

CONTRIBUTION

TO THE

KNOWLEDGE OF THE PHYSIOLOGICAL ACTION OF ATROPIA. Presented by

NO. 1. A. E. M. Purdy

ITS INFLUENCE ON PIGEONS.

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ALTHOUGH there are very few drugs whose physiological action has been studied within the last fifteen years as closely as that of belladonna, yet it does not seem that the time has come when the stamp of finished can be set upon our knowledge of the medicine. Wishing some time since to make a physiological comparison between atropia and morphia, I found it impossible to do so satisfactorily, and finally concluded to attempt to go over the whole subject, repeating all the hitherto performed experiments, trying to winnow the wheat from the chaff and, if possible, to discover new grains of truth. Whether this plan will ever fully be completed time alone can determine, but certain results have been developed already, which seem to me worthy of immediate publication, especially with the hope that they will elicit criticism, that in the fires of controversy may at last be fashioned perfected knowledge.

The first of these points, and the one to which the present paper will be confined, is in regard to the action of belladonna and its alkaloids upon birds.

In a prize paper published in the *Archives G n rale*—, M. Lemattre confirms the assertions originally made by T. Wharton Jones (*Med. Times and Gaz.*, 1857) that atropia will not dilate the pupils of birds, stating that it is because their irides contain no radiating fibres, belladonna acting on these muscles in the higher animals.

The anatomical assertion here made rests chiefly, I believe, on the researches of Mr. Jones, but I think there can be no doubt of its falsity. The general laws of homologies throw great doubt upon it, and recent

anatomists have most abundantly demonstrated the existence of such fibres. In the *Archives für Ophthalm.*, vol. 15, part I., is a beautifully illustrated paper by Alex. Ivanoff and Alex. Rollett, clearly showing their position and power, and in Max Schultze's *Archives für Mikroskop. Anatom.*, vol. 6, Heft I., 1870, is a paper by Johann Diegel, essentially corroborating the former. The anatomical explanation of Jones and Lemattre seems, therefore, to be erroneous, and the following experiments were made to test their physiological assertion.

Expt. 1.—Adult pigeon. Oct. 26, 9.20 P. M., dropped very freely three successive times a solution of sulphate of atropia in eye (gr. iij to fʒj), and held head so that solution remained in a little puddle for several minutes; 9.27 no dilatation of pupil; 9.50 there has been no dilatation of pupil.

Expt. 2.—Oct. 27. 2.30 P. M. Put 4 grs. ext. of belladonna in throat of pigeon used in first experiment, which it swallowed. 3. P. M. No visible effects from belladonna. 7 P. M. Gave by mouth 10 grs. ext. of belladonna. 9 P. M. Have examined pigeon several times; no effect from belladonna on pupil or otherwise visible. 10 P. M. There certainly has been no vomiting up to this time; no effect visible from belladonna. Oct. 27. The pigeon perfectly lively; no signs of having vomited. Oct. 28, 2.30 P. M. Gave 20 grs. of ext. of belladonna. 2.50 P. M. Pigeon reeling. 5.45 P. M. Pigeon has been running about perfectly lively ever since last entry. Gave gr. x extract of stramonium. The pupils are, I think, somewhat dilated. 6.30 P. M. Pigeon still unaffected. 10 P. M. Pupils are perfectly movable, contracting freely when brought to a light, but I think not so much so as normally. No other sign whatever of a mydriatic having been taken noticeable. No quietness or restlessness, or drooping of feathers, or apparent disordered vision. Oct. 31. Pigeon perfectly well; gave gr. jss atropiæ sulph. about 1.15 P. M., in pills of bread. 1.50 P. M. Pigeon been running about perfectly lively and eating since; no perceptible dilatation of pupil. 6.30 P. M. Assistant states that the pigeon has appeared a little stupefied during afternoon; now shows no symptoms, except that pupils are somewhat dilated; they are a little irregular and apparently do not contract as much as they ought under a strong light.

Expt. 3.—Oct. 31, 1870. Three adult pigeons were given each, by mouth, 30 grains of fresh juice extract of belladonna at 3.20 P. M. 3.30 P. M. Pigeons walking about unconcernedly. 3.50. One of the pigeons has vomited some, but evidently only a portion of the belladonna. 4.15. Two pigeons have been vomiting since; one freely the other slightly. I do not know whether one of them was the pigeon that vomited before or not. 4.30. Pigeons vomiting. Nov. 1. Pigeons do not seem different from usual.

