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Ustilago.—Ustilago. *Ustilago maydis* Leveillé (Nat. Ord. *Fungi*) grows upon *Zea mays* Linné (Nat. Ord. *Graminaceæ*). (U. S. P.)

Extractum Ustilaginis Maydis Fluidum.—Fluid extract of ustilago. Dose, ℥ x—ʒ j.

COMPOSITION.—No proper investigation has yet been made of the chemical constitution of ustilago. Some of the ingredients found in ergot have been detected, as *secaline* so called, and *trimethylamine*; but the latter is regarded by others as a decomposition product and not existing preformed. Besides other substances, Parsons has separated an acid, which he regards as similar to the *sclerotic acid* of Dragen-dorff, and a substance soluble in ether but not in alcohol.

PHYSIOLOGICAL ACTIONS.—Ustilago has been made the subject of physiological investigation by Mr. (now Dr.) Ripley C. Hoffman, of Iowa, in the laboratory of experimental therapeutics of Jefferson Medical College, under the supervision of the author. The research embraced cold- and warm-blooded animals. The preparation used was the fluid extract, made by John Wyeth and Brother, of Philadelphia, and it proved to be quite active. Both in cold- and warm-blooded animals, ustilago acts as a spinal excitant, causing convulsions of a tonic character. It also heightens sensibility and the reflex function, so that the least irritation of the skin induces general tonic convulsions of the tetanic or strychnic character. Frequent irritation and repeated convulsions rapidly exhaust the animal. On the other hand, quiet, darkness, and relief from all irritation, diminish the severity of the convulsions, and prolong life, if not prevent a fatal result. Death may ensue in a convulsion by tetanus of the respiratory muscles. Muscular tremors, general, occur in warm-blooded animals, and muscular weakness (paresis) appears in the intervals between the convulsions. The irritability of the motor nerves, and toward the end, of the sensory nerves also, declines, but is not entirely lost, and the contractility of the muscles lessens somewhat. That the convulsions are spinal, is a fact proved by destroying the cord in a frog, before admin-

istering the medicament, when no muscular action of any kind takes place. Section of the medulla or decapitation does not prevent the occurrence of the convulsions.

Ustilago slows the heart, and by numerous control experiments this action was shown to be due to stimulation of the pneumogastric and its terminal ganglia. It dilates the pupil, and affects the acuteness of vision for near objects.

We have no exact data in regard to the action of this agent on the uterine system. An impregnated cat, dying by a merely lethal dose slowly, did not abort; but it is said that pregnant cows and bitches, after eating ustilago, have dropped their young.

The modes of dying are two: in the tetanus; by exhaustion. In the former, the respiration is arrested, violent tonic extension of the voluntary muscles takes place, the head being drawn back, the toes incurved. In the latter, there is gradually increasing paresis between the convulsions, and slowing of the heart's action. The difference is largely due to the dose and rapidity of administration. A lethal dose for a rabbit weighing 25 ounces seems to be one drachm of the fluid extract.

THERAPY.—If Dr. Hoffman's study of the action of the fluid extract be confirmed by others, ustilago must occupy an important position as a remedy, possessing as it apparently does the powers of nux-vomica and of ergot combined. It is indicated in the several groups of cases to the treatment of which these remedies are now applied.

Digitalis.—The leaves of *Digitalis purpurea* Linné (Nat. Ord. *Scrophulariaceæ*), from plants of the second year's growth. (U. S. P.) *Feuilles de digitale*, Fr.; *Fingerhutblätter*, Ger.

Abstractum Digitalis.—Abstract of digitalis. Dose, gr. ss—gr. j.

Infusum Digitalis.—Infusion of digitalis contains 3 parts each of digitalis and cinnamon, infused in boiling water; after two hours maceration is strained; then 15 parts of alcohol added, and finally sufficient water to make up to 200 parts. Dose, ʒ ij—ʒ ss.

Extractum Digitalis Fluidum.—Fluid extract of digitalis. Dose, ℥ j—℥ iij.

Extractum Digitalis.—Extract of digitalis. Dose, gr. ss—grs. ij.

Tinctura Digitalis.—Tincture of digitalis. Dose, ℥ v—ʒ j.

COMPOSITION.—Digitalis contains an active principle, *digitaline*. This exists in the amorphous and crystalline form. The amorphous form—the digitaline of Homolle and Quévenne—possesses considerable activity, and, according to some authorities, is quite equal to the crystalline in strength. The crystalline digitaline (Nativelle's digitaline), physiological investigations have shown, is really an active principle which represents all of the powers of the drug. This occurs in needle-shaped crystals, and has an extremely bitter taste.

