GULSTONIAN LECTURES

ON THE

PHYSIOLOGICAL ACTIONS AND THERAPEUTICAL
USES OF CONIUM, BELLADONNA, AND
HYOSCYAMUS, ALONE AND IN
COMBINATION WITH OPIUM.*Delivered at the Royal College of Physicians, London.*

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LECTURE II.

The Physiological Action and Therapeutical Uses of Belladonna.

OBSERVATIONS were made upon man, the dog, and the horse. The effects following the subcutaneous injection of increasing doses of sulphate of atropia in man were first considered. The fiftieth of a grain of this salt is usually sufficient to produce the full effects of the plant; and, briefly summed up, the following are the effects of a full medicinal dose:—An acceleration of the pulse from twenty to seventy beats, with a slight increase in its volume, and a considerable increase in the force of the cardiac and arterial contraction; a general diffusion of warmth throughout the cutaneous surface; a slight throbbing or heaving sensation in the carotids; a slight feeling of pressure under the parietal bones; giddiness, heaviness, and drowsiness, or actual somnolency, accompanied by a tendency to quiet dreamy delirium and nervous startings; complete dryness of the tongue, roof of the mouth, and soft palate, extending more or less down the pharynx and larynx, rendering the voice husky, and often inducing dry cough and difficulty of deglutition; a parched condition of the lips; occasional dryness of the Schneiderian and conjunctival mucous membranes; and increasing dilatation of the pupils.

After continuing about two hours, the dryness of the mouth suddenly gives way to a viscid, sticky, acid secretion, of a peculiar and very sickly offensive odour; and the mouth becomes foul and clammy, and the tongue usually covered with a white fur. A short time before moisture returns to the mouth, the pulse is observed to fall, and it now rapidly resumes its ordinary rate and character. The pupils have now reached the maximum degree of dilatation; but they will still contract to a fourth, sixth, or even eighth of an inch, varying according to the original dimensions of the pupil, when exposed to the brightest light.

During the action of the medicine, there will be a slight elevation of the temperature of the surface, rarely exceeding one degree; and a still slighter and less appreciable rise of the internal temperature of the body. No difference will be observed in the rate of respiration, except, as may happen in a nervous woman, a little emotional excitement on the sudden accession of the giddiness. The breathing will be as tranquil as before the injection. The patient occasionally heaves a deep sigh, or more frequently gives a prolonged yawn as he sits still in a dull, apathetic, or drowsy condition.

After the pulse has resumed its ordinary rate, and the mouth has moistened, the giddiness and drowsiness pass off, and the patient appears tolerably lively and brisk in mind and body; but he will himself continue to feel for some hours longer such languor of body and mind as will render him incapable of active bodily or mental exertion. A little dimness of vision also remains; and occasionally there is so much, that the patient is unable to thread a needle or even to read.

As far as I have observed, headache, either during the action of the medicine or afterwards, is a rare and exceptional occurrence. The desire for food returns soon after the operation of the medicine; but, during its action, insalivation and deglutition are almost, if not quite, impossible.

If a larger dose than is sufficient to produce the above symptoms be given, there will be superadded a fluttering sensation in the cardiac region; slight delirium, manifested by picking and other motions of the hands and fingers in the air, as if they were in contact with real objects; muttering and smiling; staggering, or complete inability to walk.

The same symptoms, including acceleration of the pulse, follow the administration of belladonna or its active principle by the alimentary canal. The operation of thirty minims of a succus belladonnæ prepared by Messrs. J. Bell and Co. was noted in six adults, male and female. The belladonna action was fully developed in all within an hour. The

pulse in one was accelerated only 10 beats; in another, 20 beats; in a third, 26 beats; in two others, 40 beats; and in the sixth, a youth of twenty, the cardiac systole was more than doubled, the pulse rising from 60 to 140 beats. Associated with this acceleration of the pulse, the other effects of belladonna were fully developed; but there was no observable increase in the respiratory movements. The sixth individual, in whom the acceleration of the pulse amounted to 80 beats, did not, throughout the three-quarters of an hour during which this maximum acceleration of the pulse continued, outwardly manifest nor express the slightest excitement; the respirations never exceeded 18; and at the time when the cardiac excitement first reached its acme, and afterwards, the respirations numbered 15 or 16, and were natural and easy. Hence it is clear, first, that belladonna has no action on the vagus nerve; and secondly, that its effects are precisely the same, whether it be administered by the skin or by the stomach.