Expt. 4.—Nov. 3. 3 P. M. Gave two of the same pigeons, each 12 grs. of fresh juice belladonna extract, prepared by Ransom, of England. 5.30 P. M. Have not vomited; no symptoms from belladonna; gave each 12 grains additional. 7.30 P. M. There has been no vomiting; no effect apparent from belladonna. Gave 12 grains more to each bird. 10.30 P. M. Has been no vomiting; no effect visible from drug, save that there appears to be some slight dilatation of the pupil. Gave one pigeon 12 grains additional, the other 6 grains. Nov. 4. Pigeons perfectly lively this morning. The belladonna has not had any appreciable effect in disturbing their equanimity. There has evidently been vomiting during the night.

Expt. 5.—Nov. 4. An adult pigeon, one used in expt. 3, but not used in last, at 12.30 P. M. was given, by mouth, 10 grains of extract of stramonium. 1 P. M. No vomiting; pigeon not affected. 2.30. P. M. No vomiting; gave 10 grs. more extract of stramonium. 3 P. M. No vomiting or other perceptible disturbance. 7 P. M. No vomiting since; no perceptible effect from stramonium.

Expt. 6.—Nov. 5. 8.20 P. M. Gave an adult pigeon 3 grains of atropiæ sulph. made into pill with bread crumbs. 9.30. P. M. Has not vomited; does not seem even quieted. 10 P. M. Has not vomited or shown any effect of the atropia. 10.20. P. M. Seemingly unaffected; let loose in yard. Nov. 6. 9 A. M. Pigeon alive; has been vomiting this morning. 2 P. M. Has been vomiting off and on all morning; will not eat, is quiet, but runs away when approached. Nov. 10. Has not been well since 5th; some days eating pretty well, other days refusing; more or less diarrhœa, especially latterly; died last night.

Expt. 7.—Nov. 4. 1.15 P. M. Gave to one of pigeons used in experiment of previous day (No. 4) $1\frac{1}{2}$ grains atropiæ sulph. injected in cellular tissue of breast and thigh. A little was lost during operation, possibly as much as a $\frac{1}{4}$ grain immediate vomiting occurred. 1.40 P. M. Has been vomiting again; no other symptom save that he is disposed to be quiet in corners. 2.30 P. M. Quiet in corners; feathers look ruffled; has had very watery evacuations. 3 P. M. Allows himself to be picked up (is tame at any time) without moving, but walks well towards a corner when removed from it; is perfectly rational; no dilatation of pupil. 7 P. M. Pigeon seems well, but has some tendency to be quiet; no dilatation of pupils. Injected into breast $1\frac{1}{2}$ grains more of sulphate of atropia. Two or three drops of fluid escaped, containing probably $\frac{1}{8}$ grain of atropia. 10 P. M. No perceptible change; no dilatation of pupil; seems fairly lively; got out of basket himself and left so soon as lid was taken off. Nov. 5. All right.

Expt. 8.—Nov. 5. At 7.40 P. M. injected in three places between 12 and 14 grs. extract of stramonium, in watery solution, into cellular tissue of breast and thigh of adult pigeon. 8.20 P. M. Pigeon perfectly quiet. Pupils wide, irregular, not contracting beyond a certain limit in a strong light. 9.30 P. M. Pigeon a little quiet; more so, I think, than is due to its being night. 10 P. M. No apparent change; pigeon was let loose in yard. Nov. 6. Pigeon is a little lame, otherwise not very sick. Noon. Pigeon has refused to eat as yet. Nov. 7. Pigeon died this morning. Unfortunately assistant threw it away before I had seen it, but there can be no doubt its death was owing to local changes induced by the hypodermics, a large amount of water having been used to dissolve the extract.

Expt. 9.—Nov. 5. 2.45 P. M. Injected grains $3\frac{3}{8}$ atropiæ sulph. at three points, into cellular tissue of breast and both thighs of pigeon. 3 P. M. Pigeon lying on belly unable to rise up; when raised up it flaps its wings, but allows itself to be freely handled without resistance. When laid on side vainly tries to get on breast. Pupils contracted rather than dilated. Breathing regular, abdominal. 3.10 P. M. Heart's action irregular; lies on back perfectly quiet, except for convulsive twitchings; eyes closed; pupils decidedly small, but further contracting in a strong light. 3.22 P. M. Pigeon just dead.

Expt. 10.—Nov. 5. 9.25 P. M. Gave $2\frac{1}{2}$ grains atropiæ sulph. in solution, injected in both thighs of adult pigeon. Temperature in rectum $108\frac{3}{8}^{\circ}$ F. 9.32 P. M. No effect as yet. 9.35 P. M. Had a violent convulsion. 9.36 P. M. Another one. 9.37 P. M. Laid on side, tries only feebly to roll itself on its belly. 9.40 P. M. Temp. $107\frac{1}{4}^{\circ}$. Pigeon lies on back with no other motion than almost constant convulsive twitchings. 9.50 P. M. Temp. $106\frac{1}{4}^{\circ}$. 9.55 P. M. Pigeon dead. Temp. 106° . *Autopsy* 10 minutes after death. Heart quiescent, engorged with dark blood, not moving when pricked with knife. Intestines: Peristaltic action lively. Brain not perceptibly injected.

