secretion; in

the second place, the gland cells themselves are directly stimulated by the secreto-motor fibres to a change in activity, as a result of which the granules deposited previously in them undergo a chemical modification which renders them soluble and easily transported through the cell into the lumen of the alveolus. The constituent alveoli are bound loosely into small masses visible to the naked eye, which are termed lobules, and these lobules are divided off from one another, and at the same time united to form the gland mass, by coarser bundles of connective tissue, which unite at the outer surface of the gland to form a capsule, varying in the clearness of its definition in the different glands and in different animals, being usually but ill-defined in the case of the parotid gland.

The secreting cells of the salivary glands when observed under the microscope, either in the fresh state or after the use of hardening and staining reagents, present two distinct types of characteristically different appearance, and each type again shows distinct modifications in appearance according to whether it is observed at a period of fasting (loaded) or during a period immediately following digestive activity (unloaded).

These differences in type correspond to a difference in chemical character of the secretion yielded by the respective cells, for it has been shown that one form of cell secretes the *mucin* of the saliva, while the other secretes the *ptyalin*, which confers upon the saliva of certain mammals, including man, its important chemical action upon the starch of the food. (See *Digestion.*)

The relative extent to which the two cells are developed in the corresponding glands of different animals varies within very wide limits, the same gland being almost completely composed of one type in one animal and of the other type in another. In many cases the same gland contains both types of cells, as is particularly well seen in the human submaxillary gland, and in such a case the different characters of the two types of cell can be studied side by side in the same section. Usually the cells occupying any one alveolus are of the same type, either *mucous* or *serous*; but in the mucous alveoli a third type of cell occurs, lying outside the true mucous cells, between these and the basement membrane. From their position and the pressure applied to them by the concentrically arranged cells of their own alveolus on one hand and the adjacent alveoli on the other, these cells as they develop become crescentic in shape and have hence been termed *demilune* cells.

In a mucous alveolus, the mucin-secreting cells present in hardened sections a perfectly clear, homogeneous, glass-like appearance, except for the nucleus, which is usually shrunken and lies at the broader end of the cell close to the basement membrane. This appearance is, however, an *artifact*, and is due to the action of water, alcohol, or other reagent used in the process of manipulation, upon the cell contents; for these mucous cells when examined in the fresh state, teased out in blood serum, are filled up, provided the gland is in the loaded state, by large granules which are stated to be composed of *mucinogen*, a precursor of the mucin found in the saliva. On the other hand, if the gland has been much stimulated before the mucous cells are taken for examination, it is found, according to the degree of stimulation, that these mucinogen granules may either be few in number and confined to the inner zone of the cell, or may be entirely absent. In the process of secretion, then, the mucinogen granules are dissolved, being converted into soluble mucin, which is carried by the stream of water and salts through the mucous cell toward the lumen of the alveolus, and is thence discharged into the duct. Supporting this view, there is the fact that the viscidity and amount of mucin present in the saliva vary with the amount of these clear cells present in the gland.

Various contentions have been put forward as to the nature and purpose of the demilune cells present alongside the mucous cells in the same alveolus, and present also in glands containing no serous alveoli.

These cells differ strikingly in histological appearance from the mucous cells, especially in hardened and stained sections, being not only different in shape and position, as above described, but also smaller, free from mucin granules, and filled instead in the loaded condition with minute highly refractile granules similar to those present in the serous cells (*vide infra*) and disappearing during secretion.

One view was that they were young mucous cells designed later to be pushed toward the lumen and take the place of mucous cells which had broken down in the process of secretion.

There is, however, no good evidence that the mucous cells are disrupted in the process of discharge; no intermediate stages in the process of conversion of demilunes into mucous cells have ever been demonstrated; and, further, the charged and discharged condition of the demilunes as regards their granules, varying as it does concurrently with the state of the gland, proves that they are functionally active and not immature growing cells.

