On the administration of belladonna, and on certain causes which modify its action / by Henry Wm. Fuller.

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AND ON

CERTAIN CAUSES WHICH MODIFY ITS ACTION.

BY

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[*From Volume XLII of the 'Medico-Chirurgical Transactions,' published by the Royal Medical and Chirurgical Society of London.*]

LONDON:

PRINTED BY

J. E. ADLARD, BARTHOLOMEW CLOSE.

1859.

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Received April 26th.—Read June 28th, 1859.

In the month of November, 1858, my attention was arrested by the extraordinary tolerance of belladonna exhibited by a child to whom I was administering it as a remedy for chorea. Commencing with a quarter of a grain of the extract administered in divided doses daily, I gradually increased the quantity of the drug up to six grains a day, with no other effect than that of arresting the choreic spasm and producing very slight dilatation of the pupil. I therefore determined to institute some experiments, with the view of ascertaining whether the case in question was exceptional, or whether chorea does not exercise some modifying power in respect to the action of the drug. The results, which to me are novel and remarkable, form the subject of the present communication.

The cases on which my observations were made are twelve in number. The patients were female children varying in age from eight to nineteen; three of them had

previously experienced one or more attacks of chorea, and in five of them the symptoms of the present attack were of unusual severity. In every instance the involuntary movements were general, affecting the extremities on both sides of the body as well as the muscles of the face; in four instances the patients were unable to stand, and in three instances the violence of the jactitations rendered it necessary for the patients to be tied in bed. In eleven out of the twelve cases the disease came on spontaneously, without fright or previous illness; in the other (Case 9) the symptoms almost immediately followed the shock produced by seeing her father brought home a corpse.

In the first eleven cases belladonna was given, and the extract was the preparation employed. In the first case the drug was given in pills; in the second case half the quantity was administered in pills and half dissolved in water; in the remaining nine cases the whole quantity prescribed each day was dissolved in two ounces of water, of which half an ounce was given as a dose every six hours.

In nine of these cases the hospital extract of belladonna was used. This is obtained from Apothecaries' Hall. Its power was tested as follows: a solution of one grain to a drachm of water dropped into the eye of my clinical clerk caused enormous dilatation of the pupil, which lasted two days; a grain and a half given twice a day to a male adult suffering from sciatica produced so much vertigo and dryness of the throat and fauces, that the man was unable to continue taking it; a grain and a half taken at a dose experimentally by our Medical Registrar gave rise to dryness of the throat and fauces, and dilatation of the pupil. However, with the view of obviating any objections as to the strength of the drug, the extract obtained from J. Bell's, in Oxford Street, was administered in Case 5, and that procured from Squire's, in Oxford Street, in Case 7.

In Case 12 atropine was employed. The alkaloid was obtained at Morson's, in Southampton Row, and was dissolved by means of a few minims of the dilute sulphuric acid

in two ounces of water, of which half an ounce was given four times daily.

In neither of the twelve cases was any other remedy given except an occasional dose of castor oil, or senna draught, or a few grains of scammony and calomel when the bowels were costive.

The diet, except in those cases in which the appetite was indifferent, or in which the choreic spasm was so violent as to prevent mastication, consisted of bread, meat, and vegetable—the hospital "ordinary diet;" in the others, of beef-tea, eggs, and the hospital "milk diet."

The following brief outline of the cases will suffice for the purpose of this communication. They are given in chronological order.

Case 1.—Alice S—, æt. 11, was admitted into the Crayle Ward of St. George's Hospital, November 17th, 1858; suffering from chorea, affecting the muscles of the face and of both upper and lower extremities. She had experienced a severe attack of the disease, which nearly proved fatal, in the month of June previously, but had been relieved by sulphate of zinc administered in rapidly increasing doses. Her present symptoms commenced at the end of October, and had gradually increased up to the date of her admission. There was no cardiac murmur. She was very pale. The pupils were large. As the sulphate of zinc had proved so useful on the former occasion it was ordered again, in combination with quinine and sulphate of iron, and its dose was rapidly increased, so that by the 25th of November eight grains were being taken three times a day. At the same time the bowels were freely acted on by means of scammony, calomel, and castor oil. Nevertheless little or no improvement took place in the choreic symptoms, so on the 27th the medicine was omitted, and a quarter of a grain of the extract of belladonna was given daily. After a time this dose was given twice, then thrice, and then four times daily, and it was cautiously increased

