Calculi composed of *fibrin*, *blood*, or *inspissated albumin* are mentioned as having been met with in urine. They have a glassy fracture. Their occurrence must be regarded not only as unusual, but as anomalous.

In the description of the various urinary concretions very little has been said of the formation of mixed calculi. As a matter of fact, calculi are not commonly composed of a single constituent. The location of their formation and growth and the attending conditions upon which their formation depends so change from time to time that different substances enter into their structure, and the result is the formation of mixed calculi. Uric acid and calcium oxalate most frequently form calculi consisting exclusively of one ingredient; on the other hand, calculi composed of separate and alternating layers of these two substances are the most common example of the so-called "alternating" calculus.

The different deposits may be primary, primary and secondary, or secondary. They almost invariably have a central nucleus, while the substance of the calculus, the body, may be surrounded by an external layer or crust which is nearly always phosphatic. The nucleus varies in composition and in size. It may not differ from the body, especially in primary calculi, and on the other hand may even consist of bits of tissue, as blood clots, epithelium, or inspissated mucus. Exceptionally, foreign bodies which have found their way into the bladder become nuclei (Fig. 1485). A calculus was recently observed in which the nucleus was a snake's tail which a patient had been advised to pass into his urethra for the cure of a stiffened right arm. A form of mixed calculus that is very common is the phosphatic concretion that results from ammoniacal urine. A primary calculus, entering the bladder, or exceptionally forming within this organ, there produces such vesical irritation as eventually to give rise to cystitis with ammoniacal fermentation of the urine leading to the deposit of phosphate upon the primary formation.

Fig. 1485.—Pin Forming the Nucleus of a Calculus Composed of Calcium Phosphate, Uric Acid, and Dried Blood. (Natural size.)

Examination of Urinary Calculi.—Before proceeding to the analysis it is always well to record the color, hardness, appearance on section or fracture, and perhaps the specific gravity of the specimen. The appearance of a powdered or fractured portion under the microscope may also be of value. In the case of mixed calculi, each layer should be examined independently. The chemical analysis may be conducted as follows:

Heat a small portion of the powder on porcelain or platinum.

A. The material burns away, leaving little or no residue.

1. It melts, burns with a smoky flame, emitting an aromatic odor. It is soluble in ether, the ether leaving a fatty residue on evaporation. It is soluble in potassium hydroxide. *Urostealith.*

2. It gives off purple-red vapor. The material is soluble in sulphuric acid with the formation of a blue color, the solution showing a band before D in the spectroscope. *Indigo.*

3. It gives the odor of burning feathers. The material responds to tests for proteids: *e.g.*, Millon's, xantho-protein. *Albumin, fibrin, blood.*

4. A fresh portion, when treated with hydrochloric acid, dissolves completely.

(*a*) Also soluble in ammonia. Filtration and evaporation to remove ammonia produce a separation of hexagonal crystals. These may also be obtained by acidifying the ammoniacal solution with acetic acid. *Cystin.*

(*b*) Dissolve a fresh portion in nitric acid, evaporate to dryness in a porcelain dish over a water bath, moisten yellow residue when cool with potassium hydroxide, and an orange-red color is produced which becomes reddish violet when heated. *Xanthin.*

5. A fresh portion, when treated with hydrochloric acid, does not dissolve completely. Filter and test the filtrate as described under 4.

(*c*) After washing the residue on the filter, dissolve in nitric acid and evaporate to dryness. The yellow residue turns red when exposed to the vapor of ammonia, and the addition of potassium hydroxide produces a bluish-violet color which disappears on standing. *Uric acid.*

(*d*) In addition to the test for uric acid, the fresh material gives reactions for ammonia, *e.g.*, when heated in solution with potassium hydroxide, ammonia fumes are given off as recognized by the smell, bluing of red litmus, and production of white fumes with a rod moistened with hydrochloric acid. *Ammonium urate.*

B. The material may or may not blacken and leaves a considerable residue.

6. The original material dissolves completely in hydrochloric acid.

(*e*) With effervescence. The solution made alkaline with ammonia yields a white precipitate on the addition of ammonium oxalate. *Calcium carbonate.*

(*f*) Without effervescence.