The view has hence been put forward that these demilunes are really serous cells, occurring in chiefly mucous glands and not differing save in shape from the other serous cells which constitute the chief cells in other alveoli. Their peculiar shape can be explained from their position, while the fact that ptyalin in addition to mucin is also found in the secretion of glands containing otherwise only mucous cells points strongly to the demilunes being serous cells.

The cells of the *serous* or *albuminous* alveoli in the loaded condition are filled with minute highly refractile granules which render the cells opaque, disguise the nuclei, and make it difficult even to discern the cell outlines. When the gland is stimulated to secrete, these granules rapidly decrease in number, the cell outlines become clearly marked, soon the nuclei become visible, and the outer zone of the cell clear of granules, and capable of staining with dyes, while the portion of the cell toward the lumen is still loaded with granules. As secretion is pushed to the extreme limit, this luminal zone, however, becomes smaller and smaller, showing that there is a current of dissolution setting toward the lumen.

The intrinsic ferment of the saliva is yielded by these cells, but it is probable, as in the case of the pancreas (*q. v.*), that the ferment is not deposited in the cells in the form of this ferment in the granular condition, but is instead present in the cells in an inactive form called *ptyalinogen*, from which the free ptyalin is formed as solution of the granules takes place in the act of secretion. In some animals, however, as has been shown in the case of the horse, the active ferment is set free in an unknown manner only in the mouth, and not in the gland itself. For if the parotid saliva of the horse be collected, by means of a fine sterilized glass cannula inserted into Stenson's duct, in sterilized glass vessels, it is quite inactive upon starch solutions, and first becomes active when it is agitated by blowing air through it.

Each salivary gland is innervated along two distinct paths, receiving nerve fibres, on the one hand, from the medulla oblongata by a cranial nerve, and, on the other, fibres from the spinal cord through the cervical sympathetic. These nerve fibres have two distinct functions, some passing to the blood-vessels of the glands and regulating its blood supply, while others are purely secretory in character and pass to the secretory cells of the alveoli. The greater number of the secretory fibres are carried by the cranial nerves and are there accompanied by the vaso-dilators; while a smaller number of secretory fibres, which seem especially to be connected with the secretion of the organic constituents of the saliva, pass to the gland viâ the cervical sympathetic accompanied by the vaso-constrictor fibres to the blood-vessels.

The cranial fibres for the submaxillary and sublingual glands are carried by the *chorda tympani*, which leaves the facial nerve in the Fallopian canal, crosses the tympanum, and then joins the lingual branch of the fifth. The lingual nerve gives off a branch at the posterior border of the submaxillary gland, which contains the majority of the fibres which had joined previously by way of the chorda tympani, and this branch, which consists of a number of strands lying close together, contains most of the secreto- and vaso-motor fibres for the submaxillary and sublingual glands. These strands, often wrongly called the chorda tympani nerve, curve backward along the gland ducts and pass with them into the glands.

The cranial fibres for the parotid gland vary in their course in different animals, but frequently they arise from the ninth cranial nerve and course in the nerve of Jacobson, across the tympanic cavity, over the promontory of the tympanum, and pass viâ the small superficial petrosal and otic ganglion to the auriculo-temporal branch of the fifth, by which they are finally distributed to the parotid gland.

The sympathetic fibres to the salivary glands arise from the spinal cord in the upper dorsal region and run to the superior cervical ganglion, where a relay of nerve cells is interposed, round which the original fibres arising from the spinal cord end in arborizations. From the nerve cells of the superior cervical ganglion other fibres arise, chiefly from the lower and middle portion, and, passing to the external carotid, form plexuses upon it and its branches by which the fibres are ultimately carried to the gland without forming any more nerve-cell connections.

A similar cell station has been demonstrated in the case of the chorda tympani fibres, as lying in the many small ganglia between the point at which the fibres leave the lingual nerve and the various points at which the fibres enter the glands.

These ganglia are as a rule microscopic in size, but two can be seen with the naked eye and have been named, viz., the *sublingual*, lying in the angle between lingual and chorda, which is a cell station for fibres passing to the sublingual; and the *submaxillary*, which lies in the hilus of the submaxillary, and forms a cell station on the path of many of the fibres for that gland.