until, on the 14th of December, six grains of the extract were taken in the course of the twenty-four hours. On the 21st the notes of Mr. Seaton, my clinical clerk, report the patient as "quite steady," and on the 28th she left the hospital. Slight dilatation of the pupil was the only obtainable evidence of the action of the belladonna.

Case 2.—Ann B—, æt. 16, was admitted into Queen's Ward, November 17th, 1858, suffering from chorea of two weeks' duration. The spasms affected all the extremities; the face also was affected, and she was unable to articulate. The pupils were large; there was no cardiac murmur. The infusion of valerian with sulphate of zinc in solution was given every six hours, and the dose of zinc was rapidly increased, so that by the 2d of December fifteen grains were being taken four times daily. By the 4th, however, very little benefit had resulted, so on that day the medicine was omitted, and half a grain of extract of belladonna was given night and morning. On the 7th two thirds of a grain were prescribed three times a day, and on the 11th a grain was given four times daily. From this time the dose was rapidly increased, so that by the 16th of January fourteen grains were taken daily. By that time the spasms had almost ceased, and the patient could speak fairly. On the 17th she complained of nausea and the urine was ammoniacal. On the 18th she vomited, the bowels were much purged, and the pupils dilated. The spasms had entirely ceased. The medicine was omitted, but no other remedy was resorted to. She remained in the hospital another fortnight, in order that we might ascertain whether there would be any return of spasm, and as that was not the case, she was discharged on the 2d of February.

Case 3.—Jane C—, æt. 12, was admitted into Hollond Ward, January 12th, 1859. She had been suffering two months from chorea affecting the face and all the extremities. She had never experienced an attack of rheumatism,

but a loud systolic murmur was audible at the base of the heart, whilst at the apex an intensely loud murmur accompanied the systole, and sometimes also the diastole of the heart. Fremitus could be felt over the lower half of the præcordial region. The pupils were large. A quarter of a grain of the extract of belladonna was given four times daily, and the dose was gradually increased until, on the 7th of February, eleven grains were taken in the course of the twenty-four hours. The choreic spasms had almost wholly ceased. On the 8th the patient was sick in the morning, the bowels were relaxed, and she complained of lassitude and headache. The pupils, however, were not much larger than natural, there was not any indistinctness of vision, and the tongue was clean and moist. The cardiac murmurs were still audible, though not so loud as on admission; the heart's action was quieter, and the fremitus had ceased. No more medicine of any kind was given, and she left the hospital, on the 15th of February, perfectly free from chorea.

Case 4.—Harriet H—, æt. 19, was admitted into Crayle Ward on the 26th of January, 1859. The muscles of the face and all the extremities were affected with choreic spasm, and the fingers of the right hand were spasmodically closed. The pupils were large, the heart's sounds clear, the catamenia regular. Two grains of the extract of belladonna were ordered, and the dose was gradually increased until, by the 4th of February, she was taking seven grains daily. On the 5th I find a note by Mr. Seaton, "She is quite steady," and on the 8th she left the hospital.

Case 5.—Mary Ann F—, æt. 12, was admitted into Rosebery Ward on January 26th, 1859. Four years previously she had been in St. George's Hospital with a severe attack of chorea, which nearly proved fatal. The present attack commenced six weeks prior to her admission, and the symptoms had gradually increased in severity. The

muscles of the face and of all the extremities were affected, but those on the left side most severely. Two grains of the extract of belladonna were administered at first, and the dose was gradually increased until, by the 2d of March, she was taking forty-eight grains daily. She was then attacked with vomiting and purging, and thereupon the medicine was omitted. No other remedies were employed, but the symptoms of chorea subsided rapidly; indeed they almost ceased from the date of the vomiting and purging, and she left the hospital on the 9th of March in good health.

