

must affect the frog otherwise than man and some other animals, as the dog, the horse, etc.

It is stated by Wharton Jones, Meuriot, J. Harley, and others, but denied by Nunneley, that belladonna, when applied to the web of the frog's foot, contracts the smaller arteries, producing at first acceleration of the circulation, followed after a time by complete stasis, beginning, according to Meuriot, in the veins and capillaries; "and the circulation always continues in the artery for some time after it has completely ceased in the vein." Harley says that contraction of all the arteries follows the administration of a moderate, but dilatation after a large, dose of belladonna; the contraction being due to stimulation, and dilatation to exhaustion of the sympathetic system, resulting from its previous over-stimulation.

Meuriot is of opinion that belladonna paralyzes the peripheral branches of the vagus nerve, and by this means accelerates the heart's action. Against this conclusion J. Harley advances several ingenious arguments, and considers the acceleration of the heart's action to be due to stimulation of the sympathetic. The action of belladonna on the pupil has been variously explained, some averring that it depends on paralysis of the third nerve supplying the iris; some teaching that it is due to excitation of the sympathetic; and others maintaining that this drug, by preventing turgescence of the vessels of the iris, produces the dilatation.

Brown-Séquard considers that the sympathetic nerves of the neck are divided into two sets, one for the pupil, one for the bloodvessels of the face and neck. The congestion of the face and conjunctiva, occurring after belladonna, has been attributed to paralysis of that set supplying the vessels of those parts; but as the pupil is, at the same time dilated, belladonna is considered to act as a stimulant to that part of the sympathetic system supplying the iris. J. Harley considers belladonna a stimulant of the whole sympathetic system; but that if its action is carried to excess, this system becomes exhausted, when dilatation of the vessels ensues and the face and conjunctiva become congested.

Brown-Séquard maintains, that both belladonna and ergot of rye, exert a powerful influence on the unstriped muscular fibres of the body, instancing the power of each drug to dilate the pupil, and to produce contraction of the uterus. He has seen the vessels of the pia mater of dogs contract after large doses of belladonna or ergot of rye, and he further states that both possess the property of lessening congestion of the cord; for, after full doses of either medicine, the reflex excitability of this part diminishes. Meuriot, on the other hand, maintains that belladonna intensifies the reflex function. Moreover, Brown-Séquard adds, that one drug acts especially on the involuntary muscles of one part, and the other chiefly on those of another part. Thus, he concludes that belladonna affects, especially, the pupil, bloodvessels of the breast (and so arrests the secretion of milk), muscular fibres of bowels, sphincter of bladder (and so removes nocturnal incontinence of urine [?]); while ergot acts especially on the muscular structure of the womb and bloodvessels of the cord.

Thus, many of the phenomena ascribed by Harley to stimulation of the sympathetic, are attributed by Brown-Séquard to the effect of belladonna on unstriped muscular tissue. These speculations have led Brown-Séquard to use belladonna and ergot in those forms of paralysis depending on chronic inflammation of the cord. By giving ergot internally, and by applying belladonna along the spine in the form of plaster or ointment, he seeks to contract the vessels and to lessen the supply of blood to the cord. Meuriot believes that belladonna depresses at first the function of the ends of a nerve and afterwards its trunk.

The influence of belladonna on the sympathetic, led Dr. R. T. Smith to employ it in two cases of exophthalmic goitre—a disease regarded by some as due to paralysis of the sympathetic of the neck. The effects were striking. Five minims of the tincture hourly, affording great relief in four or five days, though the disease had lasted more than a year. In two months time the exophthalmos had much lessened. Homœopathic doctors have long employed this treatment.

Belladonna is often used to relieve pain. Dr. Anstie considers it the best remedy to mitigate every kind of pain in the pelvic viscera. Some neuralgias, no doubt, yield to this medicine; it appears to possess most efficacy over neuralgia referable to the fifth nerve. Cases are recorded of relief afforded by it in sciatica.

Trousseau recommended the following method of treating neuralgia:—To administer one-fifth part of a grain every hour till giddiness is produced, and then to lessen the dose; but to continue the medicine for several days.