The position of these various cell stations has been demonstrated by Langley by the injection of small doses of nicotine, which paralyzes the junction between nerve fibre and nerve cell, but does not affect the nerve fibres. Hence the position of a nerve station is shown after injection of this drug into a vein, if no effect is now obtained on stimulating centrally to a ganglion, while an effect is still obtainable peripherally to the ganglion, previous experiment before injection of the drug having given an effect at both places.

Experimenting by this method, Langley has shown that every fibre leaving the spinal cord, whether by cranial nerve or sympathetic, ends somewhere on its course in a peripheral ganglion. Such a fibre is termed a preganglionic fibre. From the peripheral ganglion cell a fibre arises which is termed a postganglionic fibre, and this without further interruption passes to distribution in the gland. There is hence in every case one ganglion cell and no more interposed between spinal cord and gland. The preganglionic fibres are in most cases finely medullated (2 to 4 μ), while the postganglionic fibres are probably all non-medullated.

The effect of stimulation upon the nerves has been most closely studied in the case of the submaxillary nerve, but similar results have been obtained by stimulation of the corresponding nerves in the other glands, so that a description of the occurrences in the case of the submaxillary may be taken to hold for the other two glands. Excitation of the peripheral end of the cranial nerve (chorda tympani) causes, after a very short latent period, a rapid flow of a very dilute saliva, containing a very low percentage of organic constituents. Even weak stimulation produces a copious flow, and secretion can be evoked in this manner for a long period without fatiguing the nerve, so that a quantity amounting to forty or fifty times the weight of the gland can be obtained.

Accompanying this rapid secretion there is a marked vaso-dilatation, so that the gland can be seen to become much pinker to the naked eye, and when placed in a plethysmograph shows a large increase in volume.

That the increased flow of saliva is not, however, solely due to an increased blood supply is demonstrated by the following facts:

1. After administration of atropine, the flow of saliva is no longer obtained, although the vaso-dilatation is as great as before, showing that atropine paralyzes secreto-motor fibres but leaves the vaso-dilators untouched.

2. If the cannula placed in the duct of the salivary gland be connected up to a mercurial manometer, and at the same time the carotid blood pressure be similarly observed by means of a second manometer, it is found that the flow of saliva does not stop until the pressure in the salivary manometer has risen considerably higher than that in the carotid. Now, if the secretion were merely an increased filtration due to increased blood supply, this obviously could not be so, for then the saliva would be filtering from a lower to a higher pressure.

These experiments are sufficient to show that a true secretion is taking place in the alveolar cells, under the stimulating influence of a secreto-motor nervous mechanism distinct from the vaso-dilator mechanism.

The effects of stimulation of the cervical sympathetic upon the gland are very different; there is a vaso-constrictor instead of a vaso-dilator effect, and, after a much longer latent period, there is but a scanty flow of a very viscid saliva much richer in organic constituents.

The amount of flow caused by stimulation of the cervical sympathetic is considerably increased if the cranial nerve has been stimulated a few seconds previously.

Now in the natural stimulation of the gland, as by the sight or thought of food, or by the act of mastication, it is a fairly obvious conclusion that both cranial and sympathetic nerve supplies act upon the gland simultaneously, and hence that there will be conjoined the greater flow of water and inorganic salts caused by the cranial nerve fibres, with the stimulation to increased flow of organic substances effected through the cervical sympathetic fibres.

No saliva flows between periods of stimulation, and it has been observed by inserting a cannula into the duct of Stenson in the horse that a flow of saliva occurs only when it is provoked reflexly, as by mastication.

Cutting the cranial nerve gives rise to the so-called "paralytic secretion," first observed by Claude Bernard; this commences commonly in from two to three days after the section, and lasts for a period of three or four weeks, during which time there is a constant slow secretion accompanied by a great decrease in weight of the gland, which finally becomes functionless. No permanent effect of a like nature follows section of the cervical sympathetic.