Case 6.—Jane S—, æt. 9, was admitted into Pepys' Ward on February 1st, 1859. She had been suffering from chorea about two months, and the symptoms had increased during the last three weeks. All the extremities were affected with spasm, and the muscles of the face slightly so. The heart's sounds were clear, the pupils large. Two grains of the extract of belladonna were ordered, and the dose was gradually but rapidly increased, so that by the 12th ten grains were taken daily. By this time the choreic movements had almost ceased, and the patient left the hospital perfectly well on the 16th.

Case 7.—Ann W—, æt. 11, was admitted into Crayle Ward on February 12th, 1859. The choreic symptoms, which were very severe, commenced about one month previously, and had gradually increased in severity. The whole of the limbs were in a state of violent jactitation, the skin of the hands and arms was rough, from the continued friction, and it was found necessary to tie her in bed. She was unable to speak, and could with difficulty swallow, or protrude the tongue. The pupils were large, and as far as could be ascertained, the heart's sounds were free from murmur. Four grains of the extract of belladonna were given, and the dose was rapidly increased until, by the 12th of March, sixty-eight grains of the extract were taken daily. By this date the choreic spasms were comparatively

slight, the patient could protrude the tongue and swallow without difficulty, and she was beginning to speak. On the 13th her bowels became relaxed, the motions being dark coloured, thin, and offensive; she complained of nausea, and was sick after her meals. On the 14th these symptoms had increased, and therefore, although the pupils were of their natural size, the sight was unaffected, and the tongue clear and moist, it was deemed expedient to omit the medicine. She now took no medicine for a fortnight, but the spasms continued to decrease, and the power of speech began to return. She was still unable to stand, in consequence of the choreic movements of the lower extremities. On the 28th, as she was pale and weak, a grain of sulphate of iron, and the same quantity of sulphate of zinc, was given every six hours, and the quantity of sulphate of zinc was rapidly increased, so that by the 16th of April she was taking twenty grains at a dose. Day by day the spasms subsided and her strength returned, and she left the hospital on the 20th of April in good health, and free from choreic symptoms.

Case 8.—Catherine L—, æt. 10, was admitted into Hollond Ward on February 16th, 1859. She had experienced two attacks of rheumatic fever, from the last of which she recovered five weeks before her admission into the hospital. On its cessation, symptoms of chorea began to manifest themselves, and gradually increased up to the date of her admission. The pupils were of medium size. A slight systolic murmur was audible at the apex of the heart. Four grains of extract of belladonna were prescribed, and day by day the dose was increased until, by the 2d of March, thirty-four grains were being taken daily. By this time the choreic symptoms had disappeared, and it was agreed that in a few days the patient should leave the hospital. On the evening of the 3d, however, she was attacked with diphtheria; the belladonna was omitted, and quinine with muriated tincture of iron and wine were substituted for it. On the 19th the syrup of iodide of

iron and iodide of potassium were given, with the view of getting rid of some enlargement of the cervical glands which remained after the throat affection had been subdued, and she was made out-patient on the 23d of March. There was not any recurrence of the choreic symptoms. The systolic murmur was still audible, though not so loud as on her admission.

Case 9.—Grace S—, æt. 10, was admitted into Pepys' Ward on February 18th, 1859. She had been ill a fortnight with choreic symptoms of the most violent description, which had followed immediately the shock produced by seeing her father brought home a corpse. The limbs were in a state of incessant jactitation; there was continued and violent grinding of the teeth; she had been unable to sleep or to utter a syllable since the beginning of the attack, and she swallowed with the greatest difficulty. The pupils were of medium size, and, as far as could be ascertained, the heart's sounds were clear and unaccompanied by murmur. The skin of the face, arms, and trunk, was excessively rough from continual friction, and the lips were chapped. The pupils were of medium size. Six grains of the extract of belladonna were ordered, and the dose was gradually increased, so that by the 23d twelve grains were taken daily. At this time the spasms appeared to be somewhat less severe, and the patient for the first time obtained a little quiet sleep. But the lull was of very short duration; as soon as she awoke the spasms recurred with increased violence. By the 2d of March the dose of belladonna had been increased to thirty-three grains daily, but the spasms were almost as severe as ever, the grinding of the teeth was incessant, there was the greatest difficulty in getting even liquid nourishment between her teeth, and she got no sleep. Moreover, the whole body was rough and sore from continued friction; the lips were deeply fissured; the face, chin, and upper part of the trunk, were covered with pustules, the result of friction; an abscess was forming on the neck; the skin over the right hip was abraded; and