According to Schmiedeberg, digitalis contains *digitonine*, which strongly resembles saponine; *digitaline*, which is insoluble in water, and is the chief constituent of Homolle and Quévenne's digitaline; *digitaleïn*, which is readily soluble and has the same action as German digitaline; *digitoxine*, the most powerful, and is the principal constituent in Nativelle's digitaline. Koppe has examined the action of digitaline, digitaleïn, and digitoxine, and finds that they agree in their action, and with the crude drug, but differ in degree of activity.

Digitalinum.—Digitaline. A white, or yellowish-white powder, without odor, and having a very bitter taste. Dose, $\frac{1}{60}$ — $\frac{1}{30}$ of a grain.

ANTAGONISTS AND INCOMPATIBLES.—The cinchona preparations, acetate of lead, the sulphate and tincture of the chloride of iron, are chemically incompatible. Tannic acid and the preparations containing it diminish the physiological activity of digitalis. Opium, aconite, lobelia, and the cardiac paralyzers, antagonize some of the actions of digitalis, but the antagonism does not extend throughout the whole range of their influence. The most complete physiological antagonism exists between digitalis and saponine (Köhler), the active principle of *Saponaria officinalis*, closely allied to *senegine*. Aconite antagonizes the cardiac action of digitalis, and morphine, also, to a less degree.

SYNERGISTS.—Cold, ergot, belladonna, increase the physiological activity of digitalis.

PHYSIOLOGICAL ACTION.—Digitalis has a disagreeable, bitter taste. In considerable doses, of the infusion, for example, it disturbs the stomach and gives rise to nausea and vomiting, and frequently purges. Loss of appetite results from its medicinal administration in some subjects, even when the quantity is small; but, in others, the appetite is increased. The active constituents of digitalis diffuse into the blood, but nothing is definitely known as to the action of this agent on the composition of the blood, or the influence which it has, if any, on the morphological elements.

On the heart digitalis exerts a peculiar action which requires attentive examination: it prolongs the *diastole* and increases the vigor of the *systole*. A lethal dose arrests the heart in systole, inducing a tetanic state of the heart-muscle. While digitalis increases the power of the systole, the diastole is prolonged, hence the number of pulsations per minute is reduced. With ordinary medicinal doses this slowing of the heart may be considerable, and the pulsations may descend to fifty or even forty per minute. Microscopic examination of the mesentery (Ackermann) and of the web of the frog has definitely ascertained that a marked contraction of the arterioles takes place under the influence of digitalis. The increased power of the systolic contraction of the heart and the greatly-increased resistance in front from a narrow-

ing of the caliber of the vessels produce, as might *a priori* be expected, a considerable rise of the blood-pressure. When the pulse is greatly reduced by the administration of large medicinal doses, a change from the recumbent to the upright posture causes a remarkable increase in the number, and diminution in the force, of the cardiac pulsations. When lethal doses, short of a sudden toxic effect, have been experimentally administered, the slowing of the heart and rise of arterial tension first produced are succeeded by a quick, feeble pulse, and fall in the blood-pressure. These results are obviously due to the loss of power (paresis) which results from over-stimulation.

A temporary rise of temperature follows the administration of a lethal dose of digitalis, but this rise is soon succeeded by a marked and sustained reduction. Owing to the increased resistance from diminution of the caliber of the arterioles, the actual energy expended by the heart is in part converted into heat. Subsequently the slowing of the circulation, especially through the lungs (Traube), hinders the combustion process, and hence the fall of temperature.

Digitalis in full medicinal doses produces headache, a band-like feeling around the forehead, dizziness, disturbances of vision (mistiness, vibratory movements of external objects, chromatic dispersion, etc.), drowsiness, languor, and a sense of weariness, and it may even cause hallucinations, illusion, and delirium. Digitalis lessens the reflex function of the cord, lowers the sensibility of the nerves, motor and sensory, and impairs the electro-contractility of muscles; but these effects are not produced by medicinal doses, but are toxic in character.

As might be anticipated from a study of its physiological actions, digitalis acts like ergot on the enlarged uterus; it stimulates to energetic contraction the muscular fibers, and in this way arrests uterine hæmorrhage. On the genital organs of man it has a similar action; by diminishing the blood-supply to the erectile tissue it lessens the power of erections, and, secondarily, affects the venereal appetite, producing anaphrodisia.