The same authority employed belladonna successfully in epilepsy, according to the following method:—“During the first month of treatment, the patient takes a pill, composed of extract of belladonna and powdered leaves of belladonna, of each one-fifth part of a grain every day, if his attacks occur chiefly in the daytime; or in the evening if they are chiefly nocturnal. One pill is added to the dose every month; and whatever be the dose, it is always taken at the same period of the day. By this means the patient may reach the dose of from five to twenty pills, and even more.” The dose is to be regulated by the circumstances of the patient. This treatment, it is said, even when it fails to cure, yields much relief.

Belladonna succeeds often in allaying both the cough and oppressed breathing of asthma. To ensure success, however, it must be employed in considerable doses, as Dr. H. Salter has lately pointed out, and the author has often verified his observations. Ten minims of the tincture every two or three hours, a quantity generally well borne, is often sufficient; but if any of the undesired symptoms of belladonna set in, the dose must be reduced. Sometimes far larger doses are required, where the patient is not very susceptible to the action of the drug. Thus, occasionally, half a drachm of the tincture hourly, is well and advantageously borne. A dose like this need only be taken at the time of the paroxysm; but when this lasts several days, the medicine should be given in the quantity recommended till an impression is made on the

disease. The effect is most often satisfactory, in either averting the attack or rendering it milder.

Belladonna is one of the best remedies for whooping-cough; but, to obtain any good from it, it must be employed in considerable doses, as in asthma. Thus, to children two and three years old, the author often gives as much as ten minims of the tincture every hour, and this quantity usually produces no effect, except on the disease, neither dilating the pupil, nor, so far as one can judge in children so young, making the throat dry; and it certainly does not in children a little older, who are able to express their feelings.

If drowsiness, delirium, or dilatation of the pupil occur, of course the dose must be diminished. The only symptom the author has witnessed from these large doses is dilatation of the pupil. Children, it is well known, bear belladonna much better than adults; and this fact accounts for the slight effect of so large a dose, and for the small influence which a less quantity exerts on whooping-cough—a disease of childhood. Some writers state that children become rapidly accustomed to belladonna. These large doses, however, may be given at first, and though I have employed these ample doses in a very considerable number of cases, I have never had to give less on account of any toxic effects. Under these doses the severity and frequency of the cough is often much reduced, even during the period when it is most violent and convulsive. But, like all other remedies in this disease, belladonna is of little use if the child is exposed to cold and cutting winds. If the weather is cold, the child should be confined to the house in a warm room; if the weather is mild, outdoor exercise is, of course highly beneficial; but cold must be most carefully avoided.

While there can be no reasonable doubt of the great efficacy of belladonna in many cases of whooping cough, it must be admitted that in many instances, without apparent reason, it seems of no avail. Influences at present not understood appear to modify its effect; for in some epidemics it is very successful, while in others it appears to be inoperative.

Belladonna exerts but little effect on whooping-cough, when bronchitis or any irritation exists, as that from teething, worms, etc. If the gums are red, swollen, and painful, they must be freely lanced, and the other sources of irritation removed. Belladonna is considered of especial use at the third week of the attack,—at a time, that is, when the febrile stage has passed away, and the violence of the convulsive attacks is declining.

Belladonna is often useful in other coughs, although with our present knowledge on this subject it is impossible to lay down precise rules for its employment.

It is often useful in certain forms of headache. The indications for its use are when the pain is situated over the brows and in the eyeballs, which seem as if too large for the head, and as if they would be forced out of the skull. These headaches are not due to stomach or uterine derangements; indeed, very often their cause cannot be discovered. Sometimes they seem due to weakness and overwork, being met with especially in young women. Three minims of the tincture should be given every three hours.

It is said that belladonna controls the delirium of fevers—as of typhus fever.

