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### THE PHYSIOLOGICAL AND THERAPEUTIC RELATIONSHIPS OF ERGOT OF RYE.*

A Thesis for the Degree of Doctor of Medicine; and to which was awarded the First Prize of the Boylston Medical Society for 1869.

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ONE of the first embarrassments which the student of medicine meets, and that almost at the outset of his course, is the great number and variety of the remedies presented, in the Materia Medica, for his study and use. The implements of his profession confuse him, alike by their multiplication and their complexity. From all regions of her great domain Nature gathers her remedial stores, and offers them, with profligate generosity, to him who will choose to employ them. Chemistry adds new products, and pharmacy evolves changes without number.

This unlimited variety, characterizing the Materia Medica, it is the tendency of the present medical generation to modify. Simplicity of treatment is now deemed more rational than studied complexity, and all the innovations which this century has witnessed are marked by this tendency. As compared with the customs of the fathers, the opposite extreme seems almost reached in a proper zeal in behalf of the restorative power of Nature. The professional verdict declares for the use of a limited number of remedies which are well understood, and bases its dictum on the revolutionized sentiment with regard to the treatment of disease. It is to the renewal of life that our remedies are to be directed, not to the exorcism of disease. Hence comes the dogma of expectancy. The natural history of diseases is more carefully observed and better understood, and men see that nature may be guided and aided, but not forced.

As the direct result of this advancement, come more rational methods of study into the intimate nature and relationships of the means to be used for the accomplishment of the end in view. It is part of the business of modern science to examine carefully into the processes which individual drugs produce, to see what virtue may be in them, to take them out of the hands of empiricism, and to apply them, on well-established principles of action, to the treatment of disease.

It is proposed, in this paper, to present some of the more recent views of the physiological and therapeutical relationships of a pathological product of the vegetable kingdom,—the secale cornutum.

The use of ergot as a therapeutic agent is by no means of modern date. Although there is no evidence that it was employed by the ancients, or that they recognized its virtues, it is well authenticated that scientific men of the middle ages were not ignorant of its powers. As early as A.D. 1096 it was mentioned and described by medical writers, and at a still earlier period its efficacy, under proper conditions, as a parturifacient, was known by the continental midwives and empirics.

It was not, however, until the middle of the last century that physicians consented to admit ergot into the list of the legitimate materia medica, and this recognition, at so recent date, was attended with even considerable difficulty. Its use was interdicted in France in 1774; but it was again introduced soon after, on this occasion with favor and with the royal seal of professional recommendation. Like most remedial agents, however, its success was variable until it could outlive the prejudicial conditions of novelty and the want of extended trial; and for half a century after its introduction among regular practitioners it was hardly heard of. But at the beginning of the present century, it fell to the lot of an American to put the use of ergot on a permanent basis as a therapeutic agent, and the name of Dr. Stearns, of New York, is thus associated with its early history. Since this time it has constituted a subject for scientific discussion of very great importance. Writers upon its powers have mul-

* Prof. E. H. Clarke specially recommended this paper to us for publication, and it was furnished at our solicitation.—ED.

tiplied, until the bibliography pertaining specially to ergot has acquired almost indefinite proportions. Its chemical composition, its natural history, its mode of action, its therapeutic uses and abuses have been made the subjects of inquiry, resulting in the most diverse opinions concerning its powers, its virtues and its ill effects. As has been the case with many, perhaps with most, of the really valuable remedial agents in their primitive history, ergot was thus in danger of an early decline, both in consequence of the disastrous effects resulting from its abuse in inexperienced hands, and as the result of the violent partizan opinions to which its use gave rise. In the light, however, of the best modern experience, developed from the skilful observations of such men as Parola, Bonjean, Wright and Brown-Séquard, this article properly assumes a place among the agents placed at the disposal of mankind for the relief of suffering, and it is thus rescued from the abuses of empiricism, since its manifold and often apparently contradictory indications are made to rest on a rational physiological and pathological basis.

Into the consideration of the general character, the mode of growth, and the botanical relationships of ergot, it is not proposed to enter in this paper. The chemical constitution, moreover, is as yet a vexed question among pharmacists; new constituents are discovered and urged as the active principles, and new characters serve to confuse the already accumulated mass of chemical facts.

Leaving, then, the study of the natural history and of the chemical constitution of ergot, we pass at once to the discussion of its physiological and therapeutical effects. For the more systematic consideration of its powers, it is proposed to adopt the plan as illustrated in the examination of kindred topics (Prof. E. H. Clarke's Lectures on the Materia Medica), and to investigate, in turn, the absorption of ergot, its passage through the system, the effects during its passage, its *modus operandi*, and, finally, the therapeutic uses and indications.

