

Curara, as has been stated, produces an obvious rise of temperature in the extremities. This is supposed to be due to paralysis of the peripheral vessels. In the interior of the body, however, there ensues an equally constant decline of body-heat (Tscheschichin, Röhrig und Zuntz). This lowering of the central temperature is due to the loss of heat at the periphery by the cooling of the blood detained in the superficial vessels.

Bernard long ago ascertained that curarized animals became diabetic. It seems probable that this result is due to the paralysis of the vessels of the liver. On the other hand, Bock and Hoffmann have apparently demonstrated that the production of glycosuria is the result of increased activity of the liver. It may be due to the fact that the sugar formed does not undergo oxidation, for Jolyet has ascertained that in curarized animals the excretion of carbonic acid is much below the amount in health. By reason of the changes in the vascular supply, curara affects the functional activity of various organs. The increased production of saliva, and of the nasal and intestinal secretions noted at the outset, is due, there is little doubt, to this fact.

The elimination of curara takes place chiefly by the kidneys, but some escapes with the fæces (Koch). The urine of a curarized animal will poison another animal, and this may be repeated to several subjects. The retention of the urine charged with curara, in the bladder, will continue the effects of the poison by reabsorption. This statement has been the subject of considerable controversy. It has been denied that the mucous membrane of the bladder possesses the power to absorb again into the circulation poisons dissolved in the urine in the process of excretion. Brown-Séguard appears to have been the first to prove, by direct experiment, that alkaloids could be thus absorbed, and some recent observations have confirmed the accuracy of his experiments. In respect to curara, as to other organic alkaloids, when poisoning occurs, it is an obviously proper expedient to keep the bladder empty, if necessary, by catheterization.

THERAPY.—The applications of curara to the treatment of disease follow from the results of the physiological study. Being a motor and not a sensory paralyzer, it is adapted to the treatment of *muscular cramp and spasm*. It is one of the remedies employed against *strychnine-poisoning*, and although from the theoretical standpoint such treatment may seem proper, yet in actual practice it has not succeeded. That a remedy obtained from members of the strychnos family, and a paralyzer in action, should antagonize strychnine, is a remarkable fact. In the process of preparation employed by the Indians, it is in a high degree probable that *methyl strychnium* is formed, and this substance, as was originally shown by Crum-Brown and Fraser, is a paralyzer, and acts precisely like curara. Curara has been used with a limited measure of success in *tetanus*. In the successful cases—for example,

that narrated by Mr. Spencer Wells—large doses were administered. According to the statistics of Demme, of twenty-two cases of tetanus treated by this agent, eight recovered. Other methods have certainly succeeded better. Two cases of *hydrophobia* have been reported in which a cure followed the use of curara. One of these, reported by Dr. Watson, was examined, and the diagnosis confirmed by Dr. Flint, of New York. The first dose was  $\frac{1}{16}$  gr., and subsequently  $\frac{1}{8}$  gr. and  $\frac{1}{4}$  gr. were given. The value of this statement is impaired by the fact that the different specimens vary so much in activity. M. Vella has successfully treated a case of tetanus by cutaneous absorption of the agent; but the usual mode of administration has consisted in the subcutaneous injection. This subject, as M. Vulpian has well said, has lost its interest since the discovery of the utility of chloral. It is in a high degree probable, however, that curara would be greatly more successful if it were pushed in these cases to obtain its full physiological influence, and the complete suspension of the spasms.

By Voisin and Liouville curara has been extensively employed as a remedy for *epilepsy*. The facts already mentioned in regard to the action of this agent in producing febrile phenomena were obtained from the experiences with epileptics. They find that attacks may be prevented, and the condition of epileptics much improved, by the timely administration of this remedy.

It has proved useful in *chorea*, in *tic-douloureux* (Beigel, Du Cazal), but other remedies are doubtless better.

