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ERGOT—ITS PHYSIOLOGICAL AND THERAPEUTICAL ACTION.

Read before the Southern Michigan Medical Society. By A. R. Smart, M. D., Hudson, Mich.

THIS agent, although so common and long known, has until recently been imperfectly understood, both in its chemistry and in its physiological action, and at present we have much to learn regarding the former.

Ergot consists of a blackish body, one or two inches in length, irregularly cylindrical, grooved along one side, and generally curved. It belongs to the lowest of vegetable organisms, viz., the fungi, and is the product of an intermediate condition between the formative and reproductive stages of those bodies. It is developed in the pistils of many species of the gramineæ, but one only of which is officinal, that of the secale or common rye. ' Ergot has a very complex chemical constitution, and is very susceptible to change upon exposure to the air or to dampness. This is true also of its preparations. It contains nearly thirty-five per cent of a fixed oil. It also contains propylamin in considerable quantity, to the presence of which its peculiar mouse-like odor may be attributed. Wanzell says it contains two alkaloids, soluble in water and alcohol, but insoluble in ether or chloroform; these he calls ecboline and ergotine, and says that they each exist as an amorphous brown powder, feebly bitter in taste. Eugene Handelin denies that these alkaloids are the active principles of the drug, as he found a watery solution efficient after precipitation with tannic acid and corrosive sublimate.

All of the earlier uses of the ergot, from which oxytocic effects were obtained, were with watery infusions. Levi, of Munich, says ergot contains large quantities of phosphoric acid, to which he attributes its action. A committee of the Chicago College of Physicians and Surgeons, appointed to investigate the properties of ergot, reports two preparations—a watery and an alcoholic extract, which differ widely in their nature and action. Wernich thinks the watery extract far more powerful than either the alcoholic or ethereal. He thinks the best preparation is made by

exhausting the drug, first with ether, then with alcohol, and lastly with water; then evaporating. Dr. Squibb, of Brooklyn, evaporates a watery extract on porcelain.

While the active principle of ergot is not well defined, it seems certain that two separate, distinct principles exist in the drug—the one obtained by a watery solution and the other by an alcoholic solution—which differ entirely in their nature and physiological action. Precisely what these principles are, is at present undetermined.

Physiological Action.—The older writers, in describing the action of ergot on man, speak of it as producing nausea and vomiting, with colic, and sometimes diarrhœa. Salivation was noticed in many instances; it was said to cause head-ache, vertigo and dilatation of the pupils; the heart's action was increased by poisonous doses, but slowed by smaller ones, both the frequency and force of the pulse being lessened. The effect of ergot in exciting contraction of the gravid womb, was the means of bringing the drug into notice, and has until very recently been considered its chief, if not only action of therapeutical significance. This is evinced by the name given it by the Germans, "*Mutterkorn*," or "womb-grain."

For years after ergot was known and used in medicine, its oxytocic action, which is but one link in the chain of its pathogenesis, entirely overshadowed its other properties. A few years ago Brown-Sequard announced the fact that ergot, in common with belladonna, had the power of lessening the blood supply of the brain and spinal cord, by contracting the calibre of their vessels. This he verified by actual observation of the meningeal vessels while under the action of ergot. This discovery led to a series of investigations, which have resulted in giving us an extended idea of the action of ergot, which, although as yet incomplete, has placed it in a prominent position in the list of therapeutical agents.

We may say, in formulating the action of ergot, that it acts mainly upon the ganglionic centres and upon the non-striated muscular fibre wherever found. It is a certain and unfailing vasomotor stimulant, contracting the calibre of the blood-vessels in all parts of the body with great certainty and promptitude, whenever

given in quantities sufficient to develop its action. It is equally certain in effect as a stimulant of involuntary muscular fibre. Brown-Sequard asserts that, when it is given in poisonous doses, this muscular spasm gives way to paralysis. Its action on the circulation is specially marked, invariably causing contraction of the calibre of the blood-vessels and diminution in the frequency of the action of the heart. The latter is so rapid a result that some German observers noted a fall of from four to six pulsations in one minute, from the hypodermic use of ergotine. Observers vary in their statements whether or not the force of the beat is diminished, but it is quite certain that the blood pressure is increased. In the light of these statements, the symptoms formerly ascribed to ergot are made intelligible. As we have seen, it contains two principles—one soluble in water, and to which its action on the blood-vessels and non-striated muscular fibre is due, and the other soluble in alcohol, to which the symptoms of irritation of mucous membranes and the disturbances of the cerebro-spinal nerves are attributable.