The first of these experiments was directed to test the local action of belladonna upon the pupil of the pigeon, and I think showed very distinctly that this mydriatic, used locally, fails entirely to dilate the pupil of the pigeon. The solution used was a strong one (gr. iij to ℥j) and was very faithfully applied, but the iris did not respond.

The next experiments were directed to determine whether belladonna given internally would act on the eye or not, and they appear to confirm the assertion of Lemattre. The belladonna was given in the form of extract, and of the pure salts of the alkaloid, given both by the mouth and hypodermically, and in no case produced very decided dilatation or any immovability of the pupil. In some instances, it is true, there was some apparent enlargement of the latter, but the experiments were made in the evening, when I have noticed an apparent tendency in pigeons to have dilated pupils even in a lighted room, and in those cases where the drug was given freely enough to produce very marked toxic effects, no dilatation of pupil whatever was induced. Moreover, in experiment 7, there was decided contraction of the pupil. Dr. Jones' physiological fact then seems to be accurate, although his explanation appears to be founded in error. I will not attempt to assign any reason for it, because I cannot imagine any one sufficiently plausible to be at all worthy of credence. At the present I think we must content ourselves with the bare fact.

In the earliest of these experiments I was very much astonished at the enormous doses of belladonna borne by the pigeons, and the experiments were multiplied to test this apparent inactivity of the mydriatics. The result is certainly to establish the fact that belladonna, stramonium, and of course hyoscyamus, resemble morphia in their want of action on these birds. It appears to be almost impossible to immediately kill them with the extracts, given by the mouth. Doses of over 15 grains they generally threw up, and in experiment 4, 48 grains of the best English fresh juice extract were given in a little over seven hours without any appreciable narcotic effect.

In experiment 6 three grains of a very beautiful and pure sulphate of atropia were given and retained, and yet did not appear to interfere materially with the well-being of the pigeon.

The sulphate of atropia was then tried hypodermically, and it was found, as with morphia, that although it takes enormous doses, yet it is very possible to kill the birds with the poison.

In experiment 7 thirteen grains of the extract of stramonium injected into the cellular tissue produced no direct appreciable disturbance, and in another case 3 grains of atropia ($\frac{1}{4}$ of a grain or so being lost) injected in two doses about six hours apart, induced no effects that could be called toxic. On the other hand, in experiment 9 two and one-third grains produced violent convulsions, ending in death in half an hour; but then the pigeon had been certainly weakened by previous experimentation, running through several days, and interfering very greatly with digestion. In experiment 8 the pigeon lived for a longer time after the injection of nearly 4 grains. From all the experiments I think it may be deduced that it takes not less than 2 grains of atropia, given hypodermically, to kill an ordinary robust adult pigeon. In man, the toxic action of such a dose

would at least equal that of ten grains of morphia. The power of pigeons to resist belladonna has not before been pointed out that I am aware of, although Mr. Anderson, as quoted by Pereira, asserts that blackbirds eat the berries with impunity, whilst Reil, according to Prof. S. R. Percy, declares that "sharp-sighted birds" are exceedingly susceptible. It is well known that herbivora are affected but slightly by belladonna and stramonium, whilst carnivora, like the cat and dog, are more readily influenced. Every frequenter of large cities has probably seen goats feeding freely on stramonium plants. Every experimenter knows how difficult it is to kill rabbits with the alkaloid, even when used hypodermically, and Drs. Ogle and S. R. Percy have fed rabbits for nearly a week on belladonna leaves solely without injuring them. Dr. Percy has given four ounces of dried hyoscyamus leaves to a goat and one drachm of extract of hyoscyamus to a kid without producing any symptoms save dilatation of the pupils.

Remembering this and the assertion just alluded to of Dr. Reil, I have been desirous of testing whether the same general law was true of birds, but have been unable to procure a hawk, owl, or other carnivorous bird.

The causes of the non-action of atropia on pigeons seem to be three in number: First and chiefly—absolute obtuseness of the nerve centres to its action, an obtuseness, the cause of which we shall probably be able to explain just so soon as we know why atropia acts on the nerve centres of man. Second—very rapid elimination of the poison, for I have noticed that the conjoint urino-fecal discharge becomes watery and abundant under the action of the drug. Third—when taken internally, comparatively slow absorption, so that the poison is removed from the blood by the kidneys, etc., as fast as it enters it.