the skin of the back was beginning to slough. On the 3d these symptoms had increased, and, in spite of wine which was administered freely, she sank exhausted on the following day. She was perfectly conscious throughout, and even two hours before her death recognised her friends. Unfortunately they would not permit a post-mortem examination.

Case 10.—Joanna G—, æt. 11, was admitted into Crayle Ward on February 23d, 1859. She had been suffering from chorea more or less for three months, and had been much worse during the last ten days. Her pupils were large; the heart's sounds free from murmur. Four grains of the extract of belladonna were prescribed, and the dose was gradually increased until, by the 13th of March, she was taking thirty-six grains daily. She was then so nearly free from spasm that she was permitted to carry plates and cups and saucers about the ward. In the evening her bowels became relaxed, she was sick, and began to complain of headache. These symptoms continued the next day, the motions being pale in colour, and slimy in appearance; the pupils, however, were not much dilated, there was no indistinctness of vision, and the tongue remained clean and moist. Nothing more was done than to omit the medicine, and the next day the bowels were quiet, the motions natural, and she felt much better. There was no return of choreic symptoms, and she left the hospital quite well on the 23d of March.

Case 11.—Catherine M'N—, æt. 10, was admitted into Hollond Ward, February 23d, 1859. She had been suffering from chorea one month, the spasms affecting the face and all the extremities. She could scarcely articulate. The pupils were large. The heart's sounds clear. The following were the quantities of belladonna taken, viz.—

Feb. 23d	— 4 grs.	of the extract.	
„ 24th	— 6	„	
„ 25th	— 9	„	
„ 26th	—12	„	
„ 27th	—12	„	
„ 28th	—16	„	
Mar. 1st	—20	„	
„ 2d	—24	„	
„ 3d	—24	„	
„ 4th	—28	„	
„ 5th	—32	„	
„ 6th	—32	„	
„ 7th	—36	„	
Mar. 8th	—40	grs. of the extract.	
„ 9th	—44	„	
„ 10th	—48	„	
„ 11th	—52	„	
„ 12th	—56	„	
„ 13th	—60	„	
„ 14th	—64	„	
„ 15th	—64	„	
„ 16th	—64	„	
„ 17th	—64	„	
„ 18th	—68	„	
„ 19th	—70	„	
„ 20th	—70	„	

Thus, up to this date, or, in other words, within twenty-six days, she had taken 1019 grains, or rather more than two ounces of the extract of belladonna; meanwhile her appetite had remained good, and the tongue moist and clean, but red. After the first four days she was always up and playing about the ward during the day, and at night she slept soundly, but not heavily. The pupils were always large, and somewhat dilated. She never experienced any vertigo, and on one or two occasions only, the slightest indistinctness of vision. The urine, from the first, was loaded with lithates, and was of very high specific gravity, usually about 1030; and, during the last six days of her taking the belladonna it was exceedingly scanty; so much so, indeed, that not more than seven ounces were passed each day, exclusive of what was passed at stool once daily. Its sp. gr., from the 12th to the 20th of March, ranged from 1033 to 1036. She was a long time in passing it, and seemed to experience some difficulty—not pain—in doing so. In this case the spasms were almost as severe on the 20th of March as on the day of her admission, and, therefore, although no ill effects were produced by the belladonna, its use was discontinued. After she had remained five days without medicine, the administration of sulphate of zinc in one-grain doses was commenced. The choreic symptoms at once began to subside, and as the dose of zinc was increased, which it was by the 8th of April, up to

fourteen grains four times a day, they entirely disappeared. She left the hospital in good health on the 13th of April.