It is interesting that a much slighter flow accompanies the paralytic secretion, upon the opposite side where the nerves are quite intact; this peculiar secretion is spoken of as "antilytic secretion."

There is no explanation of either paralytic or antilytic secretion, outside the region of mere hypothesis.

The mouth is probably kept moist in man between the periods of eating by the secretion of the small buccal glands, for it has been shown that the secretion of the large glands completely intermits between the meals in cases of artificial fistulæ of the gland ducts.

In man, the sight or even the thought of appetizing food causes an immediate flow; but secretion cannot be evoked in this fashion in some of the lower animals. Thus presenting meat to a dog in which a parotid fistula has been established does not cause a flow of saliva.

Sapid substances are the most powerful reflex stimulants to secretion when placed either on the tongue or on the mucous membrane of the mouth.

The vapors of chloroform and ether cause a rapid secretion when inhaled by the mouth, as a result of the stimulation of the gustatory nerve endings; when administered by the trachea, they are said not to produce this effect.

Alcohol, or water containing chloroform or ether, applied to the mucous membrane of the mouth, causes a rapid secretion.

The sapid substances produce their effect in the following descending order of strength: (1) acids, (2) neutral and alkaline salts, (3) bitter substances, (4) sweet substances; but the acids (including organic acids) are incomparably more effectual in evoking secretion than the other classes of sapid bodies.

Chemical Composition.—The composition of the mixed saliva is very variable, as can readily be understood when it is considered how many glands contribute to its formation. Sublingual saliva is richest in solids, and may contain as much as three per cent.; submaxillary saliva is stated by most observers to contain a higher percentage of solids than the mixed saliva, while parotid saliva is poorest in solid constituents (0.3 to 0.5 per cent.). The total solids of mixed saliva amount to from 0.5 to 1 per cent., and the specific gravity lies between 1.002 and 1.008.

Mixed human saliva is alkaline to litmus and acid to phenolphthalein, indicating that there is an excess of carbon dioxide present above that necessary to form sodium bicarbonate. This is borne out by the large amount of carbon dioxide obtainable from saliva, which contains more of this gas than either blood serum or venous blood. Thus Külz found in saliva 66.7 volumes of CO_2 per 100, and Pflüger 64.7 to 85.1 volumes per 100. This fact is of interest as showing the large amount of metabolism which occurs in the secreting cells, and lends a further proof, if such were necessary, that the process of secretion is not purely one of filtration and osmosis. The average amount of alkalinity to litmus is equivalent to that of a solution of 0.08 per cent. of Na_2CO_3 (Chittenden and Ely).

The organic matter of the saliva is small in total amount, and is present partially in suspension as formed elements and partially in solution.

The formed elements present include squamous cells from the buccal epithelium, salivary corpuscles, and very pale spherules resembling the granules seen in the mucous salivary cells.

The salivary corpuscles are altered leucocytes derived chiefly from the salivary glands, but possibly the tonsils also contribute to their number. The leucocytes pass from the lymph, between the alveolar cells, into the ductules, and become swollen out by imbibition from the saliva, which has a lower osmotic pressure than the lymph. For the same reason the granules which these corpuscles contain are set in active Brownian movement.

The chief organic substances in solution are mucin, ptyalin, and minute traces of proteid. The mucin can be demonstrated by its precipitation on the addition of acetic acid. The presence and action of ptyalin have been considered in the article on *Digestion*. Coagulable proteid is present only in minute traces. Urea is said to be excreted in the saliva in uræmia, and lactic acid in diabetes.

Saliva normally gives a distinct reaction for sulphocyanides when a very dilute solution of ferric chloride is added to it. The test is best carried out by wetting filter paper with ferric chloride so dilute as scarcely to color it, and then adding the saliva, when a red color is obtained. Sulphocyanates are, however, absent in certain individuals, and in the same individual are present at certain times and absent at others.