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*Gelsemium*.—Yellow jasmine. The rhizoma and rootlets of *Gelsemium sempervirens* Aiton (Nat. Ord. *Loganiaceæ*). (U. S. P.)

*Extractum Gelsemii Fluidum.*—Fluid extract of gelsemium. Dose, ℥ ij—℥ x.

*Tinctura Gelsemii.*—Tincture of gelsemium. Dose, ℥ v—℥ xx.

The so-called *gelseminine* is obtained by evaporation of the tincture, and is a very uncertain preparation; the dose is gr. ss—gr. ij. It is only used by the eclectic practitioners.

Disappointment is frequently experienced from the use of gelsemium preparations, owing to the fact that they are made from the dried root. In the process of drying, even spontaneously, the alkaloid disappears. The most trustworthy preparations are the official, prepared conscientiously from the fresh root.

COMPOSITION.—Gelsemium contains a very powerful alkaloid—*gelsemine* or *gelsemina*—and *gelsemic* or *gelseminic acid*, by some said to be identical with *asculin*; but Wormley has shown the fallacy in the evidence on which this statement was based, and Fredigke's account of gelsemic acid agrees with Wormley's in all essential particulars. It contains also an acrid resin, volatile oil, gallic acid, a yellow coloring-matter, besides some other unimportant ingredients.

*Gelsemine.*—In its pure state gelsemine (*gelsemia*) is a colorless, odorless solid, having an intensely persistent, bitter taste. It has strongly basic properties, completely neutralizing the most powerful acids, forming salts of which the sulphate, nitrate, chloride, and acetate are freely soluble in water (Wormley). Dose, gr.  $\frac{1}{60}$ —gr.  $\frac{1}{20}$ .

ANTAGONISTS AND INCOMPATIBLES.—The caustic alkalies and tannic acid are chemically incompatible. As respects the physiological actions, gelsemium is antagonized by the diffusible stimulants, by alcohol, ammonia, opium, digitalis, etc. The lethal effects are best treated by emetics, warmth, alcoholic stimulants, by faradization and artificial respiration, by morphine subcutaneously, and, according to Fredigke, by the tincture of *xanthoxylum fraxineum*.

SYNERGISTS.—Conium, physostigma, tobacco, opium, etc., when administered with gelsemium, increase its effects in the whole sphere of its physiological activity.

PHYSIOLOGICAL ACTIONS.—The preparations of gelsemium have a bitter and somewhat aromatic taste, and a narcotic odor. They do not produce gastric irritation. The active substance, being crystalloid, diffuses into the blood with facility. In moderate doses, but sufficient to produce decided physiological effects, gelsemium causes a feeling of languor and mental calm, slowing of the action of the heart, drooping of the eyelids, dilatation of the pupil, and some feebleness of muscular movements. In larger doses the physiological effects are as follows: vertigo, double vision, amblyopia, paralysis of the levator palpebræ so that the upper eyelid can not be raised, dilated pupil, labored respiration in consequence of a paretic state of the respiratory muscles, slow and feeble action of the heart, great muscular weakness, and sen-

sibility to pain and touch much reduced. These effects are produced in about a half-hour after the stomach administration, and last two or three hours, when they subside. When lethal doses are taken, the above-described symptoms occur in a more intense degree. The gait is at first staggering, but the power of muscular movement soon ceases, and a sense of numbness diffuses over the body. The eyelids close (paralysis of the levator), the pupils dilate widely, vision is lost, and the pupils cease to respond to the stimulus of light. The lower jaw drops, and the power of speech is lost in consequence of paralysis of the muscles of the tongue. The respirations are labored, shallow, and irregular; the action of the heart weak, feeble, and intermittent. Generally the skin is covered with a profuse perspiration, but no other evacuation takes place. Death occurs from asphyxia, and the action of the heart ceases after the respiratory movements. Consciousness is preserved until near the close, and until carbonic poisoning ensues. In one instance (Wormley) extreme restlessness was noted, but generally there is a condition of calm, a soporose state, or the unconsciousness of carbonic-acid narcosis, and convulsions never occur.