Considerable difference of opinion exists as to the influence of digitalis on the function of nutrition—the metamorphosis of tissue. By some an increase in the production of urea, by others a diminution, has been noted. The truth, most probably, is that it has no real influence on urea formation, and that the variations observed are accidental. The phosphoric acid and chlorides are diminished. In health digitalis affects but little the water of the urinary secretion; according to some the water is diminished, according to others increased. It is difficult to reconcile these opposing statements, in view of the fact which has recently been ascertained by Brunton, that the diuretic action of digitalis in dropsy is not due to the increased blood-pressure, but to a special action on the Malpighian tufts.

THERAPY.—Before entering on the therapeutical applications of

digitalis, there are several practical points with regard to the quality of the drug which require attention. Disappointment in the use of digitalis is frequently experienced, in consequence of the inferior quality of the drug prescribed. The wild digitalis is better than the cultivated. In this country much of the digitalis found in the shops is the plant cultivated and put up by the Shakers. It is very uncertain, and, according to the author's observation, usually inert. The English digitalis, and the preparations made from it, should alone be prescribed.

Digitalis has an undoubted power to arrest hæmorrhage (Leyden). The mechanism of its action is similar to that of ergot; it slows the action of the heart and contracts the arterioles. In hæmoptysis it is especially useful in the following state of things: frequent expectorations of bloody mucus, with occasionally a mouthful of florid blood, accompanied by fever. This group of symptoms is dependent on transudation from a number of small vessels about the site of a pneumonia due to a tubercular or caseous deposition. The same kind of expectoration, due to pulmonary congestion from mitral regurgitation, is amenable to the same treatment. In uterine hæmorrhage digitalis is also serviceable, but it is more especially indicated in menorrhagia and metrorrhagia of plethoric subjects. Like ergot, digitalis has the power to induce uterine contractions, and hence it has been used successfully to arrest post-partum hæmorrhage. Cases of menorrhagia, of a peculiarly obstinate kind, are caused by mitral regurgitation or stenosis, the mechanical result being to increase the blood-pressure in the venous system of the uterus. Digitalis is the appropriate remedy in such cases. Granules of digitaline may be prescribed for some days previously to the occurrence of the menstrual molimen, but during the attack the infusion of digitalis is more serviceable. In cases of hæmorrhage, generally speaking, the infusion is the most effective form in which to employ digitalis. If the symptoms are urgent, a tablespoonful of the infusion may be given every half-hour until four doses are taken. In ordinary cases a tablespoonful of the infusion twice a day is a sufficient quantity to maintain a constant physiological effect. In the treatment of hæmorrhage, digitalis may be combined with other remedies which are synergistic. ℞ Infus. digitalis, ℥ij; tinct. krameria, ext. ergotæ fluidi, āā ℥j. M. Sig.: A tablespoonful pro re nata.

In purpura and the hæmorrhagic diathesis, digitalis is useful when given conjointly with restorative medicines; but, as a dyscrasia exists on which the extravasations of blood depend, it is obviously necessary to correct this state of things, in order that the patient shall be benefited by a remedy which gives tone to the heart and vascular system.

The most important uses of digitalis are in cardiac diseases. In general terms it may be said that it is indicated when the action of the

heart is rapid and weak and the arterial tension low, and is contraindicated when the action of the heart is vigorous and the arterial tension high.

In simple hypertrophy, which is compensatory, digitalis has no utility. In stenosis of the aortic orifice, with compensatory hypertrophy, it is not only useless, but it may give rise to serious symptoms, and even cause a fatal result, if administered in doses sufficient to produce physiological effects (Fernet). When stenosis of the aortic orifice leads to incompetence and regurgitation of the mitral, then digitalis may be used with advantage. As respects the nature of the cardiac lesion merely, digitalis is useful in dilated heart with incompetence of the mitral, in disease of the mitral orifice with stenosis or regurgitation, and in dilatation of the right heart with incompetence of the tricuspid. As respects the mechanical difficulties which ensue from cardiac lesions merely, digitalis is useful, by reason of the increased power which it gives the auricles and ventricles to empty their respective cavities, and the longer intervals between the pulsations, which enable the auricles more perfectly to discharge their contents into the ventricles. The mechanical difficulty consists in a deficiency of blood (ischæmia) on the arterial side, and a stasis of blood on the venous side, of the systemic and pulmonary circulation. Digitalis, therefore, assists in the "compensation," or, in other words, by its action on the heart restores the mechanical balance of the circulation, deranged by the cardiac lesions. As respects the rational symptoms of heart-disease, digitalis is useful when the action of the heart is rapid and weak, the tension of the pulse low, when there are cough, difficulty of breathing, a dusky countenance, pulsating jugulars, scanty and high-colored urine, and general dropsy. As a rule, it may be stated that the rational signs furnish more conclusive indications of the need of digitalis than the physical. If given in suitable cases, the action of digitalis in heart-diseases is most conspicuous for good; but careful consideration should be given to the conditions detailed above if the practitioner would procure thoroughly satisfactory results. The form in which digitalis is prescribed is most important. The infusion is the best form in cases of cardiac disease with dropsy. It should be given in tablespoonful doses, twice a day, until some characteristic physiological effects are produced. After the subsidence of the severe symptoms, digitaline-granules may be substituted for the infusion, or the powder of the leaves may be given in pill-form. As very decided anæmia is present in these cases, the best results are obtained by a combination of digitalis with quinine and iron. ℞ Pulv. digitalis, ℔ij; ferri redacti, quinae sulph., āā ℔j. M. Ft. pil. no. xx. Sig.: One pill two or three times a day.