Certain conditions which interfered with the action of belladonna were then lightly touched upon.

1. Children, as Dr. Fuller has observed, are remarkably insusceptible to the action of belladonna. They occasionally bear very large doses before dryness of the mouth or cerebral effects of any kind are produced; but, as far as I have observed, the stimulant effect upon the heart and the dilatation of the pupil are as readily induced in young people as in adults and old people.

2. Amongst adults of apparently equal vigour, some are more susceptible to its action than others; and the ninety-sixth of a grain will sometimes produce as much effect upon one individual as double that quantity upon another.

3. The influence of pregnancy is doubtful; but, in a patient now in the sixth month of her pregnancy, I have used atropia subcutaneously a great many times; and the thirty-fourth of a grain never produced in her case greater effects than the forty-eighth of a grain in most other individuals.

4. The fixed alkalies, as Dr. Garrod has observed, by decomposing the active principle, annul the operation of belladonna. This, however, only occurs after a time; for, if the caustic alkali was mixed with the belladonna or atropia only a few minutes before it was administered, it in no way interfered with its action. Further, caustic ammonia and lime-water have the same destructive action upon atropia; and the latter, used in large quantities, promises to be the appropriate antidote in cases of belladonna-poisoning.

Elimination.—The kidneys are active in the elimination of atropia from the minute when it enters the blood until it is entirely removed from the system. In the case of a full medicinal dose, about two hours are required for this purpose. Availing myself of its dilating action upon the eye, I have repeatedly demonstrated the presence of atropia in the urines of different individuals, eighteen, nineteen, and twenty minutes after the subcutaneous injection of the forty-eighth and even the ninety-sixth of a grain of sulphate of atropia. This fact is readily demonstrated by dropping into the eye, at intervals of ten or twenty minutes, for two or three hours, one or two drops of the urine. Twelve drops of eight ounces of urine secreted during the two hours and a half that the patient is under the influence of the forty-eighth of a grain of the salt, will be sufficient to dilate the human pupil from one-tenth to one-sixth of an inch in diameter. That the ninety-sixth of a grain of sulphate of atropia—a quantity doubtless insufficient to destroy an infant—may be detected in the urine, is a fact of considerable importance in a medico-legal point of view. Nature, moreover, will commonly aid us in our search by retaining the urine within the bladder for our examination.

In ten patients, the urines secreted immediately before and during the operation of the medicine were analysed. The result was uniform. During the action of the belladonna, the urea and the sulphates and phosphates were increased; and, as a rule, the chlorine was proportionately diminished. The increase of the urea was disproportionate to, and considerably less than, that of the phosphates and sulphates.

The following analyses will show the results of the operation of belladonna upon the system, as indicated by the proportion of the solid constituents of the urine. It is to be observed, that no food was taken between 3.30 P.M. and 10.30 P.M.; and that the urine passed at 9.45 P.M. was excreted at the end of a long fast. While the amount of water remained normal, the solid constituents are observed to have undergone such an increase during and for some hours after the belladonna-action as to exceed that of the chylous urine voided at 7.30 P.M.

Thomas F. R., aged 28, the subject of chronic albuminuria. No cedema. All the urines had the same general characters—freely acid, light sherry-coloured, bright and clear, and free from any microscopical elements.

Urine passed at 8 A.M., on rising, being the quantity secreted from 11.45 A.M. to 8 A.M. next day, f. 3x; specific gravity 1015.6. 1000 gm.

measures contained—chlorine, 2.62 grs.; urea, 13.33 grs.; phosphates and sulphates, 7.2 grs.; albumen, 0.52 gr. Uric acid normal.

Urine passed at 6 P.M. the same day, two hours and a half after a hearty dinner, f. 3vii.; specific gravity 1022.8. 1000 gr. measures contained—chlorine, 4.92 grs.; urea, 20 grs.; sulphates and phosphates, 9.71 grs.; albumen, 1.30 gr. Uric acid normal.