The author's investigations have demonstrated that gelsemium is a paralyzer of motility and sensibility; that sensibility is first affected in cold-blooded animals (frogs), and afterward motility, and that in warm-blooded animals the motility is affected before sensibility. As respects the seat of the action, the author has ascertained that the end-organs of the motor nerves, and the nerve-trunks, do not lose their irritability, and that the muscular contractility is unimpaired. "Its paralyzing effect is due to its action on the motor center, and not to an action on the peripheral nerve-fibers. It acts also on the sensory portion of the cord, producing at last complete anæsthesia; but this effect in warm-blooded animals, and in man, is toxic only, and follows the paralysis of the motor functions." Applying the precise observations which are made on animals to the explanation of the lethal effects which have occurred in man, we are conducted to the following conclusions: the disorders of voluntary movement, and the more or less complete paralysis of the motor and of the sensory functions, are due to the effects of gelsemium on the motor and sensory portions of the cord, the functions of the sensory columns resisting longer the action of the poison. The labored respiration is due to the paretic state of the respiratory muscles, especially of the diaphragm. The depressed action of the heart is probably secondary to the diminished respiration movements, which produce this result by impeding the flow of blood through the pulmonary capillaries. The dilated pupil, the double vision, the ptosis, are due to paralysis of the third pair.

In rabbits and cats gelsemium, in lethal doses, affects motility in a very remarkable manner: when the paralyzing effects are becoming manifest—first in the fore extremities—these animals perform a series

of backward movements, in which sometimes a complete backward somersault occurs. In pigeons, general muscular tremors precede the backward movements. No corresponding acts have taken place in the fatal cases observed in man. A very considerable reduction of temperature occurs from lethal doses in warm-blooded animals.

The author's experimental observations on the physiological actions of gelsemium have since been fully confirmed by Ott, by Ringer, and by O. Berger, in an elaborate series of investigations. The study of Ringer and Murrell is a model of a research of this kind.

THERAPY.—Gelsemium is indicated in those maladies in which an exaltation of function has taken place in the motor and sensory spheres of the nervous system. Several cases of *tetanus* have been reported cured by this remedy; but it is impossible to say whether these were examples of *post hoc* or *propter hoc*. *A priori* it might be expected that gelsemium would prove serviceable in this disease, because its action on the spinal cord is opposed to that which takes place in tetanus. In strychnine-poisoning in animals, however, the tetanic spasms are not prevented by the administration of gelsemium. In *mania*, with great motor excitement and wakefulness, this remedy is more useful than conium. To bring about the best results from its administration, doses of sufficient strength must be given to produce definite physiological effects, viz., dilated pupil, drooping of the eyelids, and a feeling of languor. In the condition of "horrors" from alcoholic excess, in simple wakefulness, in the *insomnia* which results from over-excitement and too great physical activity, cures are not unfrequently obtained by the use of gelsemium. In the *inflammatory affections of the meninges*, and in *cerebro-spinal meningitis*, *sporadic or epidemic*, with a decided febrile reaction, this agent is extremely useful in small doses (℥ v of fluid extract), repeated every two hours so as to maintain a uniform physiological effect.

Gelsemium has been used with success recently in the treatment of *neuralgia of the fifth nerve*, but the good effects of the remedy in the painful affections of the fifth nerve are not always manifest (Berger). Cases cured by this remedy were, doubtless, not instances of tic-douloureux, but nerve-pain caused by cold, rheumatism, or temporary excentric irritation. *Intercostal neuralgia*, *sciatica*, and especially *myalgia*, are frequently cured by this agent (Jurasz); but considerable doses are necessary—from five to twenty minims of the fluid extract every three hours until the characteristic drooping of the eyelids, dilatation of the pupil, and muscular languor, manifest themselves.