Case 12. — Mary Ann S—, æt 14, was admitted into Pepys' Ward on March 2d, 1859. She had experienced repeated attacks of chorea during the last eight years, and had been thrice under treatment for it in St. George's Hospital. The present attack commenced about a fortnight ago, and the symptoms had been increasing gradually up to the date of her admission. The spasms were severe, so that she fell down yesterday, and cut her lip and bruised her face. Pupils large; heart's sounds clear. I determined to give atropine in this case, and judging from the observed effect of the extract of belladonna, I prescribed it in large doses. The following is the quantity taken each day, viz.—

Mar. 2d	—Atropine	.	gr. $\frac{1}{4}$	Mar. 11th	—Atropine	.	gr. $2\frac{1}{4}$
„ 3d	„	.	gr. $\frac{1}{2}$	„ 12th	„	.	gr. $2\frac{1}{2}$
„ 4th	„	.	gr. $\frac{3}{4}$	„ 13th	„	.	gr. $2\frac{3}{4}$
„ 5th	„	.	gr. 1	„ 14th	„	.	gr. $2\frac{3}{4}$
„ 6th	„	.	gr. $1\frac{1}{4}$	„ 15th	„	.	gr. 3
„ 7th	„	.	gr. $1\frac{1}{2}$	„ 16th	„	.	gr. $3\frac{1}{4}$
„ 8th	„	.	gr. $1\frac{1}{2}$	„ 17th	„	.	gr. $3\frac{1}{4}$
„ 9th	„	.	gr. $1\frac{3}{4}$	„ 18th	„	.	gr. $3\frac{1}{2}$
„ 10th	„	.	gr. 2	„ 19th	„	.	gr. $3\frac{1}{2}$

Thus, then, up to this date, or, in other words, within the space of eighteen days, she had taken thirty-seven grains of atropine. During the first three days the spasms were very violent, so that she had to be tied in bed, and during the first three nights she was more or less delirious; but as the tongue was moist, as the pupils were not much dilated, as there was not any indistinctness of vision, and as she was perfectly collected and sensible during the day, there was no reason for attributing the symptom to the action of the atropine. After the third night there was no return of delirium, and by the 8th of March the spasms had so far subsided as to enable her to be dressed and up about the ward during the day. The tongue had remained moist and clean throughout the attack, and the pupils, though

large, were seldom much dilated except for a short time after each dose of the medicine. She slept soundly, but not heavily. On the 19th, the last day on which the atropine was taken, my clinical assistant, Mr. Bright, reports, "She is much steadier, the pupils are of their natural size, there is no indistinctness of vision, the tongue is clean and moist, the urine clear, and the appetite good." In short there was no indication of her being affected by the drug, but as for some days it had not appeared to lessen the choreic movements its use was discontinued. She then remained without medicine until the 26th, when one-grain doses of sulphate of zinc were ordered to be taken in solution every six hours. The quantity of zinc was rapidly increased, until on the 16th of April she was taking twenty grains four times daily. The spasms gradually subsided, and she left the hospital on the 20th of April. On the 16th of March, whilst taking the large doses of atropine, she began to suffer severely from toothache, which was not relieved until the 19th instant, when the gums and face began to swell.

The following circumstances deserve to be noted. In the 1st place, feverish heat was not even temporarily produced in any instance by the administration of the medicine.

2dly. The patients were pale whilst under the influence of the drug, and in no case was any rash or erythematous blush observed on the skin, though it was looked for daily.

3dly. There was great weakness of the pulse in all the cases, and, in some, considerable quickness.

4thly. The drug did not, in any instance, exert a constipating effect; on the contrary, it appeared to prove aperient. An occasional purge was required only in Cases 1, 5, and 7.

5thly. In Cases 2, 3, 5, 7, and 10, sickness and diarrhœa were ultimately produced; but in every instance, save one, the choreic spasms had almost wholly ceased, and in the exceptional case alluded to (Case 7), had greatly subsided, before these symptoms manifested themselves. Whenever

bowel symptoms occurred, mere omission of the medicine sufficed to cause their cessation. Did the existence of spasm counteract the influence of the drug, and prevent their occurrence?

