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ESSAY LVII.

Edinburgh

A

STUDY OF DOSES.

BY

WILLIAM SHARP, M.D., F.R.S.



“All things I measure, count, and weigh.”

Motto of HENRY CAVENDISH.

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ANALYSIS.

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ESSAY LVII.

A STUDY OF DOSES.

“The question of *Doses* has not yet been settled upon a scientific basis.”
CHARLES JULIUS HEMPEL.

I. *Introduction.*

MR. CAVENDISH thought that every thing ought to be measured, counted, and weighed, and that in the minutest and most accurate manner. In this way he made the discovery that water is a compound of two gases now called oxygen and hydrogen.

Dr. Wollaston trod in the steps of Cavendish, and weighed everything minutely. I remember that it was said of him that to give him a grain of any uncommon thing was sufficient to induce him to engage in an exhaustive analysis of it. In this manner he discovered two new metals—Palladium and Rhodium—in the ores of Platinum. Weighing the small grains first in air and then in water, would suffice to separate these metals from Platinum; the specific gravity of Platinum being about 21, and that of the others about 11.

Both before and since the days of Cavendish and Wollaston, men, earnest in the pursuit of natural knowledge, have found that accurate measuring, counting, and weighing are the chief methods of discovery.

And that it is in the examination of the minutest forms of matter we are capable of recognising, that a true science of nature is brought within the grasp of our minds. We have learned much about the sun, moon, and stars, great and distant as they are, by measuring, counting, and weighing with attention to the minutest quantities.

The several steps by which the laws of gravitation were discovered are an illustration of this. The moon's

distance from the earth and its motions were at that time so imperfectly known, that Sir Isaac Newton's first calculations to test his hypothesis ended in a failure. About that time a measurement of a degree of the meridian was carefully made in France by M. Picard, from which the diameter of the earth was more correctly deduced by Newton, and a repetition of his calculations respecting the force of gravitation then confirmed his conjecture—his hypothesis was converted into the knowledge of a fact. But the moon's motions were still to some extent a difficulty. Newton applied to Flamsteed, then appointed the first Astronomer Royal, for more correct observations of these movements of the moon. Flamsteed had no instruments, and the Government would not pay for any, so he invited a friend in Yorkshire to go up to Greenwich to help him to make them. This his friend did, and there constructed a mural arc divided so minutely and accurately that, with it and some other instruments, Flamsteed was able to make the observations that Newton wanted to render the proofs of the laws of gravitation perfect. Here is an example of measuring, counting, and weighing on the smallest scale leading to the discovery of law-facts which govern the largest bodies in creation, and reach to the greatest distances in space.

These two facts—the value of *known* quantities, and the “power of littles”—have now been turned to good account in the investigations of many departments of knowledge, and it is high time that they were applied to Therapeutics.

“Doses,” it may be exclaimed, “are weighed every moment.” This is quite true. But why are they weighed? Because it is thought that we *know* what they will do, and they are weighed in order to do it. The work which has not yet been done, and which ought to be done, is to weigh doses in order *to find out what they do*.

That it is not known with any accuracy what doses do is proved by the prevalence of the belief that they differ in the effects they produce only in degree. Sir Benjamin Brodie expressed this belief in these words:—“Hitherto it has been supposed that the effects of any medicinal substance taken into the system bear some proportion to the quantity taken; that if two mercurial pills taken

daily would make the gums sore, four would make them very sore." This has been "supposed," but never verified by being put to experiment with sufficient care. Experiments of a suitable kind would have shown how great a mistake the supposition is.

Again, the doses commonly prescribed are too gross. We have to learn the effects of doses much smaller than these. We have seen that truth is discovered mainly by attention to minute quantities.

It is true that since Brodie's time immense exertions have been made in physiological laboratories, to find out the action of drugs by experiments on living animals. In my judgment this is an erroneous method; and the results from it in regard to Therapeutics are quite unequal to the labour bestowed upon it.

It is also true that unwearied exertions have been made in chemical laboratories, and very sanguine expectations have been entertained by these zealous labourers; in this way some benefit has been done to Therapeutics, but this has not been, nor is it likely to be, at all equal to the expectations. As a small illustration of this I may mention a circumstance which has just now occurred. A short time ago I had a return of the intermitting pulse described in Essay XLVII ('Therapeutics' page 80), from which I had been free for several years. On the former occasion it was cured by leaving off *tea*, and this time the experiment of taking coffee instead of tea was had recourse to, and the next day the intermissions ceased and have not returned. This being told to a young medical man he replied,—“I should have thought that coffee would come under the same category as tea, seeing that the alkaloid (which is presumably the active principle) in each (Caffeine and Theine) is chemically and physiologically one and the same.” They may be “one and the same” to the chemist, they are not so to the physician.

Another reason, and a chief one, why so little knowledge of the action of different doses of the same drug has yet been acquired by the old school is that attention has been directed only to the patient, in order to find rules for measuring doses—age, sex, predisposition, &c., and latterly, even the weight of the patient's body—these have been made to give the rules. Doubtless, these are influences not to be overlooked, but more

attention should have been directed to the instruments used—to the drugs themselves so much relied upon as remedies, and to their *doses*, if the temper of their metal, and the side which has the cutting edge, were to be discovered.

And again, the universal classification of drugs in the text-books for the instruction of medical students, under the heads of Sedatives, Astringents, Aperients, Tonics, Alteratives, &c., &c., shows how limited has been the knowledge of the action of different doses of the same drug, up to the present hour, in the old school of Medicine.

On the side of homœopathy, my readers may be reminded that from the time of Hahnemann to the present the dose has been a most difficult and perplexing subject, and on it an unceasing controversy has been carried forward. To enter upon the details of this would fill a long Essay, and would be useless. I think the prevailing judgments have been that to discover a law for the dose is impossible; that there is no necessary connection between the dose and the homœopathic law, the one existing quite independently of the other; and that the dose to be prescribed is nothing but the outcome of experience, and every practitioner must be left to create an experience for himself—this experience having no necessary influence even upon the practitioner who is his nearest neighbour.

As regards Antipraxy—the contrary action of some larger and some smaller doses of the same drug—which is now pressed upon their attention, this is thought to be at once disposed of by the remark that it has been anticipated. They say that Dr. Madden, and others, some years ago advanced the opinion that the principle of *similia similibus* is merely our guide to the *selection* of a remedy, and that it by no means expresses the part that remedy performs in relation to disease—its action, in fact, may be the opposite of the actual condition of the diseased part.

The anticipation is quite possible, but what does it amount to? It is an opinion suggesting an explanatory hypothesis, and does not pretend to be anything more. The action, in fact, *may be* the opposite of the morbid process. This does not tell us what the *fact* is. It did not lead either Dr. Madden, or any one else, *to test the opinion by experiment*. It remains nothing more than

an opinion or hypothesis, and it has been fruitless of any practical result—lifeless and useless—as all conjectures so left must remain. Moreover, it makes no reference to the *dose*. The conjecture respects the *drug*, that it acts one way in health, and the contrary way in disease, so that Antipraxy is not approached by it.

It is impossible for a law-fact thus to *remain* inoperative unproductive, unfruitful. It may be so for a time; its light shines upon objects hitherto in the dark, and they are imperfectly seen; but it continues to shine, and eyes become better able to perceive objects by it. A fact of this kind necessarily suggests practical changes, and these when seen are cheerfully recognised and adopted.

I knew nothing of this hypothesis; the hopeless confusion in which the question of *dose* was enveloped distressed me, and at every opportunity that presented itself the necessity of trying experiments in health was urged as the only way of throwing light upon the subject. At length, as no one more competent seemed disposed to undertake the task, I ventured to begin it. I had no theory, not even an opinion or conjecture, but after many experiments on myself, and on a few friends, the *fact* of the contrary action of some larger and some smaller doses of the same drug presented itself to me so distinctly in 1872, that no doubt of it has since been entertained. The following year the fact was made public, and since then I have not ceased to try experiments on myself, and to do all in my power to persuade others to try them. Surely, all this is legitimate, honest, and professional.

For many years, with the exception of one individual only—G. M. Seabroke Esq., F.R.A.S.—none seemed willing to listen. Now, at the end of 1889, a happy change has taken place, and several gentlemen, lay and medical, (all of them busy men, but it is the busy men who do the extra work), are giving some of their time and attention to this matter, and as I think, immensely to their credit, are working in earnest in this vein of experiment on themselves. They have my hearty congratulations and my grateful thanks, and there now follow extracts from their letters, and the best summary of their reports that I could make.

When, in the next century, hundreds of medical men are experimenting on themselves with three or four

hundred drugs and their different doses, first to learn the organs of the body which are the seat of the action of each drug, and next to discover the best doses for each morbid process in these organs, the little band of pioneers will not be forgotten.

II. *Experiments.*

Opium. (Papaver somniferum).

This drug is considered the most important of all drugs by the practitioners of the old school. But the uses made of it by them are in direct opposition to the uses suggested by the following experiments.

Hahnemann's remark, prefacing his provings of Opium is that "it is much more difficult to observe the effects of Opium than those of any other drug." This difficulty seems to have been experienced by him because he did not attend to the different effects of different doses.

Experiments in health.

The experimenters were Dr. Sharp, Mr. G. M. Seabroke of Rugby, Mr. J. B. Haslam of Rugby, Dr. Applebe of Coggeshall, Essex, Mr. H. C. Shann of York, and Mr. G. P. Richards of Edinburgh.