*Absorption.*—It is sufficiently clear that the active principle or principles of the secale cornutum must first be introduced into the system, by the circulation, before the well known and most obvious effects can manifest themselves. Experiments are numerous to prove that the specific action can take place only through this medium. When ergot is applied artificially to any part not in direct communication with the circulatory system, its action, so far as known, is neutral, or at best but negative. Nor is there reason to suppose that we have any subtle narcotic principle, which by sympathetic nervous transmissibility or by reflex action affects parts at a distance from each other, as some authorities suppose to be the case in tartar emetic or in some of the active poisons. But we are justified by the strongest analogy in placing ergot with the very large class of medicines which must "obtain entry into the blood or internal fluids of the body before their action can be manifested."—(Headland on the Action of Medicines, p. 59.) Chemistry, too, although as yet in a crude and imperfect manner, assists in the demonstration of the absorption of ergot, its presence in the blood having been determined by Wright, in 1840.

The action of ergot is essentially the same, by whatever avenue of absorption it reaches the blood. Applied locally in external hæmorrhage, as in epistaxis, its action is still the same as when it is exhibited by the more indirect process of absorption in the stomach; by its vital action on the bloodvessels, instead of its chemical effect on the blood, it claims a place "in the first rank of liquid hæmostatics which do not coagulate the blood, its action being wholly dynamic."—(Bonjean, "Ergotine," p. 11.) It has also been found that when the drug is administered by the rectum in the form of suppository, or as an enema; by the vagina, or by any of the mucous surfaces, absorption, although slow, is certainly followed by positive results, distant as well as local. Nor must it be forgotten that equally with other media of absorption, the stomach, obviously the most ordinary and convenient organ for the process, presents the active principle of ergot to the blood, with a consequent ready manifestation of effects identical with those produced after administration through other tissues. The numerous experiments of Wright have demonstrated, also, that the effects of the drug are the same on animals, whether it be presented directly to the blood by injection into the large veins, or indirectly by osmosis.

Another, but less obvious confirmation of the absorption of spurred rye is found in the effect of the drug in certain cases on the fœtus in utero. In discussing the use of this agent in parturition, Dr. Beatty (Contributions in Midwifery—art. Ergot) remarks that children, still-born after the exhibition of ergot to the mother in labor, vary very much in their condition and appearance from those born dead under

ordinary circumstances, and he attributes this difference not only to the mechanical causes, but, in many cases, "to the noxious influence of ergot exerted on the nervous system of the infant" through the mother. The distinguishing characteristics of the former state he indicates as follows: "general lividity of the surface, universal rigidity of the muscular system, producing the stiffened limbs and clenched hands in those infants in which life was extinguished, and the remarkable kind of alternating spasm and palsy which supervened in those which were resuscitated." These differential phenomena occurred, according to this author, after sufficient time had elapsed, in each case, to permit the influence of the ergot to permeate alike the maternal and the fœtal systems. It is not difficult to trace a marked analogy between the symptoms of ergotism thus manifested in the child, and the effects produced under ordinary physiological conditions, to be hereafter described.

The time occupied in the absorption of ergot through the healthy mucous membrane and tissues of the stomach, before it reaches the blood, is variously estimated. That it is rapidly taken up, under favorable conditions, is sufficiently clear. Thus it is stated by Churchill (Midwifery, p. 263) that sixty grains of the powder of ergot administered in tedious labor, will manifest effects in from five to ten minutes, "the pains becoming stronger, longer and more frequent." In experiments reported by Parola (Bibliothèque du Méd. Pract., p. 218) symptoms referable to the action of spurred rye were observed in a healthy adult male in two hours; and again in experiments on himself, nausea, headache, general lassitude and other indications of ergotism manifested themselves in one hour after taking fifteen grains of the powder. "Arnal's numerous experiments showed that the action of a drachm of ergot commenced within an hour." (Stillé—Therapeutics, vol. ii. p. 586.) Gubler states (Commentaires Thérapeut. p. 112) that "after an interval of ten minutes the characteristic phenomena of this convulsive poison may be seen to exhibit themselves." Upon animals the effects are much more rapid and decided. Well marked symptoms appear in from five to ten minutes, in the case of dogs, after the ingestion of large doses of ergot in powder. (Wright, op. cit.)

Of the changes which the drug undergoes in the stomach, before absorption, by which only the active and assimilable portion is selected, while the rest is rejected to be passed on through the intestines, we have no demonstration. Nor is it positive that the stomach is alone engaged in the process of elaboration and of absorption; it is tolerably certain, indeed, that the extensive mucous tract of the intestines, containing myriads of absorbents, may have some share. Whether, in this process, the tissues engaged in osmosis are subjected to any local effect, is also a question yet to be decided. It seems clear, however, that no positively irritant effect is produced, and that whatever local changes result, are only transitory and unimportant. "If the dose is sufficiently large, the subject is not slow in experiencing nausea and vomiting, which may be considered as symptoms of a promptly generalized action." (Gubler, loc. cit.) Applied externally to the skin, ergot does not appear to produce any sensible effects whatever, but if placed on an abraded surface it gives rise to profuse sloughing, the ulcers formed producing an abundant and offensive purulent discharge, and proving very slow to heal. (Wright, *Edin. Med. and Surg. Journal*, vol. liii. p. 8.)