Urine passed at 7.30 P.M., immediately before the injection of one-fortieth of a grain of sulphate of atropia beneath the skin, in quantity f. 3iii4, being all secreted since 6 P.M.; specific gravity 1023.2. 1000 gr. measures contained—chlorine, 4.64 grs.; urea, 22.33 grs.; phosphates and sulphates, 10 grs.; albumen, 3.34 grs. Uric acid, an excess.

Urine passed at 9.45 P.M., two hours and a quarter after the injection of the atropia, and when its operation had declined, f. 3liiss; specific gravity 1021.8. 1000 gr. measures contained—chlorine, 4.50 grs.; urea, 23.33 grs.; phosphates and sulphates, 11.06 grs.; albumen, 3.29 grs. Uric acid, an excess.

Urine passed at 9 A.M. next day, being all that was secreted from 9.45 the previous evening up to this time (a basin of soup, a little bread, and four ounces of light beer, were taken at 10.30 P.M.), f. 3xivss; specific gravity 1023.6. 1000 gr. measures contained—chlorine, 3.33 grs.; urea, 28.33 grs.; phosphates and sulphates, 13.95 grs.; albumen, 1.44 gr. Uric acid, an excess.

It appears from the foregoing observations that the operation of belladonna is very closely allied to, if it be not identical with febrile action, such as occurs in meningitis, in enteric or typhus fever, etc.

How far the action of belladonna illustrates the causation of the febrile condition, is a question of the highest interest. If we take the simplest view of the action of belladonna, it is that of direct and powerful stimulation of the sympathetic nervous system; and indeed, in children and many of the lower animals, this is so far the chief effect, that it may be regarded as almost the only one. During the operation of medicinal doses of belladonna the heart contracts with increased vigour, the arteries increase in tone and volume, and the capillary system fully participates in this general excitation of the circulation. A diffusion of warmth is felt throughout the body. The increase of the urinary constituents I assume to be the result partly of the excitement of the nervous centres, and, in medicinal doses, those of the sympathetic system almost entirely; and partly of the increased flow of blood through the kidneys; the former action resulting in an increase of phosphates, and the latter in an increase of the urea. The increased oxidation required in the process is a necessary consequence of the increased flow of blood through the lungs. I have already stated that belladonna does not affect the respiratory movements; but there can be little doubt, I think, that the lungs themselves are quietly eliminating an increased quantity of carbonic acid from the blood as it is rapidly passing through them.

Atropia, as we have seen, is in the true sense of the word a *diuretic*, and a more powerful one probably than any other that we possess. It does not appear to diminish any of the special secretions, not even the saliva. The inner surface of the cheeks and lips, and sides of the tongue, where the simple racemose glands chiefly reside, are rarely or never dried during the action of belladonna; and in one patient, who suffered from intense neuralgia of the temporal ramifications of the fifth nerve, associated with such excitation of the sublingual glands, if not of the submaxillary also, as to result in perpetual slobbering, the secretion from these glands was in no way diminished when, as occasionally happened, a severe paroxysm of pain occurred during the operation of atropia. The drying of the mucous membrane of the upper part of the alimentary and respiratory passages, and the exudation of the strongly acid and peculiarly offensive and sticky secretion upon these parts are facts difficult to explain. The distribution of four distinct nerves to the tongue is remarkable, and an explanation of the above-mentioned phenomena must be doubtless attributed in general terms to some disturbance of the reciprocal actions of the gustatory and sympathetic, and probably of the glosso-pharyngeal also. That belladonna can *moisten* the tongue as well as *dry* it, is a fact which I have several times observed. A quarter of an hour after injecting a small dose of atropia beneath the skin of a patient suffering from typhus, I have seen the tongue, which has been for days hard, parched, and cracked, swell out again and become moist. But this favourable change is only of short duration.