Dr. Sharp.—From many experiments the results have been as follows:—In doses varying from one drop of Opium 1 (*i. e.* one part of Tincture of Opium to ninety-nine of Proof Spirit) to one, two, and five drops of Tincture of Opium his pulse is quickened only; the bowels are slightly relaxed; the brain a little excited;—*one action.*

Mr. Seabroke.—Took six drops of Tincture of Opium, and his pulse being 54 rose to 58 and then fell to 52:—*two actions.* On another occasion he took ten drops of Tinct. of Op. and his pulse fell from 72 to 53; after some hours it returned to 64; this was attended with some drowsiness:—*one action* in the contrary direction to that of the smaller doses.

At a former time Mr. Seabroke took, without knowing what it was, one drop of Opium 1, night and morning for ten days; the effect was a considerable *increase of appetite.* A while after this he took five drops of the same centesimal dilution, night and morning for ten

days, and the result was the same—such a decided increase of appetite that he thought I had been giving him a tonic:—*one action* on the stomach contrary to the well-known effect on that organ of the larger doses. (Essay XXXII).

Mr. Haslam.—“Dec. 2, 1889. I send you a complete account of my late experiences with Opium. You will see that two one-drop doses of the centesimal dilution were followed by a complete disappearance of the minute itching spots which appeared one week after I took the one drop of the Tincture of Opium.” Mr. Haslam told me of this eruption on Nov. 23, when he had been troubled with it for a week. I showed him, in Hahnemann’s provings of Opium, this sentence—“small red itching spots on the skin here and there;” he said, “that exactly describes mine.” I advised him to take a dose of Opium 1 (a hundred times less than the dose which had produced the spots), which he did, and he reports the result:—

“*Opium*.—On Saturday evening, Nov. 9, took one drop of the Tincture in about two table spoonsful of water.

Pulse.—No appreciable alteration during the hour following.

Brain.—No certain effect—perhaps slight watchfulness.

Bowels.—Sunday, Nov. 10. Usual motion after breakfast; about 5.30, P.M. extremely loose motion; later in the evening (about 8.30) another very loose motion. Monday, Nov. 11. Loose motion after breakfast. Tuesday, Nov. 12. Normal condition. The action of the bowels struck me as being very quick.

Skin.—On Saturday, Nov. 16, very small and very itching spots appeared on left side about middle of body, spreading, during the following week, to right side chest and thighs, and small of back. Very irritable in evening, hardly perceptible on rising in the morning. Continued to Saturday, Nov. 23, when I took one drop of the centesimal dilution. Spots less irritable next night, when I repeated the dose. Very little itching next night, and without repetition of dose the spots had quite gone the following night.”

In reply to my enquiry Mr. Haslam wrote:—

"Dec. 24, 1889. I cannot remember ever having had any eruption similar to that which followed my taking the Opium. It was quite a new thing to me. The only eruptions on the body that I can remember, have occurred twice or three times after over-heating myself with walking or other similar exertion. They lasted only a day or so, and were not accompanied by any itching."

Dr. Applebe.—"Oct. 2, 1889. I have much pleasure in sending you the results of a few experiments made on myself with Opium.

"Tincture of Opium B. P. Experiments made while in recumbent posture. Age 37; healthy, vigorous; normal pulse 64.

Dose taken one drop.	Time .	5	15	20	30	40	60	120	240	minutes.	<i>Two actions</i>
	Pulse .	67	68	66	65	62	64	64	64	beats.	

Dose taken five minims.	Time . .	5	15	20	30	40	60	120	minutes.	<i>One action of larger doses</i>
	Pulse . .	66	67	70	72	68	64	64	beats.	

Caused slightly colicky pains in about fifteen minutes, which soon passed off. No drowsiness."

Dr. Applebe was requested to repeat on himself the experiment which had succeeded so well on the young milliner, as reported by him in the last Essay (LVI, page 11). "Nov. 17, 1889. I should begin by stating that I am most regular every morning after breakfast; the effect one dose of the medicine (two minims of Tinct. Op. B. P. in twelve ounces of water, a teaspoonful taken an hour before breakfast), had on me was that I had to go pretty quickly. I counted my pulse, it was about three beats quicker than normal. I think, however, this was attributable to the hurrying away so quickly."

He was then asked to continue the same dose for eight or ten days. "Dec. 8, 1889. I have been giving the Opium a fair trial. I found for five days it had the effect I told you in my last letter, viz. having to hurry off rather quickly. No appreciable effect on temperature or respiration; pulse slightly quickened. On the sixth day, strange to say, I was constipated (a most

unusual circumstance for me) ; next day I had *diarrhœa* ; this continued four days (keeping on with the medicine) : on the eleventh day I was again constipated, and had no action on the twelfth day. I took half the quantity and had relief without *diarrhœa*. I felt, whilst taking the Opium very bright and clear headed ; not at all ill-tempered, but rather looking on things through coloured glass."

Mr. Shann.—Was asked to take Dr. Applebe's prescription of Tinct. Op. two minims in twelve ounces of water, a teaspoonful every morning. "Nov. 30, 1889. I have tried the doses every morning as you suggested. I have taken it now for four days. So far it has no marked effect, certainly not caused any purging effect. I will let you know later on what may follow." "Dec. 23, 1889. I ought to have written to you before ; I had commenced a letter to you a week ago, but being called off never finished it. I apologise for my neglect, and am afraid even now my results are uninteresting. I consider that the small doses of Opium have some slightly relaxing action on me, but certainly nothing to cause anything like a *diarrhœa*."

Mr. Richards.—"Nov. 16, 1889. I have carefully carried out your directions, (he had been requested to take Dr. Applebe's prescription), and send you the result. I have taken observations upon the pulse, respirations, and temperature. Yesterday I had my old trouble—headache, and a real trouble it is to me, the pain at times is almost unendurable. I should add that it occurs periodically, *i. e.* about every five or six weeks, and has done for years. I think it depends upon the fact that I have an *oxalic acid diathesis*. I mention this matter because it *may* have some bearing upon the results of the experiments. I have naturally a bad appetite, but certainly the last few days it has increased in a wonderful way."

"November 6, 1889. Two minims Tinct. Opii in twelve ounces of water. Took a drachm (teaspoonful) of above, (bowels confined). 3 P.M. Motion, hard dark-coloured matter, instantly followed by *looseness* ; pulse good, 65.

Nov. 7. *Repeat*. Pulse, 11, A.M., 78 ; am miserable ; intensely irritable ; motion 6.50, P.M. *rather loose* ; pulse very weak all day, evening 60 ; but eat well.

- Nov. 8. *Repeat.* Bowels moved *twice* during the day; pulse better, 65; very irritable.
- Nov. 9. *Repeat.* Depressed and irritable all day; pulse good, full, rather hard, morning 70, evening 65; bowels just as usual, no looseness.
- Nov. 10. *Repeat.* Appetite still very good (unusual with me); pulse good, 74—60; *bowels confined.*
- Nov. 11. *Repeat.* Depressed again; pulse weak, better in the evening, 70—65; *bowels normal.*
- Nov. 12. *Repeat.* Pulse good, 68—62; *diarrhœa* four times during the day; appetite remains good.
- Nov. 13. *Repeat.* *Diarrhœa* continues, not so much; pulse good, 65; but fever in the evening.
- Nov. 14. *Repeat.* *Diarrhœa* better, am most irritable; troubled with large quantity of saliva all day; headache, dull throbbing in left temporal region; passed enormous quantity of urine, which is very acid, (oxalic acid mostly*) pulse 70—66.
- Nov. 15. Irritable; pulse weak, 90; temperature 99·5°; great trouble to work; but eat well; *bowels loose*, light matter; pulse at night a little stronger, 86; headache a little better."

The temperature varied much during the ten days. On the 6th 98·5°; 7th, 99°; on the 10th, 97·3°; on the 13th, 97·1°; on the 15th, 99·5°. Mr. Richards says, "I think the variations of temperature are directly traceable to the *Opium.*" A few weeks afterwards it was taken twice a day for a week and there was much less change. The respirations morning and evening for ten days varied only between 22 and 18. Mr. Richards adds "The irritable state in which I was, proved, I think, that the nervous system was in a state of excitement and from what cause? What could it be but the *Opium.*"

That the action of *Opium* in what are called *medicinal doses*, ("from 4 to 40 minims or more"), is to produce constipation and an unnatural sleep, sometimes passing on to coma, apoplexy, and death, is too well known to need proving by fresh experiments.

That still larger doses can again cause *diarrhœa* is acknowledged; that they can also cause brain excitement is strikingly proved by the following case, which I very well remember:—

* Sir Thomas Watson tells us that *Opium* renders alkaline urine acid. *Lectures*, 5th ed., vol. ii, p. 712.

At Bradford, sixty years ago, my uncle and I, were suddenly summoned in the evening to a young man, who had taken *an ounce* of Laudanum (Tincture of Opium). It was near; we went immediately; we found him in a state of very great excitement. What my uncle did I do not remember, but I have no doubt that he gave him an emetic; he then left me with the patient, saying, "walk him about all night." This, however, I could not do, for the young man took hold of my arm and walked *me* about all night in a way that I shall never forget. In a few days he was well. Here we have again *one action* of excitement.

Between the small doses which cause excitement, and the larger doses which cause sleep or stupor, we know that there are intermediate doses having both these actions, one following the other; it is, therefore, most probable that between the larger doses producing sleep and this dose which produced so much excitement, there is also an intermediate group of doses having the two contrary or "see-saw" actions.

Another experiment follows, with an enormous dose, the largest I have met with. In the first volume of the *Medico-Chirurgical Transactions* (1809) is "An account of the effects produced by a large quantity of Laudanum taken internally, by Alexander Marcet, M.D., F.R.S. Communicated Dec., 1806."