The antipyretic effect of digitalis is a fact much insisted on in Germany (Traube, Wunderlich, Thomas, Liebermeister, etc.). In the

recent elaborate work of Husemann digitalis is classed with the *Fiebermittel*—the “antipyretica.” The results which have followed its administration as an antipyretic in fevers (typhoid, typhus, etc.) do not, it appears to the author, justify its use in these maladies, notwithstanding its power to lower the temperature. Prof. Leyden regards it as unsafe as an antipyretic. The indications for its use are, according to Liebermeister, just the opposite of those which obtain in cardiac disease; that is, “digitalis is only to be used in those cases of typhoid fever in which there is no considerable degree of cardiac weakness.” He usually gives from eleven to twenty-two grains, extended over a period of about thirty-six hours.

In *scarlet fever* the utility of digitalis is very great; it lowers the temperature and maintains the action of the kidneys, thus obviating the two principal sources of danger in that disease. Dr. Daniel Lewis, of New York, influenced by the author's opinions on this point, systematically used digitalis as the chief remedy in an epidemic of scarlet fever in New York, and presented the results in a paper submitted to the State Medical Society. While the mortality from this disease, for the city at large, is 23 per cent, for Dr. Lewis's cases it was less than 11 per cent. From a teaspoonful to a tablespoonful (according to age) of the infusion every two, three, or four hours, is a suitable mode of administration. If uræmia occur, the infusion is the proper remedy, conjoined, of course, with other means. The author has seen most excellent results from a poultice of digitalis-leaves, applied to the abdomen and back, in cases of *uræmic convulsions*, the patient being unable to swallow, or the stomach so irritable as to reject all medicines.

Digitalis has been used with success in *erysipelas*, but it is by no means equal to belladonna in this affection.

In *rheumatic fever* the testimony in favor of the use of digitalis is certainly very strong. It lowers the temperature, and apparently materially shortens the duration of the disease. It may be given in powders—two grains every four hours—or a corresponding quantity of the infusion. In rheumatism, as in every other affection, very prompt effects do not follow the use of digitalis; a day or two must elapse before any marked reduction of temperature takes place, but a cessation of the joint-trouble may be looked for in seven to ten days. Digitalis is more particularly useful in the *cardiac complications of acute rheumatism*, when irregular and feeble action of the heart, difficult breathing, cyanosis, and general œdema, are present. The following is a prescription of Oppolzer in this condition: ℞ Inf. digitalis, ʒ ij; liq. potassii citrat., ʒ jss; acet. scillæ, ʒ ss. M. Sig.: *A tablespoonful every four hours.*

Digitalis has recently been much employed in *inflammatory affections*, notably *pneumonia*. On examination of the reported cases the author finds that the defervescence, produced apparently by digitalis

from the sixth to the tenth day, occurred at the time when the *crisis* in pneumonia is to be expected, and hence it is difficult, if not impossible, to estimate the precise share which the remedy had in the results. That digitalis has any power to prevent the deposition of fibrinous material, to prevent or check the migration of the white corpuscles, or to arrest the multiplication of the cellular elements of inflamed parts, seems to the author highly improbable. That it may be useful to combat some of the symptoms—high temperature, ischæmia of the arterial system from pulmonary obstruction, and low tension of the vessels—may be well admitted.

There is considerable evidence to show that digitalis is serviceable in *chronic bronchitis with interstitial pneumonia* (fibroid lung), when accompanied with difficult breathing, secondary dilatation of the right cavities, and *general anasarca*. It diminishes the cough and expectoration, tones up the weakened and laboring heart, and reduces the œdema. That digitalis has any curative power in *pulmonary tuberculosis* or *caseous pneumonia*, can hardly be credited, notwithstanding the claims which have been put forward. It may be used as an *antipyretic* when there is much hectic, but the derangement of the intestinal canal produced by it is a most serious bar to its employment in phthisis.