Belladonna is both speedier and more certain than any other remedy in removing that troublesome affection, incontinence of urine of children. It must be given in doses of from ten to twenty drops of the tincture three times a day; for small doses often fail, when large ones at once succeed. It may take a fortnight to succeed. Sometimes the incontinence is not limited to the night, but may trouble children during the day. These severe forms will often yield to belladonna; but while in fitting cases it is thus effectual, still it often fails altogether, although no worms infest the intestines, no irritation exists about the rectum, and no reason seems to exist to account for its failure. Strychnia, cantharides, turpentine, santonine, or galvanism, should then be tried.*

* In nocturnal incontinence the child should drink but little some hours before going to bed, and he should be waked in the middle of the night to pass water.

It sometimes checks the incontinence of urine of the old or paralytic.

Belladonna, used internally or externally, is certainly efficacious in erysipelatous inflammation. It may be given in combination with aconite; but when the skin is hot and pungent, and the pulse firm and resistant, aconite exerts over this inflammation an influence far more potent than that of belladonna.

Belladonna has been recommended as a preventive of scarlet fever, but so much prejudice has been introduced into this question, that it is difficult to ascertain whether it has any prophylactic virtue.

Belladonna has been found of service in the treatment of seminal emissions; a grain and a half of sulphate of zinc with a quarter of a grain of extract of belladonna, three or four times a day, is a successful remedy in most cases of nocturnal emissions.

As belladonna and opium are in some respects reciprocally opposed in their action, as on the eye, etc., it has been assumed that they must be opposed in every particular, and that one may be used as an antidote to the other. Many cases are adduced of opium poisoning, where the symptoms although very serious, were apparently removed by belladonna, and *vice versa*. Dr. Erlenmeyer is of opinion, that, in respect to their action on the brain, these agents are antagonistic, and that no coma will result when they are administered conjointly; but that they exercise no mutual counteractive influence on the sensory nerves, and hence he recommends them in combination to relieve pain. On the other hand, some authorities, among whom may be named Brown-Séquard and J. Harley, dispute this antagonism, on the ground that the cited cases are insufficient to prove it; and it has not been observed in experiments made on man and the lower animals.* The reported cases in favour of this antagonism have been severally criticised by Harley,

* But it must be remembered that these drugs so diversely affect animals and man.

who points out that many were treated by other remedies besides belladonna; in others, a fatal dose is not proved to have been taken; and the patients who recovered did not improve sooner than if no belladonna had been administered. Harley's conclusions, which are in most respects directly opposed to those of Erlenmeyer, are—"1. That in medicinal doses the essential effect of morphia (hypnosis) is both increased and prolonged by the action of atropia, whether induced previously or at any time during the operation of the former. 2. That atropia relieves, and, if given simultaneously or previously, prevents the nausea, vomiting, syncope, and insomnia, which frequently result from the action of opium. 3. That in a sufficient proportion (for most individuals one forty-eighth part of a grain of sulph. atropia to a quarter of a grain of acetate of morphia) atropia neutralizes the contractile effect of opium on the pupils; but in larger doses dilatation takes place, as if no morphia had been given. It is also to be observed that if the quantivalent doses are *successively* introduced, the drug last administered exhibits for a short time a counteracting effect. 4. That all the other effects of atropia are intensified and prolonged by the action of morphia, induced previously or at any time during the operation of the former. If, however, the dose of atropia be small, and the morphia produce considerable deranging effects on the vagus, the rapidity of the pulse is not greater than when the atropia is administered alone." Had Harley given opium in a dose just sufficient to destroy life, and then, if death had ensued after the employment of belladonna, he would have proved that belladonna would not arrest the fatal effect of opium, and *vice versa*. In no reported instance did he use enough of either substance to destroy life; hence his observations are not so convincing as they might have been; but as the coma from opium was intensified by belladonna, his observations are valuable.

On the other hand Dr. Johnston of Shanghai, who during his residence in China, has had striking experience of opium poisoning, having treated in various ways upwards of 300

cases, speaks in the strongest terms of the antagonism between opium and belladonna. It is in the worst cases of poisoning, he says, that atropia displays its wonderful effects; for instance where the immoveable pupils are contracted to a pin's point, the conjunctiva insensible to touch, the face pale, the lips, eyelids, and nails livid, the pulse weak and irregular, the breathing slow and stertorous, the extremities cold; he injects half a grain of atropia, then in ten or twenty minutes the pupils begin slowly to dilate, and in an hour or so the face becomes flushed, the breathing soft without stertor, and the pulse stronger. If within two hours the dose fail to produce these restoring effects, he repeats the injection. Where the coma is less profound he first employs a quarter of a grain of atropia.