6thly. The urine was generally clear and acid, but scanty, and of high specific gravity, varying from 1024 to 1036. In Cases 3, 6, and 8, it frequently contained a copious deposit of crystallized lithic acid. In Cases 5, 7, and 9, it was usually loaded with lithates. In Case 2, for the space of a few hours, whilst the patient was under the toxical influence of the drug, it became ammoniacal almost as soon as voided.

7thly. In Case 11 some difficulty was experienced in voiding the urine throughout the period of the administration of belladonna, but this was not observed in any other cases. This difficulty passed off when the belladonna was omitted.

8thly. The tongue was always moist, but unusually red, whilst the larger doses of belladonna were being taken, and the redness passed off when the drug was omitted.

9thly. Dilatation of the pupil was very uncertain. In almost every instance the pupils were large before the administration of the medicine was commenced, and they invariably became dilated soon after a dose of the medicine was taken. The dilatation, however, was not to the degree observed when a solution of belladonna is dropped into the eye, and in most of the cases it passed off before another dose of the medicine was due. Its ordinary duration was about two hours and a half. In Case 2 excessive dilatation occurred for some hours coincidently with the occurrence of sickness and purging. In Cases 3 and 11 considerable dilatation was pretty constant. In Case 12 the dilatation was seldom great.

10thly. In two instances only (Cases 5 and 11), did the slightest indistinctness of vision occur. In Case 11 it was observed only on three occasions, and then to a slight degree, and was not accompanied by dryness of the throat, headache, or any impairment of the mental faculties. In

Case 5 it took place more frequently, and strange to say, was most complained of when the pupils were of their natural size, and were contracting freely under the stimulus of light. It was not attended by delirium or by any other indication of the action of belladonna, and the administration of an additional quantity of the drug was almost invariably followed by its removal.

11thly. The drug did not, in any case, produce the slightest narcotic effect, and, in Case 12, it failed utterly as an anodyne.

12thly. In no instance was there any evidence of its accumulation in the system.

13thly. The tolerance of the drug was not in proportion to the severity of the choreic spasms. In Case 2, in which fourteen grains of the extract daily occasioned sickness and purging, the spasms were more severe than in Case 11, in which seventy grains were given daily without disturbance of the stomach and bowels.

14thly. The curative effect of the drug was very uncertain. In Cases 1, 2, 3, 4, 6, 7, 8, and 10, its action appeared to be curative; but, in Cases 9 and 11 it failed to exercise the slightest control over the spasms, and in Cases 5, 7, and 12, it is doubtful whether the improvement ought to be attributed to its action.

Being desirous of ascertaining whether the tolerance of the drug was due to its decomposition in the stomach, or to its non-absorption, I submitted some of the urine voided by Catherine M'N—, to my friends Dr. Marcet and Mr. Kesteven for examination. The former extracted atropine enough from three ounces of the urine to kill two white mice, and narcotise several others. The latter, from two ounces of the urine, obtained sufficient to produce dilatation of a cat's eye, to afford the beautiful filamentous crystals of atropine now laid before the Society, and to give the reactions which atropine yields with iodine water, tannic acid, chloride of gold, sulphuric acid, and bichromate of potash.

The patients being all female children, I was unable to

obtain any fæces unmixed with urine, but Dr. Marcet, who kindly undertook to analyse an admixture of fæces and urine, did not obtain a larger quantity of atropine from it than he did from the urine alone. The urine and fæces were voided at the time when the patient was taking sixty-four grains of the extract of belladonna daily, and therefore, as the drug was not found in great excess in the fæces, it seems fair to conclude, that a large proportion of it had been absorbed into the blood. At all events, its discovery in large quantities in the urine proves that its want of action is not attributable to its non-absorption.

In order to ascertain whether the extraordinary tolerance of belladonna exhibited by these patients arose from their having become habituated to the use of the drug, and to a consequently induced insensibility to its action, a solution of atropine was dropped into the eye of a girl (Case 12), who, at the time, was taking three grains and a quarter of atropine daily, but whose pupils at the time were of medium size. Dilatation of the pupil ensued as under ordinary circumstances, but was of very temporary duration.