(1) The ignition residue, treated with water, dissolves in part to a strongly alkaline solution and dissolves wholly in acetic acid with effervescence. Addition of ammonium oxalate to this acetic-acid solution produces a white precipitate. *Calcium oxalate.*

(2) The ignition residue, treated with water, does not dissolve in part to a strongly alkaline solution. It dissolves in acetic acid without effervescence. If the nitric acid solution of the original material is added to an excess of ammonium molybdate solution in nitric acid a yellow precipitate is formed when the mixture is warmed. *Phosphate.*

The solution in acetic acid obtained above or of the original material yields a white precipitate on the addition of ammonium oxalate. *Calcium phosphate.*

The filtrate from the calcium oxalate yields a precipitate when rendered alkaline with ammonia. The original material, when moistened with potassium hydroxide, does not give reactions for ammonia. *Calcium and magnesium phosphate.*

The above reaction for ammonia is strongly positive and magnesium is present. *Ammonio-magnesium phosphate* (triple phosphate). If calcium is present as well there is an admixture of calcium phosphate.

7. The original material does not dissolve completely in hydrochloric acid.

Uric acid is present and may be tested for in the residue by the murexide test described in 5 (*c*). When a platinum wire is moistened with the hydrochloric acid solution and then introduced into a Bunsen flame, a yellow coloration of the flame is produced owing to the presence of sodium. *Sodium urate.* Traces of potassium urate and even the ammonium, calcium, or magnesium salt may be present.

(Note.—The application of the foregoing scheme to the analysis of mixed calculi may call for such slight modifications of the procedure as will be apparent.)

E. E. Smith.

CONDURANGO.—The bark of *Marsdenia Condurango* Nicholson, syn., *Gonolobus Condurango* Triana (fam. *Asclepiadaceæ*). This plant is a medium-sized, milky-juiced, woody twiner of Ecuador and neighboring parts of South America. The bark was introduced as a specific for cancer, due apparently to the loose application of this term, in South America, to various minor ailments. Its trial resulted in disappointment, notwithstanding that it produces some favorable results as an alterative, in cancerous as in other diseases. Besides containing a considerable amount of resin, *condurangin* has been described as an amorphous, yellowish glucoside. This is now believed to consist of a mixture of two or more glucosides, which are similar in action, producing incoordination and loss of movement. Their therapeutical application has not been demonstrated. They are soluble in both water and alcohol. Condurango is an excellent stomachic, though only mildly bitter. Weak alcohol is the best menstruum. The average dose is 2 gm. (gr. xxx.).

Henry H. Rusby.

CONDYLOMA.—Condyloma is defined by Unna as "a pure acanthoma, appearing isolated around the mucous openings and on moist and seborrhoeic areas of skin, and tending to extend superficially." The word is here used in this limited sense, and indicates only those growths known as condyloma acuminatum. It thus becomes the name of a distinct pathological formation. The employment of the same word to designate certain syphilitic lesions (condyloma latum) is to be discouraged, except when it is properly qualified. The careful study of the histogenesis and histology of condylomata has demonstrated the incorrectness of employing papilloma as a synonym for condyloma. The formation is not a papilloma proper, the papillæ being secondarily altered by the proliferating epithelium. In the following description we have adhered quite closely to that given by Unna as representing the results of the most recent and reliable study. The growth begins as a small elevation, which later may become divided by furrows and depressions, giving when extreme a cauliflower appearance. They are usually located upon the external genitalia in either sex, or about the anus, and most often follow a chronic irritation from an inflammation of the urethra, ulcers, decomposition of the preputial secretion, etc. Bumm demonstrated that the previous idea that the gonococcus was the essential etiological agent was incorrect. He showed that they occur without gonococci being present. Kranz had apparently demonstrated the possibility of transferring portions of the lesion or its secretion with a subsequent development of condylomata at the site of introduction. This has been denied by Petters and Güntz, and they have been sustained by the experimental results of E. Bumm. Bumm found that long-continued chemical or mechanical irritation may cause the lesions, but insists upon the necessity of a predisposition being present also. If a specific agent is present, its nature is still unknown. The growth tends to extend locally by direct extension, especially in a serpiginous manner, following the folds where surfaces come in contact. In this way large tumor masses are produced, which show no tendency to become limited or to disappear spontaneously. The skin upon which they develop is usually previously altered by suppuration, eczema, seborrhœa, etc. The color depends upon the tissue where they are found during the early stage. Upon the skin they are yellowish-white, upon mucous membranes red. Later the degree of cornification determines the color, the red condyloma upon a mucous membrane becoming yellow.

