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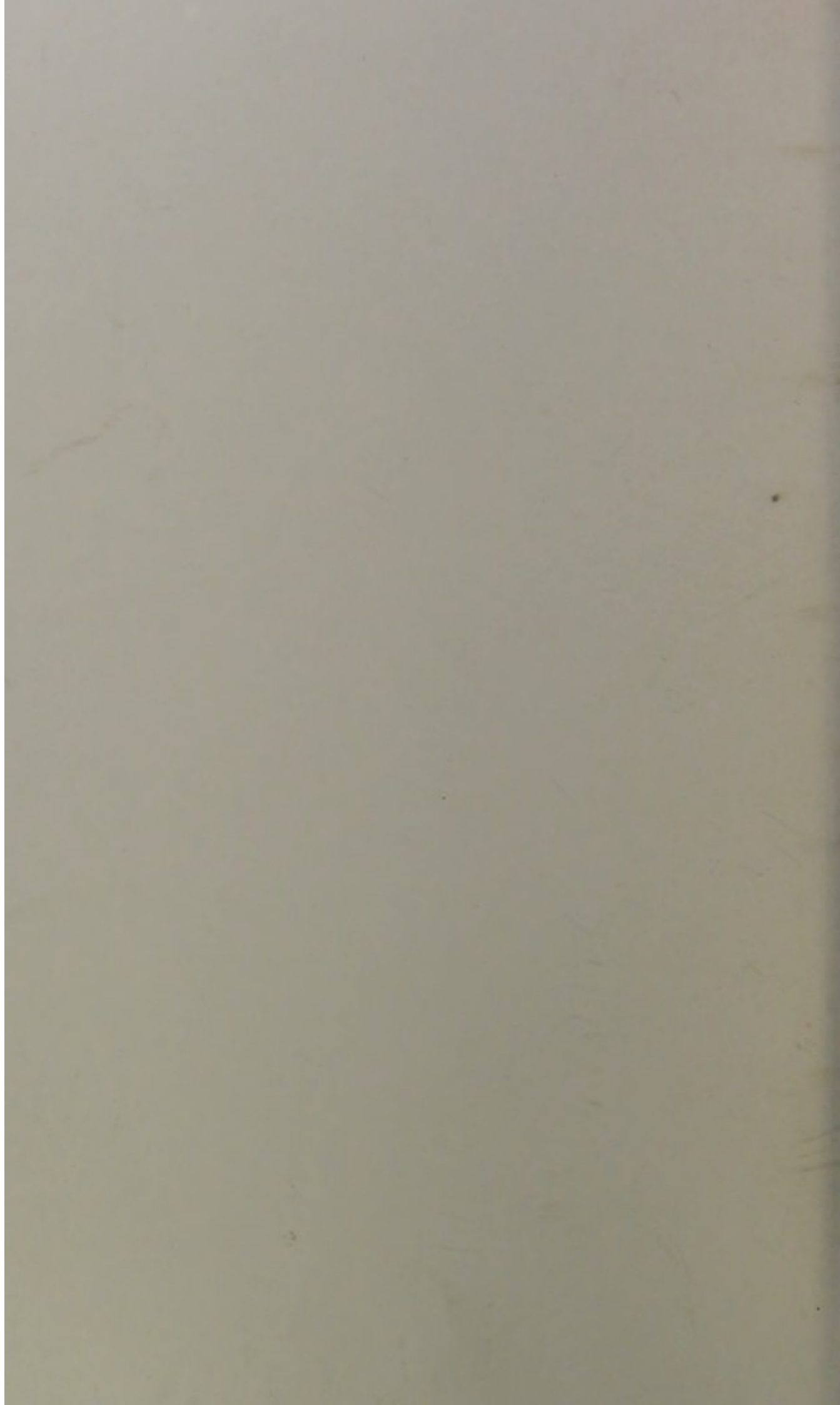
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THE
PHYSIOLOGICAL ACTION
OF
MEDICINES.

A PAPER
READ AT THE
MEETING OF THE BRITISH ASSOCIATION FOR THE
ADVANCEMENT OF SCIENCE,
AT NOTTINGHAM.

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

AUGUST 23RD, 1866.

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1866.

PHYSIOLOGICAL ACTION

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A PAPER

PRESENTED AT THE MEETING OF THE BRITISH ASSOCIATION FOR THE

ADVANCEMENT OF SCIENCE

AT NOTTINGHAM

BY WILLIAM SPENCER M.D. F.R.S.

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ON THE PHYSIOLOGICAL ACTION OF MEDICINES.

(*Read at the Meeting of the British Association, at Nottingham, August 23rd, 1866*).*

MEDICINES are substances belonging to the mineral, vegetable or animal kingdoms, which are not nutritive, or which are not assimilated by the process of digestion, and therefore cannot, in this sense, contribute to the preservation of the living body.

For the purposes of this paper they may be described by three characteristics; characteristics well known and admitted, but hitherto unexplained:—The first, that their action is more or less partial or local; the second, that this action in disease is often curative; the third, that in health it is always more or less injurious.