"On the 6th of Nov. last, Mr. Astley Cooper [afterwards Sir Astley] informed me at 4 o'clock in the afternoon, that he had just seen a young man, about 18 years of age, who had taken, at 10 o'clock in the morning, no less than *six ounces* of Laudanum, the whole of which had remained on his stomach, and had brought on symptoms which appeared to threaten immediate dissolution." Mr. Cooper, who did not see him till five hours after the accident, had made him swallow a solution of one drachm and a half of sulphate of zinc, which caused him to vomit about an ounce and a half of fluid smelling strongly of Opium, but he had fallen into a state of complete insensibility. When Dr. Marcet saw him an hour later, "his head was hanging lifeless on his breast, his eyes shut, and his countenance ghastly; his respiration slow and sonorous like apoplectic breathing; his hands cold; the pulse from 90 to 96, feeble and irregular;" 15 grains of sulphate of copper were given; in

one minute he suddenly threw up a large quantity of brownish liquid, having a strong smell of laudanum, followed by more, amounting to between one and two pints. He was then made to swallow warm water; was dragged from one room to another, and kept incessantly on his legs; on Nov. 8 he was able to walk out of doors; his appetite was not yet returned; his bowels had not been moved; in a few days he was perfectly recovered. Here we have again *one action* of depression.

It may be inferred that between the dose of one ounce causing great excitement, and the dose of six ounces causing apoplexy, there are again intermediate doses having the two contrary actions in succession.

It appears, therefore, that it is necessary to divide the doses of Opium into at least seven groups; two groups are exciting or stimulating, two are depressing or paralyzing, with intermediate doses having one action succeeded by the other.

Therapeutic uses.

By practitioners of the old school, Dr. Lauder Brunton tells us, "the general uses of Opium in disease are (1) to lessen pain; (2) to produce sleep; (3) to lessen irritation in various organs."* For none of these purposes has it been used by me for forty years. By them it is daily prescribed for diarrhœa; it is one of my best remedies for constipation. By them it is forbidden to be used for congestion of the brain†; for this formidable disease it is the best remedy I know. The above experiments also suggest it as a stomachic and tonic, and I have used it as such with success for loss of appetite from mental exhaustion. In all these cases the doses have been fractions of a drop of the Tincture.

Dr. Applebe.—"Sep. 17, 1889. I have been vastly pleased with the *purgative* effects of *Opium* in the small doses."

"Oct. 27. Since my first experiment with *Opium*, [$\frac{1}{100}$ th of a minim, given to the young milliner. Essay LVI], I have verified it again and again. I feel that I have a powerful weapon in my hand in this drug, which I knew before only as a narcotic and sedative."

In reply to my enquiries after his first case, Dr. Applebe

* *Pharmacology*, 3rd ed., p. 859.

† *Op. cit.*, p. 862.

writes :—“Jan. 1, 1890. The girl took one dose of the medicine on Friday, it acted well ; ditto Saturday ; on Sunday she had an action naturally ; and having got into the habit as it were, she went daily for a week ; at the expiration of the week, she was again constipated, but on repeating the dose as before, she had copious relief ; now, when she is at all troubled, she takes a dose of her medicine, and it never fails.”

Mr. Shann.—“Dec. 23, 1889. I gave one of my patients one-minim doses of Tinct. Op. B. P. three times a day, and he tell me that it has kept his bowels in very regular action once and sometimes twice a day, whereas he was formerly subject to constipation.”

Mr. Richards.—“Nov. 11, 1889. As regards Opium—I have constantly given it [in the small doses] to patients to cure constipation, and *nearly* always with success. This result from minute doses of Opium is the more interesting to me from the fact that a personal friend, who was most sceptical, tried *half-drop* doses in constipation and with the most satisfactory results.”

The following is a case testifying to the power of the smaller doses of Opium in apoplexy :—

Case.

1855. Summoned by telegraph to a considerable distance ; arrived at 10 o'clock at night : found a lady who had been seized with a fit of apoplexy while driving out ; she was near her confinement ; a physician and surgeon were attending her ; they would not see me ; they were requested to come down stairs. On seeing the patient she and her bedroom presented a scene of discomfort and disorder difficult to describe ; she was entirely apoplectic and unconscious, and from time to time had convulsions ; slight labour pains seemed to be coming on, and I requested that the surgeon should remain in the house. Belladonna, Aconite, and Nux Vomica were given at short intervals. Towards morning the labour pains increased and I retired. About six o'clock the child was born ; the surgeon retired and I returned to my duty. It was hoped that the birth of the child would be followed by improvement in the mother, but it was not so ; the apoplectic condition continued unabated, and there had been convulsions after the delivery. I gave *Opium* in

small doses. In a short time the patient recovered her consciousness and spoke to me; she knew nothing of the birth of the baby, which had died in convulsions before I was able to see it. Remaining over the day I left her the next morning comparatively comfortable; and she made a good recovery. This case will be found in the Appendix to the Essays (when that is published) in greater detail. It occurred thirty-five years ago, but is as fresh in my memory as if it had happened this year.

I had had already one case of apoplexy successfully treated with *Opium*, but till this second case I was not impressed with its extreme value in this disease.

Castor oil. (Ricinus communis).

Castor oil, like *Opium*, is an old medicine. Dr. Lauder Brunton says:—"Castor oil is one of our best *purgatives*." With me it is an excellent remedy for *diarrhœa*. Dr. Brunton adds:—"Its nauseous taste is its only objection." (*Pharmacology*, p. 1024). The following experiments show another and a stronger objection; they make it evident that the doses commonly given must often disappoint those who have prescribed them. On the contrary, given in the smaller doses as a remedy for one form of *diarrhœa*, success is much more certain. The cases of *diarrhœa* to which castor oil belongs may be learned from the powerful action of the *seeds* from which the oil is expressed. Twenty seeds have caused death, and the tissue chiefly acted on was the lining or mucous membrane of the stomach and bowels—*diarrhœa* from an irritation of this membrane is the disease for which the fractions of a drop of the oil are the remedy. I can testify to much success in the treatment of such cases by these doses of Castor oil. The discrepancy in the doses prescribed by the authorities is worthy of notice. Dr. Pereira gives for a dose "from one to two or three *tablespoonfuls*." Dr. Brunton says:—"Ten or twenty *drops* are generally sufficient to open the bowels."

Experiments in health.

The experimenters were Mr. Seabroke, Dr. S. H. Ramsbotham of Leeds, Mr. Richards, a Student, and Dr. Applebe.

Mr. Seabroke.—March 31, 1876. At my request took one grain of a trituration I had made of two drops (one minim) of the oil in 99 grains of sugar of milk, night and morning for three days, and his bowels *were not moved for five days*. (Essay XXXI, 1876)—*one action*, and a powerful one. Mr. Seabroke has several times repeated this experiment, and always with a similar result. These, I believe, were the first experiments of this kind ever made with Castor oil.

Nov. 20th, 1889. Five drops taken, result *no effect*.

Nov. 27th. This experiment repeated, again *no effect*.

Dec. 20th. Has taken half a teaspoonful with *no effect*. At another time a teaspoonful with *loose motion* the next morning.

The last dose taken again with the same result.

Dec. 5th. Took a dessert spoonful; on the 6th and 7th had his usual motions; on the 8th *had none*.

In Essay XXXII (1877) it was remarked “that all drugs which have been proved for this purpose, have an opposite action in smaller and larger doses; but it is not equally certain yet that all have intermediate doses with a double action. Some, as *Castor oil*, may have middle doses with no action at all.” This conjecture is now realised not only in Mr. Seabroke’s experiments but in those of two of the experimenters which follow. It will be remembered that in these Essays only *facts* are accepted; *theoretical explanations* of the results recorded are not accepted.

Dr. Ramsbotham.—“Oct. 27, 1889. I ought to premise that I never know what constipation is from my own experience; my regular habit is that the bowels are moved twice a day at least; and a very little matter—onion sauce or mental excitement—is enough to raise it to three or four times, and to make the stools quite loose.

“Taking *one drop* of Castor oil at bed-time on the 17th caused me to pass the 18th without the smallest inclination to go to stool, an unheard of thing for me. Matters righted themselves on the 19th, and on the 20th at bed-time I took the same quantity. No movement of the bowels on the morning of the 21st; but in the afternoon, after conducting a meeting of our private Musical Society at which discussion waxed warm, I went to stool, and the fæces were healthy and consistent. Had it been a

thoroughly relaxed motion, I should not have been surprised.

"You already know that *five drops*, taken during an attack of diarrhoea seemed to aggravate it; and that the *same dose* taken when in a normal state of health produced *no effect*. I did not repeat that dose, but waited a day to be sure that all effect had passed away; on the 23rd at bedtime I took *ten drops*. My usual habits were not interfered with on the 24th, but on the morning of the 25th I passed a copious stool, distinctly less consistent than usual, and having a peculiarly pungent and penetrating odour. I think I am right in attributing it to the oil, as I carefully noted that my diet contained nothing which in an ordinary way would relax the bowels; this was the only stool on that day."

"Nov. 16, 1889. My experience with Castor oil has been curious. I took *thirty drops* on Thursday night; noticed no perceptible effect on Friday, as my usual regular habits were not interfered with; on Saturday morning a copious stool, not loose, but with the peculiar odour I noticed before, followed by a slightly relaxed motion in the evening, three on Sunday, and one on Monday morning decidedly loose. This seemed to exhaust the action of the oil, and since then I have had one stool only per diem, quite natural."

Mr. Richards.—"Nov. 2, 1889. I took *one-drop* doses of Castor oil every morning for four days, when I was *obliged* to cease, and although naturally subject to looseness of the bowels it produced the most decided *constipation*, I am perfectly satisfied as to the action of one-drop doses of the oil upon myself.