Other points connected with the operation of belladonna, such as dilatation of the pupil, are too well known to require any consideration here. But I cannot leave the subject without mentioning one interesting fact which I have several times witnessed, as showing the antagonism of the sympathetic and third nerves, in the dilatation and contraction of the pupil. Just at the time when the dilatation of the pupils was beginning, after a dose of belladonna, I have called in the patient from

a subdued light, and placed him at a distance of three or four feet from an ordinary gas-lamp. On examining the pupils, I have now and then been astonished to find them decidedly smaller than they were under the same circumstances before the injection. This contraction has persisted for several minutes, when all at once the pupil has given way and become broadly dilated. It would seem from this observation, as if the third nerve had been roused to unusual exertion just at the time when the increasing influence of the sympathetic began to be first felt, and that the sudden stimulus of light had called forth its opposing energy to such a degree that for a few minutes it was able to repress the rising force of the sympathetic, which a little later on would become overpowering.

Therapeutical Use.—A study of the physiological action of belladonna has led me to regard the plant in a new light as a curative agent. First and foremost, it is a direct and powerful stimulant to the sympathetic nervous system, or, in other words, to the heart. Secondly, it is a potent diuretic. Thirdly, by virtue of its stimulant action on the circulation, it is a means for increasing the oxidising processes within the body. Its influence as an anodyne is so fully acknowledged, that I shall omit consideration of this action upon the present occasion.

First, as a *cardiac stimulant*. It is remarkable that this, the primary and essential operation of belladonna, should have been so long neglected. This plant should stand at the head of all our stimulants; for there is no medicine in the whole *materia medica* which at all approaches belladonna in its simple, direct, immediate, and powerful influence in exalting the force and rapidity of the heart's action. In all conditions and diseases, therefore, in which there is a depression of the sympathetic nervous influence, such as syncope from asthenia, or shock; in the collapse of cholera; in failure of the heart's action from chloroform or other cardiac paralyzers—the subcutaneous use of sulphate of atropia, in doses varying from the hundredth to the fortieth of a grain, is the appropriate and most hopeful means of resuscitation.

With a view more of ascertaining the influence of belladonna in progressive failure of the heart's action in inanition, than of hoping for a permanent good result, I injected the two-hundred-and-fortieth of a grain of sulphate of atropia into the arm of an infant ten weeks old, at a time when, excepting a few beats now and then, the pulse was imperceptible at the wrist, and the cardiac systoles only 80. Within four minutes, the pulse rose to 100, and each beat was quite perceptible at the wrist. In eight minutes, it had increased to 110, and was quite regular and distinct. The stimulant continued for the next three hours; and at the end of this time the pulse was 100, of good volume, and of sufficient force to bear compression without obliteration. The respiration remained unaltered, and the pupils dilated from one-twelfth to one-seventh of an inch. The stimulant effect upon the pulse continued to within half an hour of the death of the child, five hours and a half after the injection of the atropia.

As a *diuretic*, belladonna may be used in cases of *suppression of urine*, whether accompanied by uræmic symptoms or not. As both the sluggish circulation and the torpid kidney are simultaneously aroused by the medicine, there is ground for expecting a restoration of the renal secretion.

In *acute nephritis*, we may hope for beneficial results from the use of belladonna, which, coming in contact with the irritated and congested organ, will doubtless calm the nervous irritation, and at the same time contract the dilated blood-vessels. I am at the present time busily employed in determining the effects of its operation in congested and inflammatory conditions of the kidney; and, so far as my experience goes, I am led to expect beneficial results in both states.

In *chronic albuminuria*, belladonna, I believe, will prove very serviceable, provided that the kidney has not passed into the degenerative stage bordering on fatty degeneration. In one case, Charles E., aged 35, who had been under my care for three months for an acute attack of nephritis, commencing with excessive cedema of the legs and exudation of albumen, I administered a single dose of atropia with the following result. On the 10th of January, he had so far improved under the influence of astringent chalybeates and hydragogue purgatives, that there remained but slight pitting of the integuments over the tibia; and the urine, when boiled and heated with nitric acid, gave only a small precipitate of albumen—enough, however, to render the fluid completely opaque from the presence of small flocculi of albumen. At 8.30 P.M. on the day above mentioned, I injected the forty-eighth of a grain of sulphate of atropia beneath the skin; and he passed at that time urine A. The atropia produced full effects; and at 10.30 P.M., when these had passed off, he voided urine B with some difficulty and in small dribbles. Urine A had a specific gravity of 1022.4, and contained exactly a grain of albumen in 1000 grain measures. Urine B was of specific gravity 1024.4, and contained only half the quantity of albumen present in urine A. Four days afterwards, the patient presented himself at the hospital, and reported himself quite well. The