Some important results have been obtained by the use of digitalis in *nervous diseases*. The *congestive form of hemicrania* may not unfrequently be permanently relieved by the persistent use of digitaline-granules (one sixtieth of a grain *bis die*). *Acute maniacal delirium*, *chronic mania*, and *delirium tremens*, are disorders of the brain in which digitalis has proved very useful. The conclusions of Dr. Williams, of Hayward's Heath Asylum, are as follow:

“1. That digitalis is a valuable sedative in the treatment alike of recent and chronic mania, and when these forms of disease are complicated with general paresis and with epilepsy.

“2. That the average dose of the tincture is from ʒ ss to ʒ j, and this quantity may be certainly given with impunity for several days, and subsequently—adjusted to the state of the pulse—may be advantageously used for several months.

“3. That the indication by which the use of this drug is regulated is the state of the pulse, any marked intermittence requiring its immediate discontinuance.

“4. That the weakness of the circulation is no indication against its employment; on the contrary, experience shows that the most enfeebled subjects bear its administration as well as the most robust.”

In *delirium tremens* extraordinary doses of the tincture of digitalis have been used with success (ʒ ij—ʒ iv), but these large doses are unnecessary. This treatment is most useful in the young and robust, with marked cerebral hyperæmia, according to some; but, according to

others, in pale subjects with a tendency to cyanosis, the state of the brain being one of anæmia, with effusion and œdema. According to the author's observation, the latter indications are the more correct. The infusion is doubtless a better preparation than the tincture, and of this a tablespoonful may be administered every four hours.

Some supposed cases of *arachnitis* have been reported cured by digitalis, but grave doubts must exist as to the accuracy of the diagnosis.

Cases of *exophthalmic goitre* in young subjects, purely functional in character, have been cured by *digitalis*, and the cardiac irregularities, and the dilatation of the cervical vessels, ameliorated in even incurable cases. Digitaline is the form in which to employ this remedy, or powdered digitalis may be given in pill, with iron and manganese to remove the anæmia.

Since the anaphrodisiac properties of digitalis were ascertained, it has been much used in *spermatorrhœa*. It is adapted to the same class of cases as those in which ergot has been shown to be so beneficial, viz., feeble erections, frequent emissions, and cold hands and feet. The author has seen better results from the combination of bromide of potassium and digitalis, in the spermatorrhœa of plethora, than from any other remedies: ℞ Inf. digitalis, ℥ viij; potassii bromidi, ℥ j. M. Sig.: A tablespoonful morning and night, and, after a week, at night only.

Digitalis is one of the most generally useful remedies in dropsy which we possess. It is, of course, specially indicated in the mechanical dropsy of valvular lesions. In *renal dropsy* from *acute desquamative nephritis* (tubal nephritis) "of all drugs, digitalis is of the greatest value," and the best form in which to administer it is the infusion. Several days usually elapse before very decisive results are achieved, but the flow of urine is, then, often enormous. The fact that, contrary to what has been heretofore believed, digitalis has a direct action on the glomerule of the kidney, is of great interest in this connection. The author has seen very favorable results from the use of digitalis in *granular degeneration of the kidney* when dropsy supervened, but its use in this disease requires caution in consequence of the fact that the elimination of urea and of the chlorides is retarded by this agent.

The so-called Cumulative Effects of Digitalis.—The author agrees in opinion with those who hold that digitalis is not a cumulative poison in the sense in which this term was formerly used. Doses of digitalis frequently repeated, so that the effect of one is added to those before given, will certainly produce toxic symptoms. In this sense opium, belladonna, strychnine, etc., are cumulative poisons. If full doses of digitalis are given at proper intervals, and the effects of one dose are permitted to cease before the next is given, no accumulation will take

place. Sudden toxic symptoms are developed as follows: When, after the administration of large doses, the pulse is much reduced in the recumbent posture, on rising, the heart is suddenly found unequal to maintaining the circulation in face of the increased resistance in the arterioles and against the force of gravity. It must not be forgotten, further, that the irritability of the vaso-motor nervous system may be destroyed by over-stimulation by digitalis, and lethal effects be produced in this way.

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Convallaria.—All parts of the plant of *Convallaria majalis* (lily-of-the-valley). (Not official.)

THE PREPARATIONS.—It is a remarkable fact that different properties are possessed by extracts made from the various parts of the plant. An extract made from the root has very powerful emeto-cathartic property, while it but little affects the action of the heart. The same fact is true, to a less or greater extent, of extracts from the whole plant. This emeto-cathartic action is due to the presence of a rather acrid resin, and hence for the purpose now intended to be subserved by the administration of convallaria the preparation used must be freed from this resin. An extract prepared from the flowers and