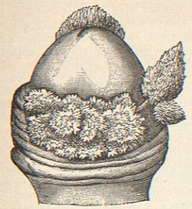

Fig. 1486.—Pointed Condylomata upon the Prepuce and Glans Penis. (After Grünfeld.)

Unna distinguishes two histological stages. In the first there is a patchy thickening of the epithelium, with a depression and flattening of the underlying papillæ. There then becomes apparent, as a very fine point macroscopically, a button-like projection of epithelium. The growing epithelial ridges do not penetrate deeply nor depress the base of the papillary body, but they are rather elevated by the papillary body which becomes more and more swollen. The surface elevation is at first mostly dependent upon swelling of the cutis, but later the epithelium is greatly in excess. While the elevation and growth in size are due in part to changes in the connective tissue, the epithelium alone is active in the formation of the lesion. Differences in resistance at various points in the cutis are factors in determining the form of the growth, but this is only in a passive way. Many minute elevations occurring at the same time cause the surface to appear finely granular.

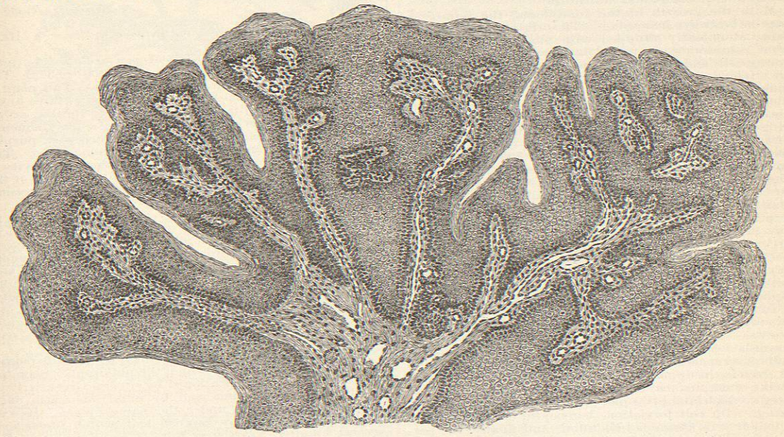

Fig. 1487.—Longitudinal Section of a Non-Specific Condyloma, Consisting of a Primary and Several Secondary Papillæ. The three layers—the horny, the epithelial, and the fibrous with its blood-vessels and lymph channels—are also represented. At the centre of the middle papilla and at the upper extremity of that to its right are seen transverse sections of the fibrous layer of tertiary papillæ arising from them. (From an original drawing by Dr. James M. French. Magnified about four hundred diameters and reduced.)

In the second stage the growth is either a cauliflower or finger-and-toe shape, or in the form of simple buttons. At this time the epithelium proliferates very luxuriantly, mitosis is found not only in the basal layer of the prickle cells, but even in the fourth, fifth, or sixth epithelial row. The prickle cells are much enlarged, some being four or even eight times the size of those in the neighborhood. There is great dilatation of the lymph spaces between the prickle cells, and the connecting bridges of the cells are unusually well developed. When the lymph spaces of the epithelium are very wide, the prickles connecting the epithelial cells may be drawn out to long threads, which may connect cells lying some distance apart and otherwise disconnected.