"I next tried *five-drop* doses—but with a *negative result*.

"I found doses of half a drachm produce slight *diarrhoea*."

A Student.—Mr. Richards writes to me:—"Dec. 15, 1889. A friend and myself took, as nearly as possible, $\frac{1}{100}$ th drop doses of Castor oil with *constipation* as a result."

Dr. Applebe.—"Nov. 17, 1889. With regard to the Castor oil, in my own case *one drop* had no effect, *five drops* caused *constipation*; *ten drops* acted freely."

We have seen that Mr. Seabroke, who was very uncomfortably constipated by the $\frac{1}{50}$ th of a drop of Castor

oil, found *five drops* to have no effect, and a *teaspoonful* to be followed by a loose motion the next morning, was again constipated by a *dessert spoonful*.

And it is well known that larger doses do constipate. In my early practice—I do not know how it may be now—it was very common for mothers and nurses to give children doses of Castor oil, which to them were large, and it was also very common for these mothers and nurses to be disappointed with the result: the children instead of having their bowels opened, had them more confined, and I heard, again and again, the exclamation “children can *digest* any amount of Castor oil!” This is an instance of the mischief done by an explanatory hypothesis. It hides the truth and stops the progress of knowledge. If the *fact* had been noticed that certain large doses constipate, and a lesson been learned from the fact, without inventing an explanation, what useful knowledge would have been gained!

Again, there are doses still larger whose action is to purge. Dr. Ramsbotham writes to me—“Oct. 1, 1889. I once was called to a patient who had taken, so he told me, *eight ounces* of Castor oil in one dose, and the effect was the reverse of constipating. I did not take notes at the time, so I now only remember the bare outline of the case, but I am sure of the correctness of the statement.”

It will be noticed that all the five experimenters have taken the “certain smaller doses” of Castor oil, and that *all* have been constipated by them. The doses forming this group have varied from $\frac{1}{100}$ th of a drop to five drops of the oil. This difference is caused by idiosyncrasy or predisposition. With three experimenters five drops had no perceptible effect; ten drops, thirty drops, and a teaspoonful respectively, acted as an aperient. A dessert spoonful, in one case, slowly constipated; it remained in the stomach the first day, as Mr. Seabroke “tasted the oil very disagreeably all the day he took it, especially after dinner;” but the constipation came on the third day. A very large dose (Dr. Ramsbotham’s case) again purged. The actions of these groups of doses are, group for group, in the opposite direction to those of *Opium*, but they alternate in a similar manner.

Therapeutic uses.

Since the first experiment by Mr. Seabroke in 1876, I have myself taken, and have given to many patients the $\frac{1}{50}$ th part of a drop of the oil as a remedy for diarrhœa, and with much success.

Dr. Ramsbotham writes,—“Sept. 24, 1889. The $\frac{1}{100}$ th minim of Castor oil has frequently stayed diarrhœa both in myself and my patients.”

Dr. Applebe writes,—“Nov. 17, 1889. In a case I had of bilious diarrhœa, *one drop* of Castor oil acted like magic. I had to give a minute dose of *Opium* to cause the bowels to act again.”

Castor oil, in the future, is to be one of our best remedies, but by no means the only one, for *diarrhœa*.

By way of offering some consolation to my brethren of the old school, a case shall be related in which *Castor oil* as an aperient, saved a life from imminent dissolution. It was a case of obstruction of the bowels caused, as so many have been caused, by large doses of drastic purgatives, which could only increase the constipation, and which cases generally prove fatal.

Case.

Fifty years ago I was returning to Bradford from the Low Moor Iron works, when a medical man rode hastily up to me looking exceedingly anxious and exclaiming,—“Mr. Sharp, I am losing a patient from obstruction, and I have given every purgative in the Pharmacopœia, and in large doses—is there anything more that I can do?” “Give him a dessert spoonful of Castor oil, and give him no more of anything else.” He rode off looking vexed. About a fortnight afterwards we met again. As soon as he saw me his countenance brightened and he came and taking hold of my hand, he said—“Mr. Sharp, I am indebted to you for saving the life of my patient; I rode as fast as I could from you to his house and gave him the dose of oil—it answered your expectations, which were not mine, and he has recovered.”

Here then, it may be said, is a successful use of Castor oil as a purgative. This is true; but such cases of obstruction *ought never to occur*. Sydenham would have said,—“These patients die, not of the disease, but of the doctor.”

Aconite. (Aconitum Napellus).

Opium and Castor oil are old and well-known medicines ; for Aconite, as a remedy in small doses for simple and inflammatory fever, we are indebted to Samuel Hahnemann. In large doses it is a very powerful poison. The root has been repeatedly eaten at dinner in mistake for horse-radish with fatal results ; in such cases of poisoning death comes with the *failing heart*.

The "larger" doses we are concerned with are the "medicinal" doses of the present medical practice, which Dr. Lauder Brunton tells us are "from one to fifteen minims." The "smaller" doses are fractions of a minim. That medicinal doses may cause death we have had painful proof in the death of Dr. Male of Birmingham in 1845, who died from not more than eighty drops taken in ten doses over a period of four days—the largest quantity taken at once being *ten drops*, (much less than ten minims).* He took it to relieve rheumatic pains. As first used it was disappointing and unsatisfactory. So lately as 1857, in the 4th Edition of Pereira's *Materia Medica* a long list of the diseases in which it has been given is recorded, and it is added, "In the large majority of these maladies scarcely any practitioner now believes in its efficacy." The exception to this is the *topical* application of Aconite in neuralgia. Pereira adds, "When the disease depends on *inflammation* Aconite will be found, I think, an unavailing remedy." As already stated, the Profession is indebted to Homœopathy for Aconite as a *febrifuge*, and so effectual is it that, so long as it is given in doses of the fractions of a drop of the Tincture, it will be impossible for *bleeding* to be had recourse to again.

Experiments in health.

The experimenters were Dr. Sharp, Mr. Haslam, Mr. Seabroke, Dr. Applebe, Mr. Shann, and Mr. Gerard Smith of London.

Dr. Sharp.—For many years (since 1872) half a drop of the first dilution of the Tincture of Aconite (Acon. 1) has made his pulse *slower* without any other effect upon the heart—*one action*.

* *Medical Jurisprudence*, by Alfred S. Taylor, F.R.S., 2nd ed., 1846.

One drop or more of the same dilution has first made the pulse *quicker*, and then *slower*—*two actions*.

Two and four drops of the strong tincture *quicken* his pulse, and this is not followed by any slowing of it beyond a return to its healthy state—*one action* only, but in the contrary direction of that of the half drop of Acon. 1.

Mr. Haslam.—“ Rugby, Dec. 8, 1889. I send you the results of my experiment with Acon. 1. The circumstances were more favourable than in any previous one. My pulse was in a normal condition, and I was lying down all the time, and had the dose close beside me, so that I could take it with the least possible disturbance. About ten minutes after lying down I found my pulse seemed steady at 60—61, that being the result of three consecutive observations: and except the slight mental disturbance referred to in my note below the record, I was quiet all the time.”

“ Took half a drop of Acon. 1 in two table spoonful of water. Pulse 60—61.

Time .	5	8	10	13	15	18	20	minutes.	<i>One action.</i>
Pulse .	60	57	60*	58	59	59	60	beats.	

“ Oct. 5, 1889. I have made three ‘provings’ with one drop, two drops, and four drops respectively, of the centesimal dilution (Acon. 1). There was in each case a very slight rise in the pulse, followed by a more noticeable depression, amounting to 4 beats with one drop, 5 beats with two drops, and 8 beats with four drops.”—*two actions*.

“ Nov. 9. Took 4 drops of Tincture of Aconite (the strong tincture). Pulse 64.

Time .	5	10	15	20	30	45	60	minutes.	<i>Two actions.</i>
Pulse .	64	64	64	64	66	62	60	beats.	

“ Nov. 7. Took 7 drops of the Tincture of Aconite. Pulse 57.

* “ This rise may very well have been caused by a slight temporary excitement occurring just after the previous observation.”

Time .	5	10	15	20	30	45	60	minutes.	<i>Two actions.</i>
Pulse .	60	57	58	54	58	*	57	beats.	

“Sept., 1889. Took 10 drops of the Tincture of Aconite about 6.20, P.M. Pulse 63.

Time .	1	5	10	20	25	minutes.	<i>One action.</i>
Pulse .	65	66	64	64	64	beats.	

“After this an unusually comfortable night of sleep.”

In this experiment there is the contrary action of the larger dose, and nothing else. Mr. Haslam has tried more experiments with Aconite, but those given above have been made under the most favourable conditions.

Mr. Seabroke.—At different times has made the following experiments, the first four with the first centesimal dilution of the Tincture of Aconite; the second three with the strong Tincture. His pulse is habitually a slow one, and such are less easily acted upon by Aconite than quicker ones.

“On the night of Dec. 22, 1889, I took half a drop of Acon. 1. Pulse 67.

Time .	5	10	15	20	25	35	60	minutes.
Pulse .	67	67	69	69	68	68	66	beats.

“These figures are quite within the limits of ordinary variation in an hour.

“Jan. 5, 1890, at 6.53 P.M., half a drop of Acon. 1 taken. Pulse 61.

Time .	Until 10	15	20	25	30	minutes.	<i>One action.</i>
Pulse .	61	59	59	59	59	beats.	

“Oct. 18, 1889, 8.15, P.M. Pulse 58. Took two drops of Acon. 1.

* Disturbed.

Time .	5	10	15	20	30	45	60	minutes.	<i>Two actions?</i>
Pulse .	55	56	58	58	56	60	58	beats.	