In *convulsive or spasmodic cough*, gelsemium often affords remarkable relief. It is beneficial in the spasmodic stage of *whooping-cough*, *reflex cough from irritation of the laryngeal nerves*, the *irritative cough of phthisis with scanty expectoration*, and the *nervous cough* of hysterical subjects. In some cases of *spasmodic asthma* great relief

is afforded by gelsemium, but, as is the case with all other remedies for asthma, it frequently fails and loses its good influence even in those cases in which it was at first successful.

The author has witnessed excellent results from the use of gelsemium in *acute inflammations of the lungs and pleura*. In *pneumonia* it affords rest by diminishing the activity of the respiratory function; it allays cough, and, by depressing the cardiac movements, it lessens stasis of the pulmonary capillaries and lowers the temperature. It is better to give medium doses (℥ ij—℥ v of the fluid extract), every two hours, to maintain a constant effect within the limits of safety. It favors, when exhibited in this way, the occurrence of an early crisis, and assists in the production of one critical evacuation—the sweat. A similar mode of administration should be pursued in *pleuritis*, in which its use is equally rational and effective.

Very great relief is afforded by the use of gelsemium in certain *pelvic disorders* in women. There is no more generally-useful medicine in *ovarian neuralgia*. The pains of *dysmenorrhœa* are also greatly alleviated by it. The evidence is conclusive that this remedy also suspends *after-pains*, and it is held by some good observers that it quiets the "nagging" pains of the first stage of labor. In these disorders of the female sexual organs, it is generally necessary to administer a quantity of the remedy sufficient to produce some of its characteristic physiological effects. According to Bulkley, it is an effective remedy for the relief of *pruritus*, and has given excellent results in the treatment of *eczema*. He prescribes from three to ten drops of the tincture, giving it every two or three hours until some of its characteristic effects appear.

The first empirical use of gelsemium was in the treatment of the *remittent* or so-called *bilious fevers* of the South. A considerable number of facts have been accumulated, which show that this remedy exercises a really beneficial influence in *remittent* and *typho-malarial fevers*. It is not an action of specificity—like quinine in *intermittent* and *remittent fevers*—and it is doubtful whether this supposed beneficial effect has any proper basis.

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**Arnicae Flores.**—Arnica-flowers. The flower-heads of *Arnica montana* Linné (Nat. Ord. *Compositæ*.)

**Arnicae Radix.**—Arnica-root. The rhizoma and rootlets of *Arnica montana*. *Racine d'arnica*, Fr.; *Arnica-wurzel*, Ger.

**Extractum Arnicae Radicis.**—Extract of arnica-root. Dose, gr. j—gr. iij.

**Extractum Arnicae Radicis Fluidum.**—Fluid extract of arnica-root. Dose, ℥ v—℥ x.

**Tinctura Arnicae Radicis.**—Tincture of arnica-root. Dose, ℥ x—℥ xxx.

**Tinctura Arnicae Florum.**—Tincture of arnica-flowers. Dose, ℥ x—3 ss.

**COMPOSITION.**—The chemistry of arnica has not as yet been thoroughly elucidated. Walz has isolated a principle (*arnicine*). The root contains an *essential oil* on which depends, in great part, its physiological activity. The oil is a complex substance. One of its most important constituents is *trimethylamine*, or an analogous principle.

**ANTAGONISTS AND INCOMPATIBLES.**—The actions of arnica are antagonized by ammonia, alcoholic stimulants, opium, camphor, etc.

**SYNERGISTS.**—Aconite, veratrum viride, digitalis, and arterial sedatives generally, increase the effects of arnica.

**PHYSIOLOGICAL ACTIONS.**—Arnica excites considerable irritation of the skin, if the contact be sufficiently prolonged. It produces when swallowed a sense of heat and acridity in the fauces, and increases the flow of saliva. It is decidedly irritant to the stomach, and causes in large doses nausea and vomiting, and choleraic diarrhoea. Its active principles diffuse into the blood. In small medicinal doses arnica increases the action of the heart and arteries, and excites the functions of the skin and kidneys. In large doses, probably after a short stage of excitement, depression of the circulation, of the respiration, and of the animal temperature, ensues; violent headache is experienced, the pupils are dilated, and paresis of the muscular system comes on. In toxic doses arnica paralyzes the nervous system of animal and organic life, and death ensues in a condition of collapse.