Dr. Kohler found Wigger's alcoholic extract or ergotine produced tonic cramps and spasm of the extremities, with greatly increased irritability of the peripheral motor nerves, while Bonjean's, or the watery extract, acted on the heart and blood-vessels, causing contraction, slow pulse and increase of blood pressure. This effect he ascribes to stimulation of the inhibitory centres of the heart and of the vaso-motor centres in the medulla. Large doses, he found, paralyzed the heart. The watery extract lessened the irritability of the peripheral motor nerves. Both extracts slightly reduce the temperature and the frequency of respiration; both dilate the pupil; both diminish the irritability of the sensory nerves. The colic, nausea, vomiting, salivation and diarrhœa produced by ergot, are the effects of the principle soluble in alcohol, as are also the cramps, staggering and trembling of the limbs, while the sense of faintness, of vertigo and swimming of the head, the disturbances in the action of the heart, and the coldness of the surface, are symptoms caused by the principle soluble in watery infusion, and are attributable to the lessened blood supply to the parts. The action on involuntary muscular fibre, of which its

oxytocic effects are a part, is also to be assigned to this watery principle. This view is supported by the fact that for years all the use made of the drug was by means of the infusion. It may be questioned whether ergot has any power over the uterine fibre, that it does not possess in common over all the non-striated muscles. It is certain its influence is not confined to that organ. It has a similar action upon the intestine, the bladder and non-striated fibre generally. In this it is an analogue of belladonna, quinia, lead, and, in greater or less degree, of many other agents. The relationship of ergot and belladonna is specially marked. We have noticed their similar action upon the blood-vessels—they each dilate the pupil, relieve pain, lessen excessive secretion, arrest hemorrhage, and act alike on organic muscular fibre and the cord.

Several observers have noticed the increased peristaltic action in the intestine, produced by ergot. Dr. Williamsky, in experiments made upon dogs and rabbits, says immediate contraction of the bladder ensued upon the injection of ergot, and it seemed to excite both the sphincter and muscles of the body of the organ. Its action upon the gravid womb is familiar; upon the unimpregnated organ it is much less marked, the susceptibility to its influence increasing in proportion to the development of muscular fibre. A Russian, with an unpronounceable name, observed as a result of full doses an arrest, and, in some instances, a suspension of the mammary secretion. He also observed the same effect in cows fed on straw containing ergot. It is as yet an undecided question whether ergot produces its results by centric or peripheral action. Eberly found that after division of the *par-vagi*, large quantities of the drug failed to produce cardiac arrest, and in frogs and mammals, after paralysis of the peripheral vagi by atropia, ergot was powerless to effect the system of the heart. We know the pneumogastric is the inhibitor of the heart, and the fact that ergot in smaller (stimulating) quantities, slows its action, while in quantities sufficient to paralyze the vagi its action is accelerated, would tend to show that its action on the heart was through the vagi. Paul Vogt found the vessels in the ear of a rabbit from which he had extirpated the cervical ganglion, could not be made

to contract by the hypodermic use of ergot. Dr. Drashe, in some experiments with ergot, found a strong solution when brought in contact with a bleeding surface, even a severed artery, had the effect of lessening its calibre and checking the hemorrhage. Other known local uses of ergot seem to favor the view of its peripheral action, yet it is probable that its chief activity is centric. If ergot is given for a long time, or in very large quantities, disastrous results may follow. From large doses the vaso-motor stimulation and tonic muscular spasm caused by smaller doses, may pass over to a condition of paralysis and relaxation. If the action be long continued, the blood supply may be so much interfered with as to arrest the nutrition of the tissues, while softening from anemia of the brain and nerve structures, with paresis of muscles, results. It produces in the extremities a form of gangrene, which Simon says exactly simulates that caused by arterial obstruction.

Therapeutical Uses.—Having now briefly glanced at the physiological action of ergot, we will notice some of the therapeutical uses of the drug, which may thus be suggested. The statement may safely be made that we have no hemostatic so prompt and reliable as ergot. It has been tested so many times, and in so many varieties of hemorrhage, that such an assertion is fully warranted. Nor is this more than we should expect when we consider its unfailing, universal power of contracting the calibre of blood-vessels and lessening blood flow. Its use in uterine hemorrhage, both ante and post-partum, is familiar, acting both by contracting the muscular fibre and directly upon the vessels. It is much more prompt and efficient if used hypodermically, especially if the hemorrhage has been excessive, absorption in such cases being slow. Dr. Williams, of Baltimore, reports some cases of its hypodermic use in post-partum hemorrhage with complete success. Dr. Boardman, of St. Paul, records a case of placenta previa in which, after failure with other means, the hemorrhage was arrested upon different occasions, and the patient finally brought within two weeks of full term by means of ergot used hypodermically. In all forms of hemorrhage occurring during gestation, and in threatened abortion, ergot is invaluable. A fre-