"Oct. 25, 9, P.M. Pulse 56. Took ten drops of Acon. 1.

Time .	5	10	15	20	30	60	minutes.	<i>Two actions.</i>
Pulse .	59	57	55	56	55	55	beats.	

"Oct. 3, 8.15, P.M. Pulse 54. Took four drops of Tinct. Acon.

Time .	5	10	15	20	30	45	60	minutes.	<i>Two actions?</i>
Pulse .	50	53	54	52	53	53	56	beats.	

"Oct. 4, 8.15, P.M. Pulse 55. Took six drops of Tinct. Acon.

Time .	5	10	15	20	30	45	60	minutes.	<i>Two actions.</i>
Pulse .	52	57	58	56	55	56	55	beats.	

"Oct. 6, 8.10, P.M. Pulse 58. Took eight drops of Tinct. Acon.

Time .	5	10	15	20	30	55	minutes.	<i>One action.</i>
Pulse .	65*	62	59	60	61	60	beats.	

Dr. Applebe.—October, 1889. "My normal pulse in recumbent posture, at 7, P.M., is 64. *One minim* of Tinct. Acon. B. P. in ten minutes reduced the pulse to 60: at 8, P.M., pulse again 64"—*one action.*

"*Three minims* reduced pulse in five minutes to 60; in half an hour pulse was 68; in one hour pulse still 68; in two hours 64"—*two actions.*

"*Six minims* taken, in five minutes pulse was 66; in half an hour pulse 70; in two hours pulse still 70; in two

* "He was immediately conscious of the quickening of the pulse."

hours and a half pulse 68 ; four hours pulse normal (64) ”
—*one action.*

Here it appears that the action of one minim would have been what is desired, namely, the slowing of the pulse only. That the action of three minims would have been beneficial in the first instance by reducing the frequency of the pulse, but soon afterwards the fever would have been increased. Six minims would have aggravated the fever and inflammation from the first taking of the dose. All this on the supposition that the action of drugs is not more powerful in cases of illness than it is in health ; but the contrary, that it is more powerful, is generally what is experienced.

Mr. Shann.—“ October 23, 1889. With regard to my experiments with Aconite, they seem to me very unsatisfactory as regards any deduction to be drawn from them. It seems as if my pulse, in its most normal condition is so varying as to frequency that, drugs or no drugs, I get a variation in number of beats nearly every time I take it, and I have taken it most carefully each time. My pulse just now is 65, only a short time ago it was 72, and that while writting this letter to you, so that I fear that I am not reliable on the point of pulse action.” Of the five experiments Mr. Shann has sent me the last may be given, as from it this inference may be drawn, that *six minims* of the Tincture of Aconite of the British Pharmacopœia, if it acted at all, increased the frequency of the pulse, so that, if given to a patient in inflammatory fever, must do harm and not good. This experiment, therefore, confirms Dr. Applebe’s experiment with the same dose.

“ Oct. 23, 9, P.M. Pulse 68. Six minims of Tinct. Acon. B. P. taken.

Time .	5	10	15	20	30	45	60	minutes.
Pulse .	66	71	65	64	64	69	70	beats.

The last rate (70) “ continued for nearly half an hour. Aconite sensation at back of the throat, as after chloroform inhalation.”

Mr. Gerard Smith.—“ Jan. 1, 1890. I now send you the result of two experiments with *one drop* of Acon. 1^x (the decimal dilution of the Tincture of Aconite, one

drop containing the tenth part of a drop of the strong Tincture). I repeated the experiment twice in the day, six hours apart, with the same result.

“Dec. 31, 1889, 11.30, A.M. Pulse being 64. Took one drop of Acon. 1^x.

Time .	5	15	20	35	50	55	65	75	80	minutes.	One action.
Pulse .	64	64	63	61	58	58	59	62	64*	beats.	

This is distinctly the lowering action desired from Aconite from a dose about midway between my dose (half a drop of $\frac{1}{100}$ th of a drop) and Dr. Applebe's (one minim of Tinct. Acon. B. P.). This, therefore, constitutes the group of small doses, so far as the present experiments teach us, out of which, doses to be prescribed for inflammatory fever may be chosen. The idiosyncrasy of each patient must decide what dose belonging to the group is the best for that patient.

In reply to a question about the larger doses allowed by authority to be prescribed, (“from one to fifteen minims”), Mr. Smith writes:—“Dec. 11, 1889. I have seen *fifteen minims* of the B. P. Tincture of Aconite given as a dose; it does not kill a man, but it produces a slight delirious state; it does not produce perspiration; and the well-known vascular relaxation of the lesser doses is absent.”

It is obvious that it is absurd to give such doses as these to a patient and expect them to do any good. They cannot but do harm.

The largest dose of Aconite taken voluntarily that I am acquainted with was reported in the ‘Standard’ newspaper for Oct. 9, 1889, as follows:—“A schoolmaster in the village of Caersws, Montgomeryshire, walked into the surgery of Dr. Snow and asked to see him, but he was away from home. He then took a bottle containing Aconite and drank the contents, about an ordinary tea-cupful. He then walked into the street and commenced screaming and yelling horribly. Asked what was the matter he replied, ‘I have taken my last dose.’ He was taken to Dr. Ferguson’s surgery, and the stomach-pump was used, but he shortly afterwards died in great agony.” In reply to my enquiry Dr. Ferguson courteously wrote:—

* “At which it remained.”

“October 10, 1889. With regard to the painful occurrence of Mr. — poisoning himself, I did not see him until about a quarter of an hour after his having taken the poison. He was just able to say that he had swallowed about a teacupful of Aconite. It was not the Tincture, as the bottle was afterwards discovered. It was the ordinary ‘Liniment of Aconite.’ He never complained of any tingling of lips or mouth, but I noticed that his hands became rapidly benumbed; the breathing was also very laboured. His pulse when I first saw him, was extremely weak; as the poison passed into the system it became faint and flickering; *the heart and pulse impulse could not be distinguished at least half a minute before life was extinct.* He was covered with a cold clammy perspiration.”

In a second letter, dated October 14, 1889, giving me leave to publish what he had written, Dr. Ferguson adds —“I cannot say whether the bowels or kidneys were acted upon previous to the taking of the poison, but certainly not after. So far as I have been able to ascertain, he lived about thirty-five minutes from the time of coming into my surgery.”

The heart dying half a minute before the rest of the body is worthy of note. Every experiment with Aconite testifies that the *heart* is the great seat of its action. I think the four ounces of Liniment of the British Pharmacopœia, if well made, would be equal to $14\frac{2}{5}$ ounces of the Tincture. It is to be earnestly hoped that such a painful case will never happen again.

Therapeutic uses.

The choice of doses of Aconite, as learned from these experiments, lies between the $\frac{1}{100}$ th of a drop of the Tincture, or less, and one minim. This choice is abundantly confirmed by its use as a remedy. I have never given a larger dose than the centesimal dilution. These doses of Aconite will often arrest “a cold,” *if it is a feverish one.* The orthodox duration of a cold is well known to be three weeks. For croup in children Aconite in the second or third centesimal dilution, alternately with Spongia every five or ten minutes until relief is obtained, and followed by a few doses of Hepar Sulphuris are admirable substitutes for emetics, warm baths and

tracheotomy. For inflammatory fever *Acon.* 1, alternated every two, three, or four hours with some drug the local action of which is on the part inflamed, and also given in the smaller doses having a contrary action, will cure in a way that those who have not seen it find it very difficult to believe. Let me take this opportunity to repeat once more, that Aconite should not be given in low or typhoid fever; I have seen it do great harm in that.

Cases.

Pleurisy.

When this inflammation is incipient and there is pain—the characteristic *stitch* between the ribs on inspiration—rendering it impossible to take a deep breath, and before the pulse has begun to quicken, I have found one drop of *Bryonia* 1 (the first centesimal dilution) effect a complete cure in a very short time. When the stage of inflammation is further advanced, and there is fever, it is better to begin with *Acon.* 1 and *Belladonna* 1, in half-drop doses alternately, every hour and a half or two hours. The Aconite will slow the pulse, and the Belladonna will lessen the inflammation, and the pain will abate, probably in a few hours. Then a few doses of *Bryonia* 1 will usually complete the cure, unless other complications arise. With this treatment it will be found that bleeding, leeches, cupping, blistering, large doses of drugs, and paracentesis, are unnecessary.

Titanium.

This metal was discovered in 1791. It is found chiefly in clay iron stone. The specimen I obtained was found at the bottom of a large smelting furnace at the Low Moor Iron works, which had been burning many years and was blown out for repairs. The metal was in small cubic crystals of a copper colour but deeper red, and having a very brilliant lustre. The crystals were triturated for me by Mr. Turner of Manchester who told me they were difficult to triturate from their hardness; the proportion was one grain to ninety-nine of sugar of milk. I have lately got more specimens.

Experiments in health.

The experimenters were Dr. Sharp, and Mr. G. P. Richards.