There are, of course, conditions by which the absorption of this, in common with all drugs, is essentially modified. For example, the state of the system in general, whether of stimulation or of depression, the amount of the dose, the degree of its dilution when administered or subsequently in the stomach, depending on the relative fulness of that viscus, the idiosyncrasy, age, or habits of the patient, and, finally, the relative health of the medium of absorption, are all modifying conditions so obvious, and of such general application, that they need no extended discussion.

*Passage through the System.*—Once in the blood, the efficient constituent principles of ergot are conveyed by that fluid to every part of the system, thus exercising their legitimate effects everywhere, and giving rise to characteristic phenomena of action. What becomes of the drug in the passage through the system, whether its elements are resolved chemically, and used up in the blood, or are eliminated as they were absorbed, are questions yet open for solution. The experiments of Wright appear to indicate the presence in the blood of the oil of ergot, which Bonjean deems the poisonous element, but concerning the ultimate fate of this and of the other principles we are not yet enlightened. Nor do we know that any of the ordinary emunctories are concerned in the act of elimination. No increase of the secretions appears to indicate

the process, as is so plainly demonstrated with other agents, and we do not find functional or organic changes in the glands other than those referable to the general action. It has, however, been observed that the perspiration acquires a perceptibly sour odor after the injection of ergot. (Wright.)

We are equally uncertain concerning the time occupied by the processes of absorption and elimination, all observations being approximative only. Thus in labor, according to Trousseau and Pidoux (*Thérapeutique*—art. Ergot), the duration of the action of the drug varies from half an hour to an hour and a half. Prescot, after an analysis of fifty-nine cases, fixed the average duration of the effects at "an hour and a little more." But these sensible effects on the gravid uterus, although more obvious than phenomena developed elsewhere, do not probably indicate the only influence, or its actual extent and duration, while the cumulative effect is sufficiently shown by the symptoms in chronic ergotism, as well as by those pertaining to the nervous centres in the ordinary exhibition of the drug.

*Effects on the System.*—Experiments in this direction are reported in great numbers, although the results attained are essentially the same. A single observation recorded by Parola (*Bib. du. Méd. Pract.* p. 218) will suffice in illustration. "A single man, aged 24 years, tall, slender, lymphatic and always healthy, took one gramme and a half of powdered ergot; his pulse being at the time sixty-seven, and his respiration twenty. Two hours after, he felt general depression, shivering throughout the body, coldness of the surface with 'goose-flesh,' illness at the epigastrium, loss of appetite; pulse sixty, soft and feeble; countenance pale; pupil dilated. On the day following, he took another dose, with the same effects somewhat aggravated; and during the next forty-eight hours, a feeling of debility, with slow pulse, and diminished respiration, showed the lasting depressing effect of the drug." Gubler (op. cit. p. 113) enumerates the symptoms of acute ergotism as follows:—"Nausea and vomiting, pain in the abdomen, alvine dejections, dryness of the fauces, thirst, aversion to food, itching of the limbs, numbness, lassitude, heaviness of the head, vertigo, dilatation of the pupils, delirium, drowsiness, stupor, rarely acceleration of the pulse, almost always, on the contrary, diminution in the frequency and force, tendency to syncope, pallor and lividity of the face." Nor must we forget the specific action of ergot, that for which it was first employed, whether empirically or regularly, and which has given it nearly all the distinction which it possesses—its effects on the gravid uterus.

Experiments on the physiological effects on animals give results no less striking and interesting than those above enumerated. The numerous observations of Wright gave symptoms almost constantly identical; dilated pupils, convulsions, rapid pulse, staggering, paraplegia, prostration, coldness of the surface, death. The prolonged exhibition of ergot produced analogous phenomena, differing only in degree of intensity.

[To be continued.]

## A CASE OF HERPES ZOSTER OPHTHALMICUS, IN A PATIENT 80 YEARS OF AGE, CAUSING FATAL PROSTRATION; WITH REMARKS.

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(Continued from page 292.)

I think, very naturally, medical gentlemen may be inclined to doubt the correctness of my diagnosis in this case, or perhaps even the existence of so curious and sometimes so formidable a disease. I shall, therefore, in support of my views, take the liberty of here quoting gentlemen whose opinion and observation will be unquestioned. Mr. Jonathan Hutchinson, in the Royal London Ophthalmic Hospital Reports, says, of herpes zoster affecting one or all the branches of the ophthalmic nerve: "This most interesting disease has as yet received but little attention from writers on skin diseases, and, as far as I am aware, scarcely any from ophthalmic surgeons." "The disease is, I am persuaded, more frequent than is generally supposed. In proof of this I may mention that, during the last year, no fewer than three patients have consulted me in private on account of its effects. I have found most surgeons very incredulous as to this disease, and free in asserting that they had never seen it, and that it must be extremely rare. My conviction is that it is often misnamed. It is often considered to be erysipelas. Three patients who came to me with the unmistakable marks of herpes on one side of the forehead had been treated for a disease which had been said to be erysipelas, and several others in my series had also had a similar diagnosis given. Yet it is easy enough to distinguish the one from the other, if attention be once drawn to their differences. Herpes frontalis is always limited to one side—never transgresses the median line of the forehead and nose. It never affects the cheek, although there may