Everything indicates an exceptionally luxuriant nutrition of epithelium and a growth of the prickle layer in all directions from abnormally numerous points. The granular layer is broad, associated with delayed cornification. The horny layer is of normal thickness or only moderately thickened. There is no hyperkeratosis. The connective tissue is rich in blood and lymph, and penetrated by wide vessels and lymph spaces. The capillaries of the papillæ are sometimes as large as cutaneous veins and pass to the free ends of the papillæ. Nets of fibrin and fibrinous lumps with much granular fibrin are found in the wide lymph spaces, and the connective tissue is sometimes penetrated by fine fibrin threads. In the connective tissue there are found an excess of spindle cells, and an abnormal number of leucocytes, which wander into the epithelium. The action of caustics, etc., may be followed by a more extensive accumulation of leucocytes. Mast cells are always found in the newly formed connective tissue in considerable numbers, rather round in form than elongated, but large and multiform.

With the growth of the condyloma, the number of papillæ is always increasing. The original main papillæ, being abundantly supplied with blood and lymph, become considerably increased in size by the formation of young cells and the emigration of leucocytes. They also are divided by the ingrowing folds of epithelium, and thus the number of papillæ becomes increased. There is never, however, an independent growth of papillæ into the epithelium, as the name "papilloma" suggests. The irregular formation of condyloma is finally due to the succulence and marked swelling of the connective tissue and of the uncornified epithelium. The direction of growth is not limited, but is unlimited in all directions. The external form varies as widely as its internal structure. Rarely the horny layer is firm enough to form a continuous covering for the swelling, and a mushroom or pear-form results. More often the horny layer gives way, and after penetrating into the divisions between the larger main papillæ, it falls off, leaving the finger-and-toe form. If the horny covering of these again gives way, and the horny layer penetrates into the younger epithelial buds and between some of the newly furrowed papillæ, a cauliflower surface is the result.

Unna gives as the characteristics by which the condyloma may always be distinguished from verruca vulgaris as follows: "The thin horny covering and absence of hyperkeratosis; the remarkable size of the prickle cells and the interspinal spaces; the numerous and ever-present mitoses, even in the upper prickle layers; the complicated furrowing of the surface; the constant active dilatation of the vessels, which later gives place to a regular chronic inflammation, with cell formation, leucocytic emigration, and abundant sero-fibrinous exudation; and finally, the persistent papillary furrowing by the growing epithelium."

Treatment.—If the irritant acting upon the involved surface is removed, and the parts kept dry, or an astringent is applied, the smaller lesions may disappear without further treatment. The further means to employ for their removal are excision, erosion, or caustics (nitrate of silver, alkalies, acids, etc.). For larger growths, ligature of the pedicle may be required. Removal by the Paquelin cautery is followed by an eschar, which protects the surface and prevents hemorrhage. The electric needle is also useful at times. *George H. Weaver.*

CONIFERÆ.—*The Cone Family.* (*Pine Family*, in the broad sense. According to some authors, and probably correctly, it is subdivided into the *Pinaceæ* and *Taxaceæ*, but, for convenience, we here follow Engler and Prantl, in considering both under the title *Coniferæ*.) The family contains between thirty and forty living genera, and ten times as many species, besides a number of fossils. They grow mostly in temperate climes, especially the northern. Probably no other family is of greater interest. These trees represent a flora for the most part extinct, and are closely related to those which produced our coal. They are not so well adapted to present conditions as most plants, and their tenure of life may be regarded as on the whole weak, and themselves destined, for the most part, to early extinction. The largest known trees are members of this family. They yield almost all of our soft building lumber. They yield our vegetable tars, pitches, and turpentines, though apparently some of the trees yielding these will be practically extinct within a few years. Through extinct relatives, their relations to coal tar explain the close similarity between the two classes of products. The seeds of a number constitute important foods. Medicinally the family is of great importance, being very rich in volatile oils, of which those of juniper, cedar, turpentine, savin, cypress, and others, are important drugs. Empyreumatic oils similarly used are represented by those of tar and cade. Amaroids, glucosides, and at least one alkaloid, with an abundance of tannin, also occur. Because of the close similarity in nature and properties between these products, only the most important are treated in this work. The number of pines, spruces, firs, larches, cedars, and related plants in use is very great. *Henry H. Rusby.*