Dr. Sharp.—This metal was experimented with by him in 1856, and an account of the effects was published in a “Reply to a Letter of Sir Benj. Brodie” in 1861. The account was also given in Essays XIV, and LVI. He took two grains of the first trituration (*i. e.* $\frac{1}{80}$ th of a grain of the metal) once a day for a week. He was made very ill by what is now called blood poisoning, one of the consequences being albumen appearing in large quantity in the urine, and which continued, in spite of all treatment, for two years, and until a few small doses of the second trituration of *Titanium* were taken, after which the albumen and all other symptoms disappeared in less than a week. All this has been burnt into his mind, and the readers of this Essay will imagine with what deep interest he received the following letter:—

Mr. Richards.—“Nov. 5, 1889. In regard to *Titanium*.—Last April I had the charge of a physician’s practice (Newcastle) and in the surgery noticed a bottle labelled *Titanium 2^x*. (This is the same as *Titanium 1*). I candidly admit that at the time, if there was a drug that I knew hardly any thing about, it was *Titanium*, but of simple curiosity I took about *two grains* ($\frac{1}{80}$ th of a grain of the metal), at about 3, P.M. At this time I was in a poor state of health, and thought I had symptoms of incipient Bright’s disease—or something equally unpleasant. Consequently, I examined my urine daily, but there was no albumen until the day following the one upon which I took *that* *Titanium*, when I found a distinct trace of *albumen*, which continued more or less until the first week in July last (three months). Although I thought the *Titanium* might have had something to do with it, I knew so little about the drug that I was not certain. I was, therefore, astonished to find that it had treated you in the same way. I certainly think that I will not play with *Titanium* again—it is too serious a matter.”

In reply to my enquiries Mr. Richards has written again. “Jan. 2, 1890. To the best of my knowledge there has been no return of the albumen since July, but it did not pass away *per se*, the fact being that I took

three-minim doses of Acid. Phosporic. (B. P.) for about ten days, four times a day; the albumen then passed away. That I was threatened with Bright's disease was what I did think at the time; of course I do not think so now. I have not any doubt that the albuminuria was caused by the *Titanium*. I have just now examined my urine, and cannot discover the slightest trace of albumen although I have used various tests."

It will be noticed that the single dose taken by Mr. Richards was the same—the fiftieth part of a grain—as that taken by Dr. Sharp once a day for a week. One suffered from albuminuria for three months, the other for two years, and neither of them has had any return of the complaint since—Mr. Richards for six months, Dr. Sharp for thirty-three years.

Therapeutic uses.

In the Reply to Sir Benjamin Brodie (1861) the action of *Titanium* was summed up as being upon:—

"(1). The *stomach*; bringing on nausea, loss of appetite, and feeling of discomfort.

"(2). The *brain and nerves*; giddiness, imperfect vision, the peculiarity being that *half an object* only could be seen at once, desire to keep the eyelids closed.

"(3). The *blood*; a perceptible derangement of the system, which could not, without danger, have been carried further."

And a case is given in considerable detail of serious blood disease, which had continued seven years after an attack of typhus fever, and which was very rapidly cured by small doses of *Titanium* 2.

When the notes quoted above were written I was suffering still from great debility, and had the discharge of albumen, but I did not then attribute the latter to the *Titanium*. This did not become clear to me till some time afterwards. The following is another case of blood disease nearly as quickly cured as the earlier one.

Case.

1860, Sept. 14. Mr. H—. Consultation. Feels altogether out of condition; has lost thirty pounds in weight in a year; has no strength; perspires on the least ex-

ertion; has pain across the loins; but has a good appetite; can sleep well; no excess of urine (which unfortunately was not analysed or tested for albumen); no diarrhoea. He had been a very robust and vigorous man. *Titanium* 2 night and morning.

Oct. 10. Consultation. Is much better in every way; the pain is gone; the perspirations are gone; he feels much stronger; and has already gained from three to four pounds in weight. The *Titanium* 2 (the second centesimal trituration) was given him for another week, and he needed nothing more.*

III. Summary of the Experiments.

With Opium.

There were six experimenters, and by their careful statements the following facts seem to be made clear:—

There are certainly five, and probably seven or more, groups of doses of Opium, each with characteristic actions.

There is a group of small doses whose action is exciting or stimulating on the brain, the heart, the stomach, and the bowels—this group includes doses from $\frac{1}{100}$ th of a drop to five drops of the tincture. (Dr. Sharp and Mr. Haslam).

A second group has first a stimulating and then a sedative action. This group includes doses of from one to six drops of the tincture. (Dr. Applebe and Mr. Seabroke).

A third group has again one action only, but this is the contrary of the first,—it is sedative and narcotic. It includes doses from five minims or ten drops to the so-called “medicinal doses.” (Mr. Seabroke and Dr. Applebe).

A fourth group has one action, and that a repetition of the smallest doses, but instead of being slightly is vehemently exciting, especially on the brain. The dose in the case given was an ounce of the Tincture. (Dr. Sharp).

A fifth group is again dreadfully narcotic. The dose

* Some of the Titanium used in these experiments has been given to Messrs. E. Gould and Son, 59, Moorgate Street, London, E.C., who can supply the triturations.

in the case reported was six ounces. (Dr. Alexander Marcet).

Between the third group and the fourth, and between the fourth and fifth, it is highly probable that there are intermediate doses having both actions. It is possible that between these very large doses there may be also other alternations of doses with one action.

Then there are the experiments with repeated doses, and these have some important features. Their effect on the stomach in increasing the appetite (Mr. Seabroke and Mr. Richards) is suggestive of a new use of Opium as a stomachic and tonic. Their effect on the bowels is very remarkable; the small dose, after acting as a purgative for four or five days, caused constipation on the fifth or sixth day, and then became again purgative for some days (Mr. Richards and Dr. Appleby), and after that again constipating. (Dr. Appleby).

The value of these experiments is very great in reference to the difficult question of repeating the doses of a medicine. They show that repetition may undo the good that has been done, and so may increase the original mischief. This I have often noticed with regret in my own practice; it is a sin, I fear, we are all guilty of; it is so extremely difficult to persuade either oneself or one's patients to discontinue a medicine as soon as it has done good. This opportunity may be taken to remark that the repetition of small doses may be followed by effects in one case directly opposite to those in another case, *e. g.* I have taken small doses of *Arsenic*, which, as single doses, have tonic or astringent effects on the stomach and bowels, until they have had the action of the larger doses, and have caused diarrhoea; and I have taken the small doses of *Digitalis*, which, as single doses, are tonics to the heart, and diminish the secretion of the kidneys, until they have caused suppression of urine, which is the extreme action of the smaller doses, and the opposite of the action of the larger doses. Both these results are strong protests against the common practice of the continued taking of doses—even when the doses are small ones.

The small, red, itching spots of Mr. Haslam are a very interesting fact. They prove that small doses can not only "augment and diminish" functions, but that they can on a small scale also produce a "perversion"

of functions. If they can thus produce, they may also remedy opposite perversions caused by larger doses, or by other causes. The cure of these spots by a dose of *Opium* a hundred times less than that which caused them, ought to attract notice as an example, as *Titanium* was, of small doses of a drug being an antidote to the poisonous action of larger doses of the same drug.

Mr. Shann's experience is valuable. Along with that of Mr. Richards, we probably have the two extremes of the influence of idiosyncrasy or predisposition. The subject is a discouraging one to physicians of all schools, but it is there, and has to be faced. It affects all methods of treatment alike. The value of Mr. Shann's experiments on this occasion is that they anticipate and reply to similar apparent negatives, should such be put forward, as contradicting the views of this Essay. It will not be forgotten that negatives are not negations.

The extreme of sensitiveness to the action of *Opium* in Mr. Richards is also valuable. It shows that such predisposition may be met with among patients, when a necessity will exist for the use of doses even smaller than those which he took. The state he was thrown into was an extreme one, but it was entirely consistent; it was excitement all round.

Nothing can be less doubtful than the reports of the new therapeutic uses of *Opium*. There is only one testimony concerning these, and that of the very strongest kind. They have been "verified again and again." No evidence of the use of *Opium* in apoplexy could be stronger than that given in the case reported. Nothing could be more satisfactory proof of its value as a remedy for constipation than that furnished by the medical experimenters. On this topic perhaps it may be well to remark that constipation arises from various causes, and that one drug cannot be a remedy for them all. There are cases for which other drugs—such as *Nux vomica*, *Sulphur*, *Lead*, *Podophyllum*, &c.—may be better adapted as remedies; but for torpid constipation we need not seek a better medicine than small doses of *Opium*.

With Castor oil.

There were five experimenters. The results of their experiments show that the various doses of *Castor oil*

may be classified in groups in the same manner as those of *Opium* have been.

There is a group of small doses whose action is astringent upon the bowels causing constipation of a very decided character, both in health and in sickness. This group includes doses from the $\frac{1}{100}$ th of a drop to five drops. (Mr. Seabroke, Mr. Richards, and a Student, Dr. Ramsbotham, and Dr. Applebe). Four of these also took five-drop doses; with three the dose had no effect; one (Dr. Applebe) was constipated by it.

A second group has no perceptible effect. This group includes doses from five drops to half a teaspoonful. (Mr. Seabroke, Dr. Ramsbotham, and Mr. Richards). Some will immediately exercise their ingenuity upon this apparent neutrality, and will put forward sundry bright but imaginary *explanations*. With a respectful bow I decline to listen to any of them.

A third group has an action contrary to that of the first group. It acts as an aperient. The doses range from ten drops to a teaspoonful. (Dr. Ramsbotham and Mr. Seabroke).

A fourth group acts as the first, and again constipates. The dose in one experiment was a dessert spoonful. (Mr. Seabroke).

A fifth group again purges. The dose taken was eight ounces. (Dr. Ramsbotham's case).

It is probable that there are groups of doses having different actions, between the fourth and fifth.

The therapeutic use of *Castor oil* in the small doses, as a remedy for diarrhœa is sufficiently established. (Dr. Sharp, Dr. Ramsbotham, and Dr. Applebe). The taking of the larger doses as a purgative is a very disagreeable process, and may be entirely discontinued.