cedema of the legs was entirely gone. He passed urine in the pre-scribing-room; and repeated examination by my clerks and myself showed that the albumen had quite disappeared. The patient has not attended since, from which I infer that he continues well. He had presented himself regularly at the hospital the previous three months, and the urine was regularly examined. The albumen was observed to be slowly diminishing in quantity, but it had never been absent from the secretion. It appeared, in this case, that the kidneys had received a sudden impulse to healthy action.

In another case, that of John B., aged 25, who had been under my care for two years continuously for acute, passing into chronic albuminuria, the albumen, which had long been stationary, began to decrease rapidly in amount under the influence of the same treatment.

The effect of a powerful dose of atropia upon the kidneys in chronic albuminuria is well seen in the analyses above given. It will be observed that there was a decided diminution of the albumen during the operation of the medicine. The result by the operation of belladonna in these cases must be accepted as the best proof of the condition of the blood-vessels generally during that operation. It is quite clear that there is no impediment from contraction of the arteries on the one hand, or from dilatation of the capillaries on the other, to the flow of blood through the kidney. On the contrary, it appears that the vessels of the gland are aroused by the action of the drug into a healthy state of excitement; a condition highly favourable for the nutrition of the organ, and the removal of chronic disease. As a means of promoting oxidation of the blood, belladonna will doubtless prove of essential service in the uric and lactic acid diatheses. I have employed it in rheumatic fever with marked success. I inject the fiftieth or fortieth of a grain of the atropia salt into the integument over the affected joint, as soon as the first indication of inflammatory action arises in the part. The anodyne action is so direct, speedy, and enduring, that the use of opium, which, excepting for its anodyne and hypnotic actions, is decidedly objectionable in this disease, is altogether unnecessary. The subcutaneous use of atropia in other acute diseases is a wide field for inquiry, and promises, as far as my observations extend, to be a most interesting and encouraging one.

FURTHER OBSERVATIONS ON THE CÆSAREAN SECTION.

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INFANTILE MORTALITY.—Infants *in utero* may die during pregnancy from disease within their own bodies, or from any morbid cause existing in the placenta or funis which can interrupt the supply of blood from the maternal system. Undue protraction of labour is extremely hazardous to the lives of infants, and especially so after the discharge of the liquor amnii. The five infants which are stated to have been dead were so before the performance of the operation. Of this number, two were doubtless destroyed by long continued pressure during protracted labour. One presented with the arm, for the delivery of which manual and instrumental attempts had been unsuccessfully made. One presented with the feet, in which case, after drawing down the body, craniotomy was performed; and afterwards the body was dragged away by the feet, leaving the perforated head behind. In another, craniotomy was unsuccessfully performed. It is quite evident from the above statement, that there is not a single infantile death which was caused, either directly or indirectly, by the operation; and there is little doubt that all of them would have been saved, if they had been living at the time of its performance.

OPERATION.—I shall not here enter into all the details which are requisite to be observed before, during, and after this operation; but I shall confine my remarks to some of the more important points. (See observations, *BRITISH MEDICAL JOURNAL*, vol. i, 1865, p. 263.)

Frequent examinations *per vaginam* are extremely injurious, from the contusions which the vagina and pelvic tissues sustain. There are cases recorded which forcibly prove the necessity of this precaution. When the uterus is deflected, as it generally is in cases in which there is extreme distortion of the pelvis from mollities ossium, this organ must be raised up before the incision is made; so that the fundus, which abounds with large anastomosing veins, may not be incised. Neglect of this rule doubtless would produce hæmorrhage by the division of this portion of the uterus, which is so vascular and eminently contractile, and consequently would interrupt the efficient contraction of

the organ, which is so important to produce a nice adaptation of the edges of the wound, and thereby, in some measure at least, to prevent it from assuming the gaping character which occurred in some of the tabulated cases.