quent cause of hemorrhage and premature uterine action is a lax, feeble state of the uterine fibre, with relaxed vessels, or in other cases a congested, over-full state of the organ, in either instance allowing oozing of blood and partial separation of membranes, which provokes uterine action. In these cases the use of ergot in quantities sufficient to produce a tonic contraction of the vessels and fibre of the organ, arrests the mischief, and, together with the use of opiates to lull pain already commenced, will generally prevent farther trouble. No fear need be felt with the moderate use of ergot here; the uterine fibre is undeveloped, at least during the earlier months of pregnancy, and much more danger will arise from the hemorrhage and its results than from the action of ergot. It has happened, doubtless, many times, that after the administration of ergot in cases of supposed certain abortion, for the purpose of hastening the result, the physician has been surprised to see the hemorrhage and pain cease, and the process become suddenly arrested. I can call to mind one case in particular, occurring during the later months of gestation, in which I repeatedly arrested attacks of pain and hemorrhage which threatened premature labor, and succeeded, by the use of ergot and morphia mainly, in nearly completing full term.

In congestions, displacements and enlargements of the unimpregnated uterus, ergot is often of value used in the form of suppositories, and in combination with quinine and belladonna, it is a most useful application in cervical congestion, displacements, imperfect involution, leucorrhea. It is used in these various uterine diseases by the Italians with alleged great success; the use of ergot in the treatment of fibroid tumors of the uterus, a practice introduced by Hildebrandt, may be considered fairly established. If the success claimed for this treatment by its originator has not been fully realized in the hands of others, yet so large a measure of success has been attained, as to place its value beyond question. Of one hundred and three cases of uterine fibroids collected by Prof. Byford of Chicago, and reported by him to the American Medical Association at the last meeting, twenty-three were cured; in thirty-eight hemorrhage was arrested and the tumors decreased in size; nineteen were benefited, while twenty-one resisted treat-

ment. In some of the cases he injected the ergotine into the cervix or into the tumor itself, instead of the surface of the body. He prefers for hypodermic use the watery extract. Dr. Parvin records three cases successfully treated with the watery extract, and says the addition of glycerine caused abscess. Dr. Reeves Jackson, of Chicago, reports five cases treated, three of which were successful; used watery extract prepared by Squibb. I have used ergotine in one case of interstitial uterine fibroid, occupying the posterior wall of the organ; the cavity was increased to four and one-half inches. The patient, a lady of fifty-three years, had suffered over a year from exhausting hemorrhages, and was very anæmic and much reduced in strength. For some weeks before commencing the use of ergotine, she had been partially aphasic, and had suffered incomplete hemiphlegia. The injections were made over the lower portion of abdomen with a solution of ergotine in glycerine and water at first, which irritated so much that it was changed for the fluid extract. The injections were repeated every second day for about six weeks. The hemorrhage then having entirely ceased for four weeks, and the general appearance being much improved, they were omitted. The hemorrhage soon returned, and the injections were resumed and continued for two months with immediate effect in arresting the metrorrhagia. The patient then passed from my observation, but I have since learned that up to July last, over three months afterward, she had been free from a return of the trouble.

According to the experience of most observers, ergot is most certain to benefit when the growth is firm and elastic and has not degenerated, but remains vascular. When its seat is sub-mucous or interstitial where the uterine walls are healthy and capable of contraction, the ergot acts not only by directly cutting off blood supply to the tumors, but also in causing contraction of the uterine wall, and exciting atrophy.

Dr. Collins, of New York, reports a case of sub-mucous sessile fibroid, which, by the use of ergot, he converted into a polypoid, form, which he readily recovered. It has been said that the oxytocic action of ergot is due to its power of lessening the quantity of blood in the uterus, and allowing its muscular fibre to act.

Whether this view be correct or not, ergot is by no means certain or desirable as a parturient. It produces a tonic unremitting contraction of the uterus, being very unlike in character the alternate contraction and relaxation of true labor. I have often queried after the use of ergot in tardy and irregular labor; if it did not rather impede than facilitate the progress of the case. Further than this, the use of ergot during labor is not wholly devoid of danger. The rigid prolonged contraction which it induces may seriously compromise the safety of the child, by cutting off its blood supply, and causing asphyxia. The alternations of contractions and relaxations in labor are not without a purpose, and the unremitting pressure upon the lower segment of the womb, and upon the soft parts may be productive of mischief. It is said that its use in small doses is best during labor to simply excite contraction, without inducing its tetanic character. This is perhaps true, but as a parturient, ergot is much inferior to cohosh, quinia, morphia or stimulants as may be demanded; or if these fail, the timely use of the forceps. I apprehend that at no distant day, what was considered the chief use of ergot, will come to be one of the least of its therapeutical features. However undesirable ergot may be during labor, it is certainly invaluable afterward in inducing a firm tonic contraction, which lessens the dangers of hemorrhages, and tends to expel any clots or shreds of membrane that might remain and cause pain, inflammation or septicemia. It will likewise prove of value if continued until involution is completed; given in quantities that will maintain freedom from relaxations and engorgements.