As was remarked of constipation, so it may be said of diarrhœa, that it has many causes, and differs much in kind, so that there can be no one remedy for all cases. The kind for which *Castor oil* seems to be adapted has been explained; other kinds may be cured by other drugs; such as that arising from a more severe degree of irritation of the mucous membrane by *Arsenic*; that caused by exposure to cold, by the favourite purgative of Hippocrates—*White Hellebore* (*Veratrum album*); that from summer heat by *Cinchona*; that by indigestion by

Pulsatilla or *Nux vomica* ; the chronic diarrhœa of children by *Rhubarb* ; &c.

With Aconite.

There were six experimenters with *Aconite*, and the following groups of doses were distinctly observed :—

A group with one action—that of slowing the pulse. The doses ranged from half a drop of Acon. 1.—the first centesimal dilution—(Dr. Sharp, Mr. Haslam, and Mr. Seabroke), to one minim of the Tincture of Aconite of the British Pharmacopœia, (Dr. Applebe).

A group with two actions. The doses varied from one drop of Acon. 1. (Dr. Sharp and Mr. Haslam) to three minims of Tinct. Acon. B. P. (Dr. Applebe).

A group with one action—the contrary of that of the first group. This group included doses from two drops of Tinct. Acon. (Dr. Sharp) to six minims of Tinct. Acon. B. P. (Dr. Applebe).

Mr. Shann's experiments were again of value, because they are an example of some of the results of such experiments as these, made by men varying so much as men do in their sensitiveness to the action of drugs. To me it is surprising that so many individuals, entirely separated from each other, so that one did not know what the others were doing, and all of different temperaments and most actively engaged but in different kinds of work, should have presented me with a series of results so confirmatory of each other.

Dr. Ferguson's melancholy case terminated fatally in a short time. It is, doubtless, the largest dose of *Aconite* ever taken ; its effects have the same character as those of all the smaller ones ; the heart is the chief organ acted upon—it dies first—the contrary of the action of *Opium*, from which, if recovery takes place, the heart is the organ of those most affected, which recovers first.

The therapeutic use of *Aconite* in inflammatory fever is emphatically testified to by the whole body of homœopathic practitioners.

With Titanium.

The experimenters have been Dr. Sharp and Mr. Richards. This is the first introduction of the metal

into the *Materia Medica*, and, of course, its use as a medicine is in its infancy ; but enough has been ascertained respecting its properties to show that, for the diseases which belong to it, it is a very powerful remedy. As a poison taken in health its action is on the blood, which it rapidly disorders, and disorders so much that the most important organs and their functions are greatly disturbed. The brain and nerves, and the digestive organs are especially attacked, so that great debility and excessive nervousness are soon produced. Dr. Sharp became so weak that at one time he could scarcely cross the road, and so nervous that he almost shrunk from going into a booking office at a railway station to take a ticket.

As a remedy, the second trituration ($\frac{1}{10000}$ th of a grain) has shown a power of healing as remarkable as the power of poisoning possessed by the first trituration ($\frac{1}{100}$ th of a grain). All the debility, loss of appetite, and nervous timidity experienced by Dr. Sharp for so long a time passed away, together with the albuminuria, in a surprisingly short time after a few doses of it had been taken.

Titanium is not a *polychrest*—I do not think there are any drugs really such—and the greatest danger it has to encounter is that of being given as *Conium* was, when first introduced into medicine by Baron Stöerck, for many other diseases besides that for which it is adapted.

IV. *Reflections.*

1. The experiments reported in this paper demand the attention of the Medical Profession. They are not theories but facts. They are not speculative but practical. They are not abstruse and difficult to be understood ; they are as plain to the youngest as to the oldest practitioner. They are of the highest concern to every medical man's patients. The inferences obviously to be drawn from them may be startling, but, assuredly, they are true. They may be thus stated :—

(1). The small doses of drugs used in these experiments have power to act on the living human frame both in health and disease.

(2). The effects of these actions are sufficiently distinct to admit of classification.

(3). The commonly received opinion that these effects are simply increased in degree, and not altered in character, by increasing the dose, is an error.

(4). It is necessary to arrange doses into groups in order to classify them, on account of the varying sensitiveness to their action of different individuals.

(5). Each of these groups has characteristic actions either in kind or in degree, which distinguish it from the others. Some groups have actions contrary to others; some are intermediate and have both actions in succession; the groups which are alike in their kind of action differ in the amount of energy; the large doses which act in the same direction as the small ones, act violently, and their action is accompanied with more or less serious complications.

(6). The doses which have both actions are not well adapted for use as medicines. Even when the drug is rightly chosen, such doses must either first aggravate the disease before it can alleviate it, or after giving relief it must make the malady worse.

(7). The large doses which have energetic and complicated actions do more harm than good.

(8). Doses which are small, and have only one action, and that action a known one, are the doses fit for use as medicines; these doses if chosen because their action is contrary to that going on in the disease, will do good and not harm, provided they are discontinued as soon as the good is observed.

2. A very serious thought forces itself at once upon our notice, namely, that the use hitherto made of drugs as medicines has been a mistaken one. They have been given for diseases for which they are not designed. This error has been continued from age to age, by the large doses it has always been the custom to administer. In the drugs here experimented with, we see that *Opium*, hitherto given to put patients into an unhealthy kind of sleep, ought to be used as a stimulant to rouse a torpid brain; that instead of being given for diarrhoea it should be given for constipation. The same, with *Castor oil*; and with many other drugs. This thought may be condemned as presumptuous, but that will not prove it to be untrue.

3. Another very painful, but alas ! very obvious thought, is the prodigious amount of harm which is annually done to their patients by the medical men who thus mistake the use to be made of medicines. As commonly administered it would be better for patients if there was not a drug in the world. By a section of the Profession the use of them is all but abandoned ; but until now the only result of this abandonment is an excessive recourse to surgical operations.

4. These two thoughts are indeed painful and dark, but a bright one comes after them. The experiments here recorded, made with different doses of the same drug, open a wide door of hope. Medicines have been given us for our diseases, as much as food has been given us for our hunger, and these experiments point to a method of using them incomparably superior to all the older methods. The large doses hitherto given, even when they have seemed to do good, have always done some accompanying mischief. The small doses can do good without doing harm, and the good they can do is conspicuously greater than any which has either been experienced or expected from the larger doses.

5. I hear it exclaimed—"This is a revolution !" True, it is a revolution in Science ; it is not a political revolution, it has not the slightest connection with that ; our Royal Colleges have nothing to fear. It is such a revolution as was brought about when Astrology became Astronomy, and when Alchemy became Chemistry. "But how can *you* expect to work a revolution in Medicine, and with such trifling experiments as these ?" The answer is, by trusting in God. This Essay shows what eight men have done in a few weeks by experimenting on themselves with four drugs, and soon six or eight other volunteer experimenters may do as much, in as short a time, with three or four other drugs ; and when the ball has thus been set rolling, these may be followed by a greater number. In this manner, in a few years, we may become acquainted with the properties and the proper use of a sufficient number of drugs to make the "revolution" not only possible, but easy of accomplishment. As to the assertion that the experiments themselves are trifling, Sir Humphry Davy shall answer that,—" *Experiments,*" he says, "*even the most trifling can hardly fail to be useful ;*" and again he says,—"*The*

grandest as well as the most correct views are those that have been gained by *minute observation*." (*Life*, pages 152, 153).

6. It must be remembered that, in these experiments, doses are not regarded as they are commonly regarded. It has already been remarked that the different doses of a drug to be prescribed in ordinary practice, are settled by the age, or the sex, or the idiosyncrasy of the patient, or, as Dr. Brunton looks at them, by the weight of the patient's body. It is evident that these views are confined to the patient. The kind of disease also is allowed to influence the dose. We are not looking either at the patient or at the disease, but at the *doses themselves*, and the different powers of action inherent in them, and we are concentrating our attention upon this view—not despising other views, but for the present putting them aside. The questions to which we are seeking an answer are these—What is the action of the several groups of doses of a drug when taken by themselves in health and in disease? And when this knowledge is obtained, what practical use of it can be made?

7. The double action of intermediate doses, on careful examination presents a difference which is remarkable. With Dr. Sharp, Mr. Haslam, and Mr. Seabroke, doses of a few drops of *Acon. 1* have this double action, and with it the beats of the heart are first quickened and then retarded. Doses of the strong Tincture have the same succession of action with Mr. Haslam, but with Mr. Seabroke and Dr. Applebe the reverse action appears; the pulse is first made slower, and then it is quickened.

What do these diverse phenomena teach? If the succession had been with all the experimenters the same with *Acon. 1* and the contrary with the Tincture of Aconite, the cause of the reversed successions would have appeared to be in the change of the size of the doses only. But there has not been this uniformity in the successions—with Mr. Haslam it was the same with both sizes of doses: with Mr. Seabroke and Dr. Applebe it was the reverse action with the strong Tincture. This seems to show that the cause is in the predisposition of the experimenters. It does not show that the steady alternation in the groups of doses is broken. Any two men starting together with the right foot and stepping

at nearly the same rate, will be approximately in step for some time; by and by, they will be quite out of step: but it is no less true for all that, that each of them has taken regularly alternate steps, first with one foot and then with the other, for the whole time.

So far as experiments have been made, a succession of four groups of doses form a cycle, which is then repeated.