Thus, then, up to this point, five facts appeared proved—1st. That in cases of chorea extraordinarily large doses of belladonna and atropine are tolerated. 2dly. That the drug is absorbed into the blood; and therefore, that the tolerance of it is not attributable to its non-absorption, nor to its being decomposed in the stomach. 3dly. That it does not accumulate in the blood, but passes out of the system with the urine and fæces, and probably with the other excretions. 4thly. That it does not exercise that amount of control over the choreic spasms which would have been expected, from the readiness with which it is tolerated by the system. 5thly. That the tolerance of the remedy is not in proportion to the severity of the choreic symptoms.

Another question, therefore, arose, viz., whether the existence of chorea had any part in producing tolerance of the drug, or, whether that tolerance may not have been due to the age of the patients, or to some other circumstance.

Case 13.—With the view of determining this point, I gave a child, Mary Ann F—, æt. 10, in Queen's Ward, convalescent from acute rheumatism, a quarter of a grain of the extract of belladonna, in four equal doses, and increased it day by day, until, at the expiration of thirteen days, she was taking twenty-eight grains of the extract daily. When she commenced taking the belladonna she was quite free from rheumatism, and remained so until the date of her discharge from the hospital. On the first and second days of its administration dilatation of the pupil and some degree of furring of the tongue were observed; but these symptoms had passed off before the fourth day of its administration. On the tenth day, when she was taking twenty grains of the extract daily, I find a note by Mr. Bright, my clinical assistant, to the effect, that "she is quite uninfluenced by the medicine;" and on the 29th day of March, the day preceding her discharge from the hospital, at the time when she was taking twenty-eight grains daily, my clinical assistant, Mr. Leighton, made a note as follows: "Pupils natural and of medium size; no indistinctness of vision; tongue clean and moist; no dryness of throat; appetite good."

Case 14.—To another child, Elizabeth O—, æt. 7, in Crayle Ward, convalescent from scarlatina, I gave, on the 28th of March, half a grain of the extract, and increased the dose gradually, until, on the 5th of April, she took thirteen grains of the extract daily. The tongue remained moist and the appetite good throughout; there was no vertigo or indistinctness of vision, and no dryness of the throat. On the 5th of April, the day preceding her discharge from the hospital, there was not any evidence of her being affected by the drug, except slight dilatation of the pupils. She slept soundly but not heavily.

With the view of having the matter tested with children on a larger scale than is possible at St. George's Hospital, I requested my friend Mr. ——, who is attached to a large

public institution for children, to administer it cautiously and favour me with a report of the results. Accordingly, on the 24th of March he gave eleven children, varying in age from three to six, one eighth of a grain of the extract in solution three times daily. To four other children, from eight to twelve years of age, he gave, at the same time, one quarter of a grain of the extract, and increased the dose up to one grain, three times a day. These children were all in good health; the dose of the medicine was gradually increased, and the only effect observed was dilatation of the pupil, which continued for about two hours after each dose of the medicine was taken. On the 30th many of the children left the institution, and the experiment was discontinued.

On the 5th of April he gave seven children, from five to seven years of age, one third of a grain of the extract of belladonna twice a day, and continued it until the 7th, without perceiving any effect from its administration beyond that of slight dilatation of the pupil, as on the former occasion. On the 7th he prescribed two thirds of a grain to be taken twice a day, but the nurse by mistake gave a quantity of the mixture equal to a grain and a third of the extract at a dose. The result was that the children were all seized with sickness and vomiting, some of them had diarrhœa, and one of them had the violent uncontrollable delirium characteristic of belladonna. Stimulants were at once administered, the belladonna was omitted, and on the following day the toxical effects of the drug had passed off and the children were perfectly well.