In diseases of the bladder, the stimulant action of ergot may be, and has been, utilized. Dr. Williamsky used it with success in the atony of the bladder, frequently referred to as paralysis. The fact that cases of poisoning from ergot are generally found to have disturbed bladders would seem to contradict this assertion, but this is to be attributed to its action on the vesical sphincter, an effect I have observed several times when using it hypodermically in the abdominal region. The possibility of this condition should be kept in mind when administering ergot during parturition, and the state of the bladder be carefully watched. May it not be true that cases of vesico-vaginal fistula have occurred from this cause?

The hemostatic action of ergot is as marked in other localities and conditions as in those recited. It has been used in the hospitals at Vienna with success in the treatment of hemorrhage from the lungs, nose, kidneys, and in intestinal hemorrhage during fevers (*Medical and Surgical Reporter*, Vol. xxx, p. 173). Dr. Ritchie, of Manchester, England, reports twenty cases of hemoptysis treated with prompt and decided success by means of the hypodermic use of three to five grains of ergotine (*Amer. Jour. Med. Science*, April, 1872; p. 538). The late Dr. F. E. Anstie says ergot is the best known remedy for hemoptysis. He advises its hypodermic use. In the *Medical Recorder* for May, 1875, a case of purpura is reported. It occurred in a child of seven years, and had resisted various plans of management. The hypodermic use of one grain of ergotine, twice in twenty-four hours, completely arrested the hemorrhage. The case is described as a severe one, and when first seen, blood was issuing freely from nearly all the mucous orifices of the body. The writer believes the idea that this disease is the result of fatty degeneration of the capillary vessels is untrue. He suggests vaso-motor paralysis as the condition, and ascribes the beneficial effect of ergot to its power of inducing vaso-motor spasm. In the same journal is recorded a case of epistaxis in an adult, where, after failure of other means, the use of twenty-drop doses of fluid extract of ergot at once controlled the bleeding, the same result following the use of the remedy in a subsequent recurrence of the hemorrhage. Prof. Voigt, of Griefswald, reports an extensive varix of the leg which had existed for years, and was cured by two injections of ergot, and remarks that in various other cases results equally remarkable followed this treatment. He says the cure was accomplished in part by the contractions of the arteries and veins, and in part by the pressure of the infiltration caused by the injection. Whether the cure was permanent or not, the professor does not know, as sufficient time had not elapsed to determine that fact. He further says that he has used ergot with good results in hemorrhoids and varicocele. For the latter disease ergot has been frequently used successfully by the Italians. The use of ergot in prolapsus ani, by Von Langenbeck, was the means of suggesting to Hildebrandt its use in

uterine fibroids. Von Langenbeck states that he has astonishing success with the use of ergotine in prolapsus ani. He uses five to fifteen parts of ergotine, to one hundred distilled water, or sometimes in aneurism, ergot two and one-half parts, and alcohol seven and one-half parts. He throws the fluid into the cellular tissue at the side of the rectum, at intervals of three or four days for as many weeks. Dr. Semple, of Virginia, says rectal injections of fluid extract ergot will accomplish the cure with less pain and inconvenience than results from Von Langenbeck's method.

Ergot has been recommended by Langenbeck for the treatment of some forms of aneurism, especially the intra-cranial variety. Ergot has been found of service in many kinds of inflammation. When we consider its influence over the heart and blood-vessels, and its power of lessening the blood supply of parts, it theoretically would seem of value in inflammatory conditions, and this has, to some extent, been verified in practice. Dr. Wysick employed it in the treatment of croupous pneumonia, and says it lessens exudation and subsequent expectoration. In one instance an excessive albuminous expectoration ceased in two hours after the administration of nine grains of powdered ergot, repeated every fifteen minutes. He cautions against its use in debilitated and emphysematous subjects. Dr. T. Curtis Smith, of Middleport, Ohio, recommends ergot in all inflammatory diseases of the air passages. He says it relieves congestion and prevents exudation. One of the essential conditions of inflammation is stasis, dilated capillaries, vaso-motor paralysis and exudation. Ergot, we know, directly antagonizes this condition, and that it should relieve inflammatory states is palpable. Dr. Bonjean, the originator of the extract that bears his name, states that in the Hospital St. Andre, at Bordeaux, the mortality after amputations had been largely reduced by the administration of fifteen to forty-five grains of ergotine, daily, for fifteen days succeeding the operation, the effect being to lessen inflammation, and to diminish, and sometimes wholly prevent, suppuration (*Med. News and Library*, April, 1869). Dr. Luton, of Rheims, found when administering ergot for the relief of a uterine hemorrhage in a patient, who, at the same time, was suffering from dysentery, that both conditions were alike