**THERAPY.**—In *febrile diseases* and *inflammations*, when there is sthenic reaction, arnica in full doses depresses the action of the heart and lowers the arterial tension. It is, therefore, *antipyretic*. For the production of this effect, an infusion is probably a better preparation than the tincture. When, however, in febrile diseases there is present the condition of *asthenia*, small doses of the tincture (five minims) are to be preferred. That this remedy will produce different results, in

small or large doses, need not occasion surprise. It is conceded on all sides that the effects of opium differ according to the size of the dose, and the frequency with which it is repeated.

Good results have been obtained from the use of arnica infusion in *mania* and *melancholia*. The tincture of arnica is exceptionally serviceable in *delirium tremens*, with depression.

In *rheumatism* and *rheumatic gout*, very decided curative effects are sometimes procured from arnica. The fact that it contains *trimethylamine* is probably the true explanation of its utility in these affections. It has also proved very efficacious in *acute eczema*, in *erysipelas*, and other cutaneous affections of gouty and rheumatic origin. *Dysmenorrhœa* of the congestive form, *acute metritis*, and other acute pelvic inflammations, are also favorably influenced by the administration of arnica.

The tincture of arnica has a popular reputation for the relief of *sprains*, *bruises*, and external inflammations. The author has known violent erysipelatous inflammation to follow its application to a sprained ankle. It is extremely doubtful whether the good effects are more decided than those of a spirit-lotion. The infusion or decoction does not, it is said, cause local irritation. Planat has demonstrated that arnica is a remarkably effective application to *boils*. He directs one part of the extract and two parts of honey to be thoroughly incorporated, and the paste spread on some adhesive plaster, leaving a margin to secure its adhesion to the skin. The plaster is renewed every twenty-four hours. To increase the effect, Planat gives by the stomach the tincture of arnica.

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**Trimethylamine.**—(Unofficial.) This is an ammoniacal substance, having a strong, fishy odor. It is isomeric with *propylamine*, which is also an ammonia. As the propylamine of commerce is a mixture of various substances, and is of uncertain composition, trimethylamine only should be used (Spencer). The dose of trimethylamine is four to eight minims. Its disagreeable taste may be disguised somewhat by peppermint-water.

**PROPERTIES.**—Trimethylamine is a colorless liquid, having the composition  $C_3H_9N$ . It dissolves freely in ether, alcohol, and water, has a strong alkaline reaction, and is inflammable.

*Chloride of Trimethylamine* is a stable salt which crystallizes in long needles; it is very deliquescent, and its solution when concen-

trated has a caustic action on the skin and mucous membrane. It is free from odor, except when heated or mixed with an alkali, when the fishy smell is evolved. The taste of a solution of this salt is alkaline, but not disagreeable (Dujardin-Beaumetz). Dose, grs. ij to grs. v every three hours.

**ANTAGONISTS AND INCOMPATIBLES.**—Chemically trimethylamine is incompatible with the mineral acids, the salts of the metals, the alkalies (chlorides), and vegetable infusions. It should always be prescribed alone, in solution in some aromatic water. Therapeutically, it is antagonized by the stimulants, opium, belladonna, digitalis, etc.