8. In former Essays analogies have often been used as illustrations, for, though they are not proofs, they help to make a subject more interesting and easier to be understood. The following extract from the Address by Sir Frederick Bramwell as President of the British Association for the advancement of Science, at the Meeting at Bath in 1888, will, it is hoped, answer both these objects on this occasion:—

“I have already spoken to you, when considering steel as a mere alloy of iron and carbon, as to the value of even a fraction of 1 per cent. of the latter; but we know that in actual practice steel almost always contains other ingredients. One of the most prominent of these is Manganese. It had for years been used, in quantities varying from a fraction of 1 per cent. up to 2·5 per cent., with advantage as regards ductility, and as regards its ability to withstand forging. A further increase was found not to augment the advantage; a still further increase was found to diminish it; and here the manufacturer stopped, and, so far as I know, the pure scientist stopped, on the very reasonable ground that the point of increased benefit appeared to have been well ascertained, and that there could be no advantage in pursuing an investigation which appeared only to result in decadence. But this is another instance of how the *application* of science reacts in the interests of pure science itself. One of our steel manufacturers, Mr. Hadfield, determined to pursue this apparently barren subject, and in doing so discovered this fact—that, while with the addition of Manganese in excess of the limit before stated, and up to as much as 7 per cent., deterioration continued, after this latter percentage was passed, *improvement again set in.*”

Here are groups of doses of Manganese, with their characteristic actions, when they are added to Iron and Carbon in the manufacture of Steel, and it is remarkable that there is a repetition of the same kind of action in

successive groups, having between them groups of contrary action, and groups of no action at all.

9. Finally, it is evident that henceforward, a group of small doses of *Opium* may be given as a remedy for constipation with good expectation of success, because, from experiments with them in health, it has been found that to relax the bowels is the natural action of this group of doses, notwithstanding that other groups of larger doses of this drug have other actions, and some of them even in the contrary direction. A group of small doses of *Castor oil* may be prescribed for diarrhœa, because the natural action of these doses in health is to cause constipation, and this may be done with confidence, in spite of the fact that groups of larger doses are known to be laxative. In like manner, a group of smaller doses of *Aconite* may with safety be administered to a quick beating heart, with the assurance of making it beat less quickly, because the natural action of this group of doses in health is to slow the pulse, though we are not to forget that larger doses of this poisonous drug have other and fatal effects upon the heart.

These Essays are nothing if they are not practical, but here are practical results of the extremest value, which my colleagues have so ably helped me to make certain, and to whom I again offer my most grateful thanks. Surely, other men will do the same with other drugs, until this happy revolution in Medicine has been fully accomplished.

V. *Reply to two Letters.*

“ Oct. 23, 1889.—My dear Dr. Sharp,—I have to thank you for your Essay LVI. . . . I for one, distinctly admit the contrary action of large and small doses, and that in health as in disease, though as yet I have been unable to see how or why it is to upset Hahnemann’s teaching ‘*Similia*’ &c. Admitting Antipraxy, I still seem to be doing what I have done all along; prescribing the same drugs, in the same manner, to meet the same emergencies, and that too in the same doses. True, it gives me a reason for doing all this which I never had before; and for this I am deeply grateful to you. Your establishing this fact has enabled me to understand

clearly what 'Rational Medicine' is, and to meet those who try to enter into controversy with me on medical topics, with a reason perceptible by their understandings, and free from all mysterious principles. To be thus freed from saying, 'I don't know how or why small doses act, but I know by experience that they do act,' and to be able to say, 'I know the action of small doses of a drug is in the contrary direction to that of the large doses' is truly a gain, for which I am, and I think others ought to be, thankful. 'Primary and secondary' action has always seemed to me doubtful, if not 'unthinkable'; 'contrary action' I can grasp, and feel myself on firm ground. Believe me, affectionately yours,

— — — ”

“Nov. 2, 1889.—My dear Dr. Sharp,—I wished to read your Essay 56 over carefully twice before thanking you for your kindness in sending it to me. This I have done My understanding has not enabled me to go beyond this, that Antipraxy and Homœopathy, as far as Therapeutics is concerned, not Pharmacology, mean the same thing. They both say that a drug in a certain dose given to one in health causes certain symptoms. They both say also, that when like symptoms exhibit themselves in disease, that same drug will remove those symptoms if given in a smaller dose. Here is a wonderful similarity between Antipraxy and Homœopathy. But then comes the point of disagreement, Antipraxy says that cure is explained by the doctrine of contraries; Homœopathy that it is by the doctrine of similars. I feel myself as a kind of outsider in this dispute.

But I cannot help congratulating myself on the fact that my therapeutics would be the same whether I agreed with you or not, for I believe that the same drug causes and cures like symptoms, the curing dose being smaller than the causing dose.

Ever affectionately yours

— — — ”

The same thought is the burden of these letters. One says, "I still seem to be doing what I have been doing all along;" the other, "my therapeutics would be the same whether I agreed with you or not."

Pardon me, my dear Friends, if I express some surprise at your letters, and suffer me to put the matter before you in as clear a light as I can.

You know perfectly that Hahnemann's Homœopathy consists in making an inventory of your patient's symptoms and in finding a corresponding inventory of symptoms in his provings of drugs in health; and when this is found, prescribing the drug as the true remedy. You know perfectly how he rejected *pathology*, and how his "law of similars" says nothing about the *dose*. The dose is to be found out by experience, that is, by *experiments on the sick*. Hahnemann began by giving the usual doses, but was compelled by the aggravations these caused, to make them less, and with these lesser doses there has been great success in practice, and this is still called Homœopathy—"similia, &c." But experiments with these small doses *in health* have shown that they cure by acting *contrary* not *similarly* to the disease. The success you have had belongs to Antipraxy, its rightful owner; it has been stumbled upon by Homœopathy and appropriated for want of a true owner.

The present practice of Homœopathy has, I think, been arrived at mainly by experiments on the sick, which have been so diligently pursued for many years. This is the old way of learning *ab usu in morbis*. It is called Homœopathy, but it is Antipraxy unperceived. *Similia* has to be dismissed as making a false claim. Antipraxy not only explains the success of the treatment of small doses, but it also explains some of its failures. When a drug has been selected, whose small doses *do not act contrary but similarly* to the morbid process going on in the patient, it must fail. This, surely will be a gain. Consider the experiments reported in these pages, for example, those with *Castor oil*. You see that with three experimenters out of four, five drops produced no perceptible effect, while with one it caused constipation, and all smaller doses down to the hundredth part of a drop, also constipated. And as in another experiment five drops taken for diarrhœa, instead of abating it increased it, it is clear that in future you will select for a patient suffering from looseness of bowels some dose less than five drops, and probably even less than one drop. If you gave such a dose before, you did it blindly; now you will give it with a distinct reason and with quiet confidence that you know what you are doing and why.

It is said that Antipraxy explains Homœopathy; this

is saying that *contraria contrariis* explains *similia similibus*. Antipraxy explains and accounts for the success of the treatment of diseases by *certain small doses of drugs*. It contradicts Homœopathy, and is independent of it. The present practice is called Homœopathy because the true action of these small doses was unknown.

But it is said, the law of similars still holds good as a rule of *selection* of the drug. The experiments recorded in this Essay ought to be sufficient to show that this guide cannot, without great difficulty, any longer be followed. The actions of a drug are seen to be so frequently changed in successive groups of doses, that before a similarly acting dose can, with any certainty, be found, the characteristic actions of these several groups must be experimentally discovered. With respect to three drugs this has now to some extent been done, and what is the result? That small doses of *Opium*, *Castor oil*, and *Aconite* may now be very confidently prescribed without thinking of, or caring for, any "similar" at all. They can be given because they are known, by experiments made with them in health, to have a contrary action to that of the diseases for which, in future, we shall prescribe them. What we want to know of all drugs is the *seat and kind of action* of their small doses, and that which has been done for these three may be done for the rest, and will, I trust, be done. Each drug will then be selected on the principle of *contraria*, not of *similia*.

The contention that *similia similibus* is still the rule of selection is the last refuge of Homœopathy. You can see now, I think, that this refuge must be abandoned.

I fear you will say, this is a long preface to your argument—"I still seem to be doing what I have been doing all along;" and "My therapeutics would be the same whether I agreed with you or not."

This will appear to be true of you for some time to come, but you will have other and clearer thoughts about what you are doing than you have hitherto had. You will know that you are practising Antipraxy not Homœopathy. The examples of *Opium*, *Castor oil* and *Aconite* will perpetually be rising up in your minds, and, if I mistake not, you will become impatient under the conviction that more drugs must be brought into the same condition.

Antipraxy, in one sense, is not opposed to Homœopathy, but is to be substituted for it. Homœopathy was the result of experiments with *drugs* in health. Antipraxy is the result of experiments with *doses* in health. In another sense it is opposed to it. The inference from the first experiments was *similia*; the inference from the second is *contraria*. You know that Hahnemann rejected pathology and trusted entirely to symptoms. Antipraxy was preceded by Organopathy—the *local action* of all the causes of disease among which are drugs,—and Organopathy depends upon pathology for teaching us the *seat* of diseases, and the *seat* of the action of drugs; and in these, when we are prescribing, there is not to be *similarity*, but *identity*. Antipraxy also depends upon pathology for teaching us the *kind* of morbid process going on in disease, and *that* caused by small doses of drugs; and between these, for our guidance, there is not to be *similarity* but *contrariety*. Farewell.

* * * * * *

I am this day eighty-five years old. Forty of these years have been devoted to a practical investigation of Homœopathy. The conclusions successively arrived at have been recorded, from time to time, in these fifty-seven Essays. The result is, to me, both clear and satisfactory.

In the future, any medical man who can disentangle himself from the prejudices of his education, who can observe, experiment, and think for himself, and who has the moral courage to face opposition with a quiet mind, may accept Organopathy and Antipraxy as law-facts—not theories—and may practise by their guidance with success and satisfaction, without becoming a homœopathist, and he may safely leave the consequences to the overruling Providence of God.

HORTON HOUSE, RUGBY;
January 21, 1890.

BY THE SAME AUTHOR.

ESSAYS ON MEDICINE.

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