Amid all this diversity of opinion, it must be admitted that, on the subject of this antagonism, more proof is needed. But while there is room for doubt concerning the antagonism between opium and belladonna, the interesting experiments of Fraser have demonstrated beyond question that atropia is an antidote to physostigma. He experimented on dogs and rabbits; but, as the action of these substances on man and animals is identical, he concludes that atropia will neutralize the fatal effects of physostigma on human beings. His experiments were conducted in three ways: (1) He administered the atropia before the physostigma; (2) He administered them together; (3) He administered the physostigma, and, after the animal was completely paralyzed, he injected atropia. In each series of experiments atropia averted the fatal effects of physostigma, although physostigma was employed in fatal quantities, as was afterwards proved by administering to the animal the same or a smaller dose by itself, when in every instance the animal speedily died. Fraser concludes that "the lethal effects of doses of physostigma greatly in excess of the minimum fatal, may be prevented by doses of atropia greatly below the minimum fatal." He recommends, "in treating cases of poisoning in man, the sulphate of atropia should be given by subcutaneous injection, in doses of from

one-fiftieth to one-thirtieth part of a grain. The exhibition of the antidote should be persevered with, in repeated doses, until the pupils are fully dilated and the pulse rate increased, and probably also until the hypersecretion of bronchial mucus, which greatly impedes respiration, is completely checked."

He thus summarises the antagonism between these two substances: "That physostigma increases the excitability of the vagi nerves, while atropia diminishes and suspends this excitability; that physostigma diminishes the arterial blood-pressure, while atropia increases it; that physostigma greatly augments the secretion of the salivary, bronchial, intestinal, and lachrymal glands, while atropia diminishes and even completely checks these secretions; and that physostigma contracts the pupils, while atropia, to a much greater relative extent, dilates them. Besides these effects of the action through the blood, various opposed topical effects have been observed, among which is the contraction of the veins by physostigma—the existence of which rests on the high authority of Mr. Wharton Jones—and the contraction of the arteries by atropia."

Dr. Fraser has recently published some further experiments on the antagonism between physostigma and atropia, being led to this investigation by the following considerations. While no doubt the more active and poisonous effects of physostigma are antidoted by atropia, still it seemed possible that physostigma might possess some properties—might affect some part of the body in a manner not opposed by atropia—and both poisons might possibly possess certain properties in common, so that while some of the poisonous properties of each substance being antagonistic, other poisonous properties might not be opposed, nay, might be similar in kind and assist each other. His experiments confirm these conjectures. Thus he found that after a minimum fatal dose of physostigma death could be averted by a dose of atropia varying greatly in quantity; but as he increased the dose of physostigma so the range of antidotal doses of atropia became diminished, and that so far from requiring a larger

maximum antidotal dose, the greater the quantities of physostigma administered the smaller became the maximum antidotal dose of atropia, till at last a point was reached when atropia ceased to avert death. For instance, with a minimum fatal dose of physostigma a dose of atropia varying from nine-thousandth to five grains prevented the rabbit's death; but on increasing the dose of physostigma to one and a half times the minimum fatal dose the antidotal dose of atropia ranged from one-fiftieth of a grain to four grains; and on augmenting the dose of physostigma to two and a half times the minimum fatal dose, the antidotal dose of atropia ranged from one-fortieth to two grains and a half. With three and a half times the minimum fatal dose of physostigma the range of atropia sufficient to avert death was reduced from one tenth of a grain to one-fifth of a grain, and with four times the minimum fatal dose of physostigma, atropia failed to avert death. Here, while atropia prevented the more powerfully fatal effects of physostigma, yet on increasing the dose of this drug a point at last is reached when its properties not antagonized by atropia become fatal. But the fatal issue is due not only to increasing the non-antagonized properties, of physostigma, for the range of an antidotal dose of atropia became lessened as the dose of physostigma was increased, showing that the atropia, assisted the physostigma. This fact is also shown by the experiment of injecting simultaneously one half the minimum fatal dose of each substance, when the animal died.