Labour unduly protracted, from any cause whatever, is nearly always attended or followed by some danger to either the mother or to her infant, or to both. The degree of mischief inflicted on the maternal structures is in general in a ratio proportioned to the period of protraction; and, doubtless, in all cases it is aggravated by the nature of the obstructing cause. We ought, therefore, to be extremely watchful, in all cases of protracted labour, but especially so when the impediment arises from a mechanical cause; and we should timely adopt appropriate measures for the delivery of the woman before irreparable mischief is done. (See former observations, *BRITISH MEDICAL JOURNAL*; also Cases of Laceration of the Uterus, etc., *Obstetrical Transactions*, London, vol. viii, p. 210.)

In ordinary labours, where the infant can pass *per vias naturales*, certain organic changes are waited for; the os uteri must be more or less dilated; but, in those cases which demand the Cæsarean section, it is not only a very great folly to wait, as dilatation cannot be effected, but it is a very great evil.

An early performance of the operation is of the utmost importance. Supposing the woman at full term of pregnancy, it should be commenced as soon as the labour is declared—before, or at least immediately after, the membranes are ruptured. By so doing, the uterine incision would be relatively considerably diminished after the complete contraction of the uterus, and all the dangers of protraction avoided. My friend Dr. Greenhalgh has suggested the performance of this operation before the completion of pregnancy. He says: "I have a strong conviction that greater success would attend our endeavours if all cases were operated upon at, or shortly after the completion of, the eighth month of utero-gestation, when the vessels are smaller, the contractile power of the uterus greater, and the liquor amnii relatively larger in proportion to the size of the child. By pursuing such a course, a smaller incision would be required, less blood would be lost." I am inclined to agree with the above suggestion, especially if the obstructing cause of labour be epithelioma of the os or cervix uteri. Two successful cases are recorded (p. 14) in which the operation was performed before the completion of pregnancy—one at the end of the eighth month, by Dr. Greenhalgh; the other at six and a half to seven months, by Dr. Newman. There is, however, one objection, either real or imaginary, against having recourse to the operation before the completion of pregnancy, when the os uteri is closed by the mucous plug, and the cervix is undeveloped; which condition would tend to prevent the lochial or other fluids from issuing from the cavity of the uterus. In consequence of this opposition, the fluid would accumulate up to a certain amount, and then be discharged into the abdominal cavity. Such an event happened (closing of os and cervix uteri) on the second day after the operation in Case 95. Care must, however, be taken to keep open, if possible, the oral and cervical portion of the organ by some means or other.

Before the incision is made, it is of great importance to ascertain the location of the placenta. Its position in sixteen cases was as follows. In eight, it was placed anteriorly; in seven of which it was central, in one a little to the left. In eight cases, it was fixed on the posterior part of the uterus; in three of which it was centrally situated; in two, it was towards the fundus; in one, to the left; and in two, to the right side.

During the operations, the placenta was unfortunately cut in two cases; it was partially separated in four cases; and in two cases it was completely detached and removed before the extraction of the infant, which is most hazardous to the mother (see remarks on Hæmorrhage), and also to the infant. In order to avoid as far as possible cutting the placenta, the stethoscope ought to be used; and doubtless, in the great majority of cases, satisfactory information, either negative or positive, will be obtained. If the "placental soufflet" is not heard, the infant being still alive, it is fair to conclude that this organ is not within the reach of the knife. If the infant is dead, there is not much risk of cutting into the placenta.

In sixteen cases, the incision was made longitudinally in the centre along the linea alba; in three cases, it was made a little to the left of it. I prefer the left side, at a little distance from the linea alba.

It is of the greatest importance that the operation should be completed as expeditiously as possible, in order to avoid the hazard of inducing rapid and irregular contraction of the uterus before the incision is made sufficiently long, so as to safely extract the infant. It is of great consequence not to have again to incise the organ when the infant's body is in a great measure brought out. This has happened. In Case 96, the uterine tissue was torn, in consequence of the incision being too small; it was only four inches long.

* Concluded from page 297 of last number.