On adults the medicine acts much more powerfully than on children, and a tolerance of it is not easily established. An opportunity has not yet occurred to me of administering it in full doses to patients between the ages of nineteen and thirty, but in the few persons between the ages of thirty and sixty to whom I have given it, one or two grains daily have produced vertigo or dryness of the throat and fauces, and in one instance only have I been able to increase the dose beyond four grains daily. The instance alluded to

was that of a nervous woman, aged thirty, a patient in Hollond Ward, suffering from hysterical contraction of the left arm; and in her case the dose was gradually increased up to ten grains daily. This quantity, however, occasioned so much vertigo, loss of appetite, and dryness of the throat and fauces, that I was soon obliged to discontinue its administration.

Thus, then, it would appear—1st, that the tolerance of belladonna is not attributable to the counteracting influence of choreic spasms, but is in some way connected with the age of the patient; 2dly, that a much larger dose than is usually prescribed is well borne from the first by children of tender years; 3dly, that in children, though not so in adults, a tolerance of the remedy is speedily established, so that the dose may be safely increased rapidly, but gradually; 4thly, that special care should be taken in apportioning the dose to the age of the patient and in not increasing the dose too rapidly, inasmuch as the usual toxical effects of the drug will be produced if too large a dose be given before a tolerance of the drug has been established; 5thly, that the milder toxical effects produced by the drug are of little importance, and subside without remedies as soon as the administration of the medicine is discontinued; 6thly, that adults cannot tolerate the doses of the drug which can be taken with impunity by children.

If I were to state the opinion I have formed from a close and careful observation of the cases recorded in this paper, coupled with the information supplied by Mr. —, I should say that the commencing daily quantity of the extract for a child—

Between the ages of	3 and 5	ought not to exceed	one third of a grain.
„	5 „ 8	„	one half „
„	8 „ 10	„	two thirds „
„	10 „ 15	„	one grain;

but that in each instance this dose may be safely given, and may be increased on alternate days, by an equal amount, until loss of appetite or some symptoms of the action of the

drug, other than moderate dilatation of the pupil, begin to manifest themselves. In hospital practice, where the patients are seen by a medical man three or four times daily, and in the intervals are under the eye of an experienced nurse, considerably larger doses may be given without the slightest risk. In every instance, however, the daily quantity ought to be given in at least four equal doses, for the effects of the belladonna pass off so rapidly, as evidenced by the cessation of dilatation of the pupil, that much larger doses may be thus administered daily, than it would be safe to exhibit at a single dose, or even in two or three doses.

The extraordinary difference in the tolerance of the drug observed at different periods of life is probably explicable by the medicine passing off with the urine, as also with the other excretions, more rapidly in childhood than it does in adult life.

Several questions of practical importance arise in connexion with this inquiry: 1st. May not full doses of belladonna be exhibited with advantage in hooping-cough? It is admitted that the drug is often productive of signal benefit even in the minute doses in which it has been hitherto prescribed, and it seems fair to conclude that a corresponding increase of benefit would result from the administration of larger doses. 2dly. In epilepsy, laryngysmus stridulus, and other spasmodic affections, full doses of the extract may possibly prove serviceable. It is obvious that they may be taken with impunity if due caution be observed in their administration, and they certainly deserve a trial. 3dly. May not the drug, if perseveringly employed in full doses, be productive of relief in certain forms of dyspepsia connected with infra-mammary pain, flatus, and spasms in the abdomen? Combining, as it does, antispasmodic, sedative, and slightly purgative properties, it seems likely to be useful in many such cases; and although at present my experience is too limited to warrant an opinion on the subject, I may state that I have found it give relief to two patients who had abnormally clean tongues, but were suffering from an irritable state of the stomach and of the

nerves connected therewith. 4thly. It exercises a remarkable power in controlling seminal emissions and incontinence of urine. This I can attest from oft-repeated observation, and as the experiments already detailed prove that the drug is excreted with the urine, the question arises whether, in the cases alluded to, its curative action may not be due in great measure to its topical effect, and if so, whether it might not be applied locally with advantage?

In conclusion, I would add that my best thanks are due to my colleagues at St. George's Hospital, and to other of my friends, for kindly furnishing me with cases of chorea, and for offering many valuable suggestions in aid of my investigations.