The foregoing experiments, moreover, make it apparent that atropia is an antidote for only a given quantity of physostigma, and that, if the physostigma is increased, a quantity at last is reached the more active properties of which no doubt are neutralized by atropia, but the other properties in conjunction with similar ones of atropia are sufficient to cause death.

It is a most singular fact that while the minimum fatal dose of extract of physostigma is 1·2, and that of atropia at 22 grains, yet nine-thousandth of a grain of atropia injected five

minutes before a minimum fatal dose of physostigma prevents its fatal effects, in fact a quantity of atropia which produces no perceptible effects can avert many of the serious effects of a fatal dose of physostigma.

Although it is experimentally proved that atropia can avert death from physostigma, it yet remains to be proved that physostigma can prevent death from atropia.

Dr. Fraser conceives that "with regard to the counteracting actions themselves it is to be observed that various of the facts mentioned in the record of experiments (of his paper) tend to make mutual antagonism, probable not only of one, but of several of the actions of physostigma and atropia; and it is legitimate to suppose that with a given dose of physostigma, the counteraction produced by a certain amount of atropia will be more perfect in the case of one or more of the antagonistic actions, than in that of others; and that with certain doses of the two substances such incompleteness of counteraction may exist as would even without the occurrence of *non-antagonized* action suffice for the production of death."

Preyer maintains that atropia, by paralyzing the peripheral branches of the vagus nerve, will prevent the arrest of the heart's contractions by hydrocyanic acid; and is thus an antidote to prussic acid.

That atropia is separated from the body in part by the urine may be proved by putting into the eye some of this secretion voided by one to whom belladonna has been given. J. Harley states that within two hours atropia is separated from the body, as none is to be found in the urine after that time.

Dr. Garrod has shown that caustic fixed alkalies destroy the active principle of belladonna, hyoscyamus, and stramonium, but that carbonates and bicarbonates of potash and soda do not destroy it. Lime-water too is equally destructive; hence it has been recommended as an antidote in poisoning by belladonna. (J. Harley.)

STRAMONIUM.

STRAMONIUM produces symptoms very similar to those induced by belladonna. A stramonium ointment, made by mixing half a pound of fresh stramonium leaves with two pounds of lard, and gently heating till the leaves become friable, then straining through lint, is used spread on lint and applied thrice daily at the Middlesex Hospital to relieve pain. Stramonium, smoked with or without tobacco, is mainly used to reduce spasm in asthma. It is especially useful in pure asthma, that is, when the lungs are structurally free from disease, and is useless when the dyspnoea is owing to heart disease. Twenty grains of the dried leaves, or ten of the powdered dried root, may be smoked, inhaling meanwhile into the lungs; or the fumes puffed into an inverted tumbler until it is filled may be placed over the mouth, and the contents inhaled by a deep inspiration. It excites a good deal of cough. The inhalation may be repeated again and again. It is preferable to smoke the plant unmixed, as few persons can draw the fumes of tobacco into the lungs without great discomfort. There is no doubt that stramonium is very successful in many cases of asthma; but in others, without apparent reason, it fails; and even when it succeeds, its influence, gradually diminishes by use. Sometimes *datura tatula* succeeds when *datura stramonium* has failed. Dr. Salter believed that stramonium often failed, owing to the badness of the preparation, and he advised asthmatics to grow and prepare their own stramonium. Its effect is more manifest when employed at the very commencement of an attack, affording but little relief when the paroxysm is fully developed, cold stramonium smoke can sometimes be inhaled when the hot is intolerable. It has been used in neuralgia.

Like belladonna and hyoscyamus, its active principle, as Dr. Garrod has shown, is destroyed by caustic potash and caustic soda.