**SYNERGISTS.**—All agents depressing the vascular system and the temperature are synergistic.

**PHYSIOLOGICAL ACTIONS.**—Applied to the skin, mucous membrane, or areolar tissue, trimethylamine produces decided caustic effects, comparable to those which result from the action of ammonia. It excites gastric pain when taken into the stomach in considerable doses, and will, doubtless, cause a high degree of inflammation if incautiously administered. The most characteristic effects are the lowering of the action of the heart, the depression of the temperature, and the diminution in the amount of urea excreted. In the physiological state Dujardin-Beaumetz found, in some experiments on himself, that the chloride of trimethylamine lessened the temperature and the pulse, but these results were much more decided when it was administered in cases of acute rheumatism. The influence which this agent has on the excretion of urea is still more remarkable. The observations of Dujardin-Beaumetz show that a gradual but considerable decline in the excretion of urea is a constant result of its administration. On the other hand, Spencer says that the excretion of urea is sometimes increased, and, in one case in which the urinary discharge was carefully studied, the urine was almost trebled, and the urea more than doubled by the use of this remedy. If the diminution of the amount of urea were a constant result, as claimed by Dujardin-Beaumetz, the influence which trimethylamine has on the body temperature might be due to an interference with the combustion process. But the facts do not as yet justify the construction of a theory as to its mode of action.

**THERAPY.**—Thus far almost the only application made of trimethylamine is in the treatment of *acute rheumatism* and *gout*. In some cases it appears to produce almost complete relief after the administration of a few doses, but generally a longer time is required (Awenarius, Dujardin-Beaumetz, Spencer, Leo). It moderates, at once, the fever and the joint-pain, and very decidedly shortens the duration of the disease. It is said to diminish the tendency to cardiac complication.

This agent, having so decided an influence on the pulse, temperature, and excretion of urea, will in the future doubtless be applied to the treatment of other maladies.

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**Pilocarpus.**—Jaborandi. The leaflets of *Pilocarpus pennatifolius* Lemaire (Nat. Ord. *Rutaceæ*, *Xanthoxyleæ*). (U. S. P.)

**Infusum Pilocarpi.**—Infusion of pilocarpus ( $\frac{3}{4}$  ij—Oj). Dose,  $\frac{3}{4}$  ss —  $\frac{3}{4}$  ij. (Not official.)

**Extractum Pilocarpi Fluidum.**—Fluid extract of pilocarpus. Dose, 3 ss — 3 ij.

**Tinctura Pilocarpi.**—Tincture of pilocarpus ( $\frac{3}{4}$  iv—Oj). Dose, 3 ss — 3 ij. (Not official.)

**COMPOSITION.**—The important constituent is the alkaloid—*pilocarpine*—which possesses the physiological properties of the drug. It combines with acids to form salts. The salts of pilocarpine crystallize in the oblique system. In 1880 another alkaloid was discovered, and to this the name *jaborine* was given (Harnack und Meyer). Subsequent researches fully confirmed this (P. Castaing). These alkaloids are closely related in composition: probably identical, but having a different molecular arrangement. By heat, merely by concentration of an acid solution, pilocarpine is converted into jaborine (Hans Meyer); and by washing with absolute alcohol they are separated, when united, as is very often the case in the commercial article. As these two alkaloids differ very greatly in properties, it is not surprising that the observations made with pilocarpine at first were very discrepant. Chemically they differ in that the salts of jaborine do not crystallize, and they dissolve more easily in ether and less easily in water. Physiologically, they differ even more decidedly. Jaborine acts like atropine, to which pilocarpine is a physiological antagonist.

**Pilocarpinæ Hydrochloras.**—Hydrochlorate of pilocarpine. Minute, white crystals, deliquescent, odorless, having a faintly bitter taste and a neutral reaction. Very soluble in water and in alcohol, but almost insoluble in ether or chloroform. Dose, gr.  $\frac{1}{2}$ —gr. ss.

**ANTAGONISTS AND INCOMPATIBLES.**—The caustic alkalies, the persalts of iron, and the salts of the metals generally, are chemically incompatible. A remarkable antagonism has been shown to exist between pilocarpine and belladonna (Ringer and Gould).

**SYNERGISTS.**—Aconite, veratrum viride, gelsemium, and remedies