CONIUM.—Conium Fruit (incorrectly "*Seed*"). Hemlock. *Poison Hemlock.*

"The full-grown fruit of *Conium maculatum* L. (fam. *Umbelliferæ*) gathered while yet green" (U. S. P.). The leaves, formerly official, are no longer so. This plant is a stout, erect, biennial herb a metre or more (three to six feet) in height, with a long, simple or forked, rather fleshy, yellowish-white root 2 cm. or so in diameter, and a smooth, branching, striated or furrowed, purple-spotted, dark-green, hollow, slightly glaucous stem. The spots are small and rather numerous; the pith cavity is closed at the joints of the stem. The characters of the leaves and white flowers are well displayed in the accompanying cut.

Hemlock is a common Old-World plant, occurring in the temperate portions of Europe, Asia, and even Africa. It is also rather common in many places, as an introduced weed, in the United States. It affects rich and moist waste places, especially swamps and brook-sides and damp and shady gardens. It is easily distinguished from most harmless *Umbelliferæ* by its spotted stem, short, thick, disagreeable-smelling fruits, and the absence of oil-bearing vittæ in the latter. Cicuta (see *Poisonous Plants*) is very easily mistaken for it, but both are similarly poisonous.

Conium is notorious as an ingredient of the state poison of the ancient Greeks, by which the philosopher Socrates met his death. It is mentioned by several Greek writers of about the same time, and by numerous Latin ones since—by these often under the name *Cicuta*. It was used as a medicine by English and Scotch physicians several hundred years ago, but its employment under modern ideas of medicine dates from the time of Stoercke, about seventy-five years since. The use of the term *Cicuta* as the name of the hemlock by Latin authors has created some confusion, which was not diminished by Linnæus when he gave the latter name to the related genus.

All parts of hemlock are active, and have been employed in medicine. The drug should be carefully and quickly dried, without heat. As the active principles are volatile, conium deteriorates rapidly, and should be considered inferior if more than one season old. The intensity of odor developed by moistening it, and especially by treating with potash, is a rough way of estimating its value. The leaves are especially unstable; their odor, when fresh and green, is strong and disagreeable, and developed still more so by the potash; when dry they often have no strength or value. The fruits are alone

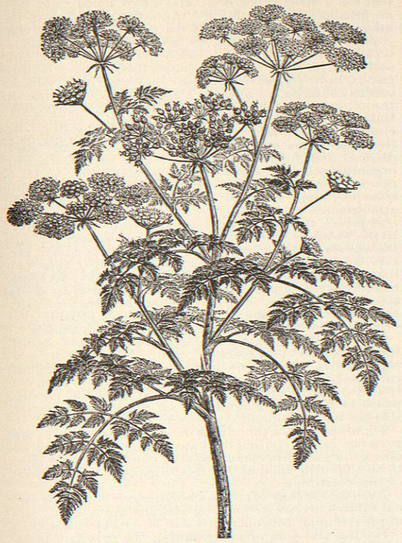

Fig. 1488.—Conium maculatum L.

official in the United States, the dried leaves having proved to be generally worthless in this country. They are thus described in the Pharmacopœia: "About one-eighth of an inch (3 mm.) long; broadly ovate; laterally compressed; grayish green; often divided into the two mericarps, each with five crenate ribs, without oil tubes, and containing a seed which is grooved on the face; odor and taste slight." They hold their strength comparatively well, and yield, on the whole, more uniform preparations than even the fresh leaves.

Composition.—Conium contains but very little *essential oil* compared with the aromatic members of the order, and that little is neither pleasant nor useful. Its most important constituents are two or three closely related alkaloids.