relieved by the action of the drug. He afterward gave ergot in powder, forty-five grains per day, in a case of dysentery, and found it promptly quieted the tenesmus, and arrested the bloody discharges. It may also be of benefit in dysentery by exciting peristaltic action in the bowel, above the seat of inflammation—a locality usually in a state of inaction and torpor in this disease. Dr. Jacobi, of New York, says the antiphlogistic action of ergot is marked. He has used it in spinal meningitis, in infantile paralysis dependent on congestion of the cord, and in some cases of chorea. He declares that intermittents may be arrested by it, that have resisted the action of quinia and arsenic. He uses it in large doses, giving ℥ij of fluid extract to children, and has no fear of producing ergotism. He continues ℈j doses of ergotine daily to adults for a long time, without bad results. Dr. Dubone, of Pau, says of fifteen cases of palustral fever treated with ergot, fourteen were arrested. Dr. Reed, of Boston, a year or more since reported several cases of cerebro-spinal meningitis successfully treated by him with ergotine and belladonna.

The controlling power of ergot over the circulation of the brain has been utilized by many observers. Dr. Kitchen, of Utica Insane Asylum, says of one hundred patients with plethoric congestive types of headache, who took ergot, in nearly all the attack was cut short in one-half hour. He uses it also in epilepsy, and in some forms of insanity. Dr. Mann, of New York State Asylum, on Ward's Island, uses ergot in acute mania of congestive form, with marked benefit. He gives from ℥ss to ℥j of fluid extract, or five to ten grains ergotine three times daily. J. Crichton Browne, of West Riding Asylum, England, uses ergot in many forms of mental diseases. In mania he says it calms excitement, shortens the attack, and widens the intervals of their occurrence. Other observers make similar statements, and, perhaps, in no disease has ergot attained a better reputation, than in acute congestion of the brain and cord. Dr. Hampel says he has derived great benefit from ergotine in whooping cough and in laryngeal spasm, and thinks it lessens congestion and increases normal secretion. Dr. DaCosta reports two cases treated by ergot, one a case of diabetes insipidus, successfully treated by ℥j fluid extract ergot, *ter in die*; the second,

a case of that obscure disease of the blood, leukemia of the splenic variety, treated with ergotine, five grains, given on alternate days, and which was cured after the eighth injection (*New Rem.*, April, 1875, 105).

As regards administration, ergot may be best given internally in the form of fluid extract, of which the acetic is the most reliable; or the alcoholic or watery extract may be given internally according to the action sought. When ergot nauseates, or when a prompt effect is needed, the hypodermic use is the best, and will sometimes succeed after other forms of administration have failed. It may also be used in suppositories, rectal or vaginal. Professor White, of Buffalo, has used ergotine in this manner, in the treatment of uterine fibroids, and remarks that, used in the rectum, it sometimes incidentally cured an obstinate constipation. The chief objection to the hypodermic use of ergot is the tendency to inflammation and abscess. This may be avoided by using the watery extract, made after Squibb's method. The addition of a small quantity of alcohol increases its activity, renders it less prone to change, and does not increase irritation.

Hildebrandt advises that the needle be thrust deeply into the tissues to avoid abscess, a proceeding I have found successful. Although sometimes used, I am certain the addition of glycerine adds to the irritation produced; in the absence of any other preparation, the fluid extract may be used hypodermically. As to the locality, I am disposed to believe it should be as near the diseased tissue as possible.

In conclusion, gentlemen, permit me to say I have no disposition to assign to this drug a more prominent position in therapeutics than it merits. My object, in thus calling attention to it, and in reviewing its action, both physiological and therapeutical, is to subject it to the only real test of a supposed valuable agent, viz., clinical experience. If it shall prove to be as valuable in certain diseased conditions as its physiological action would lead us to believe, then shall we have added another to our list of specific curative agents. If not, then it must be consigned to the obscurity of so many vaunted specifics in the past.