The inorganic salts present consist chiefly of chlorides, phosphates, and carbonates of the alkalies and alkaline earths, the chief constituent as usual being sodium chloride. The most interesting of the inorganic constituents is calcium bicarbonate; it is this salt which gives rise to the cloudiness observed when saliva is allowed to stand for some time. The precipitation is due to the escape of the excess of carbon dioxide, which had previously held the calcium carbonate in solution. A certain amount of calcium phosphate is similarly precipitated. Such a precipitation occasionally leads to occlusion of the gland ducts by the formation in these of salivary concretions, which consist of a mixture of calcium carbonate and calcium phosphate. When the precipitation occurs on the teeth it is termed tartar; this also contains silica in addition to the calcium salts mentioned above.

Benjamin Moore.

SALIVARY GLANDS AND THEIR DUCTS, DISEASES OF.—*Increased Secretion of the Salivary Glands* (Ptyalism; Salivation).—The normal amount of salivary secretion is from one to three quarts in twenty-four hours, though under exceptional conditions the quantity may be as much as five quarts. While food is being taken the saliva is normally greatly increased, which may also occur during the menstrual period and during gestation. Salivation, likewise, occurs in connection with quite a number of different diseases, such as acute fevers, diseases of the liver, spleen, genital organs, and pancreas, and in all inflammatory conditions of the oral cavity. It is likewise sometimes seen in bulbar paralysis, in diabetes, and in melancholia. Quite a number of drugs are also capable of giving rise to an increased salivary secretion, among which are muscarin, tobacco, pilocarpine, potassium iodide, the salts of arsenic and copper, and mercury and its various compounds. Of all the causes the last mentioned is the one that most frequently occasions the condition, and it is true that the amount necessary to produce this result varies very greatly in different instances — some individuals tolerating large quantities of the drug, while others are affected by very minute doses.

(For the treatment see article on *Mouth, Diseases of*, in THE APPENDIX.)

Decreased Secretion of the Salivary Glands (Xerostomia; Dry Mouth).—The secretions of the salivary and buccal glands may be greatly diminished, or, in some instances, entirely suppressed. The condition is most commonly observed in nervous women, though it is occasionally seen in men as well; it may follow shock or may occur in connection with diabetes and febrile states. As a natural consequence of the arrest of the secretion the tongue and mucous membranes of the cheeks and palate become dry, and mastication and articulation are exceedingly difficult. Osler speaks of a case observed by him in which, on account of the absence of the normal secretion of the mouth, food collected along the gums and became exceedingly hard, presenting somewhat the appearance of a new growth in the oral cavity of the patient; in this instance the affection was cured in about three weeks by the application of the galvanic current.

Treatment. For dry mouth pilocarpine may be used, and, as in the case above cited, electricity may be employed with advantage. Oils applied to the mucous membrane of the mouth are of service in ameliorating the very disagreeable dry state of the oral mucous membrane. The condition is very obstinate.

INFLAMMATION OF THE SALIVARY GLANDS.—There are several distinct and separate varieties of inflammations of the salivary glands at present recognized, and there can be no question but that, as our knowledge increases, many conditions which are at present regarded as being identical will be found to be the result of causes differing widely from each other. There are specific parotitis (see *Mumps*), symptomatic parotitis, and chronic parotitis.

Symptomatic Parotitis.—Symptomatic parotitis is an affection that occurs in connection with a large number of different diseases, though the relationship between inflammations of the glands and the causes that apparently determine them are exceedingly obscure. The condition occurs most commonly during the course of the infectious fevers, such as typhoid, typhus, scarlet fever, rheumatism, pneumonia, peritonitis, pyæmia, septicæmia, and syphilis, but it is also sometimes seen in connection with consumption and gout. When the affection results from acute fevers, the inflammatory phenomena are quite severe, and, as a rule, suppuration results. If the pus be not evacuated by surgical means, it not uncommonly burrows into the tissues of the face to a considerable distance. Inflammations of these glands likewise very curiously often follow laparotomy, and operations upon the genital organs in both men and women. It has also been found associated with facial paralysis, and may occur during pregnancy or follow menstruation.