The most important of these in quantity and activity is coniine, also called conicine and cicutine, which in the plant exists combined with one of the common vegetable acids, probably malic, to the extent of about one-fifth to one-half per cent. in the fruit. The leaves contain much less. It is a strongly basic, colorless, oily liquid, of penetrating odor, closely resembling that of urine or the nests of mice, and a sharp, burning, tobacco-like taste. It is volatile at ordinary temperatures, and boils at 166° to 166.5° C. *In vacuo* it can be redistilled without change, but in the air a portion is decomposed. It becomes thicker and yellow upon prolonged exposure, and, finally, resinous looking. Specific gravity, 0.88. Chemical composition, $C_8H_{17}NH$, CH_3, CH_2, CH_3. It is freely soluble in alcohol, chloroform, the essential oils, etc., but only to the extent of one per cent. in water. It, on the other hand, dissolves in from twenty to thirty per cent. of cold water, which may be separated by heating. It unites with acids, forming neutral salts, which are often crystallizable. That most used is the hydrobromate, in white needles, soluble in two parts of water or of alcohol. Complete purification of coniine is difficult to accomplish.

The second alkaloid, *conhydrine* or oxyconiine, is solid and concretes in the head and tube of the retort in pearly, iridescent, white, foliaceous crystals. It has a faint, conium-like odor, melts at 118° to 121° C., and boils at 220° to 225° C. It is soluble in alcohol and slightly so in water. Conhydrine can be converted into coniine by abstracting the elements of water with phosphoric anhydride. The proportion of conhydrine in conium is much less than that of coniine. Methyl coniine is usually present in commercial coniine and is probably a constituent of the drug itself. The coniine of the market is also apt to contain some pseudo-conhydrine dissolved in it, which can be separated by freezing. This is white, crystalline, soluble in alcohol and water.

The physical properties of coniine and conhydrine are very nearly those of an essential oil and its camphor.

Action and Use.—The action of conium may be regarded as entirely that of coniine; conhydrine and methyl conine, besides their smaller proportion, are physiologically only coniine reduced; the oil and other constituents (vegetable acids, etc.) amount to nothing.

It is very difficult to interpret and harmonize the phenomena attending the action of coniine. Pharmacologists are not agreed as to the mode of their production, and they will be considered here only in their practical bearing. The drug is promptly absorbed from the stomach, very slightly if at all locally, circulates as coniine, and is rapidly excreted through the kidney. It is a nauseating depressant, the effect varying in degree from slight languor and weakness, through nausea, salivation, weak perspiration, vomiting, great muscular weakness, results in general similar to sea-sickness, up to complete collapse and death by respiratory failure, after preliminary stimulation. There is dilatation of the pupil, perhaps after temporary contraction, especially upon local application. There are evidences of vaso-motor depression. There is slight depression of the cardiac ganglia. There may be temporary and slight tremors and muscular twitchings, though the later, and strictly speaking physiological effect is opposed to these, destroying them when they already exist. There is little disturbance of sensation proper, and intelligence is little or not at all affected. The one important element is depression, or paralysis of the motor nerve endings. There is apparently, at first, central stimulation, followed by depression, beginning below and passing upward. The peripheral paralysis referred to also apparently proceeds gradually along the nerve trunks. The best authorities agree that conium has failed in nearly all the therapeutic uses to which it has been put. Most of these uses have centred about the theory that it relieves pain, in spite of its failure to affect sensory nerves. The fact is that when pain is kept up through muscular twitchings, commonly themselves induced by existing pain, conium prevents this aggravation by cutting these movements short. In any case, this appears the only use for which it can be recommended.

In administering conium, it is most important that the nature of its constituents be remembered. Coniine, the most important, is volatile, so that careless manufacture is destructive to activity. Long exposure to the air also induces destructive changes. The greatest care should thus be taken in selecting preparations, and only those which are assayed should be accepted. Conium and its fluid extract should contain 0.5 per cent. of total alkaloid, the extract 2.5 per cent. The Pharmacopœia supplies an extract, the dose of which is 0.02–0.06 gm. (gr. ⅓–i.), and a fluid extract, the dose ♏ i.–v. *Henry H. Rusby.*