I. The action of medicines received into the body is local; to borrow an old chemical phrase, there is sort of elective affinity between certain organs of the body and certain drugs. This fact is as well known, though as unexplained, as the parallel fact that each organ selects from *the same current of blood* the elements of its own nutrition; organs differing as much as the brain, the muscles, the bones, the ligaments, the

* It is a rule of the British Association that the papers proposed to be read shall be sent about ten days before the meeting commences, that the committee of the section to which each paper belongs may have an opportunity of accepting or declining it. The committee of the physiological section accepted this paper, but requested me to omit reading the early part of it, for the reason that "it was historical and preliminary."

skin, the organs of the senses, appropriate from the same liquid the materials for their own construction and constant reparation; so with respect to medicines, one organ appropriates one, and another organ a different one; and this fact is proved both by the effects produced upon the organs during life, and by chemical analysis after death. Upon this fact is founded the use of drugs as medicines by all schools and upon every doctrine. This is the first characteristic.

II. The second, drugs used as medicines in disease often have a curative effect. This also is an admitted but unexplained fact.

On these two characteristics I need not detain you longer by any further observations.

III. To the third characteristic I beg leave to call your serious attention. It is this, the action of drugs, when taken in health, is always more or less injurious,—hence the name of *poisons* given to the more active among them. This also is a notorious fact, and alas! one which often produces consequences inflicting severe grief and irreparable loss. Consequences so painful, that they have hitherto directed men's attention almost exclusively to the discovery of antidotes for their prevention or removal.

But it has been again and again suggested that there is another aspect in which the action of drugs in health must be contemplated, namely, with reference to the employment of them as medicines. Drugs have been diligently investigated by the students of toxicology and medical jurisprudence; they require to be as diligently studied with regard to therapeutics.

The first who suggested this view of the subject and its importance, so far as I can discover, was HALLER, about a century and a quarter ago. These are his words:—

“In the first place, *the remedy is to be tried on the healthy body; without any foreign substance mixed with it; a small dose is to be taken; and attention is to be directed to every effect produced by it; for example, on the pulse, the temperature, the respiration, the secretions.* Having obtained these obvious phenomena

in health, you may then pass on to experiment on the body *in a state of disease*.”*

Eminent physicians, from time to time, have expressed their approval of this suggestion; and in 1842, about a hundred years after its proposal by Haller, it was more formally recognised. A public assemblage of medical men, at the scientific congress held at Strasburg in that year, announced the adoption of the proposal in the following resolution:—

“The third section (the medical), are unanimously of opinion that experiments with medicines on *healthy* individuals are, in the present state of medical science, of urgent necessity for physiology and therapeutics; and that it is desirable that all known facts should be methodically and scrupulously collected, and with prudence, cautiousness, and scientific exactness, arranged, written out, and published.”

Such was the resolution, passed unanimously, at the scientific meeting at Strasburg. Twenty-three years after the passing of this resolution, namely, at the meeting of the British Association at Birmingham last year, Dr. ACLAND introduced the subject from the chair of the section, and the following resolution was agreed to, and was afterwards presented as a Memorial to the General Medical Council, by Dr. Acland, on the 17th of May of this year:—

“Having regard to the observations of the President, Professor Acland, in his inaugural address, the Committee of the sub-section of physiology, desire respectfully to intimate their opinion of the great advantage which would accrue to physiological (and thereby to medical) science, if the General Council should think fit, by pecuniary grants and the appointment of suitable persons, to undertake investigations into the physio-

* “Primum, *in corpore sano* medela tentanda est; sine peregrinâ ullâ miscelâ; exigua illius dosis ingerenda; et ad omnes quæ inde contingunt affectiones, quis pulsus, quis calor, quæ respiratio, quænam excretiones, attendendum. Inde adductum phænominorum *in sana* obviatorum, transeas ad experimenta *in corpore ægroto*.”

logical action of medicines. A few agents when administered in poisonous doses have alone been made the subjects of such research; and whilst the remedial effects of even such well-known agents as quinine have been admitted for ages, their modes of action are still unknown. Even to this moment our knowledge of the action of remedies rests only upon ordinary observation and general inferences. The Committee is well aware of the extreme difficulty of prosecuting exact physiological enquiries *in states of disease*, and, above all, of the necessity of devising *new modes of investigation*; but, bearing in mind recent researches of an analogous nature *in health*, they do not doubt there are physiologists and physicians of approved ability in such researches, who would be able to devise the methods, and bring the results to a satisfactory conclusion. The Committee also venture to suggest that no experiments should be regarded as satisfactory which (in addition to others) are not made in ordinary medicinal doses in the diseases for the relief of which the remedies are administered, (as well as in poisonous doses), and which are not performed with all the care and exactitude known in modern physiological research. That this resolution be signed by the President, Vice-President and Secretaries, on the part of the Committee, and that the President be requested to present it to the Medical Council."

The presentation of this Memorial to the Medical Council was followed by an animated discussion, in which the importance of the subject was admitted on all sides; and though the adoption of the proposal was negatived by sixteen votes, on the ground that to undertake the task suggested would be to exceed the powers given to the Council by the Act of Parliament, five members voted in its favour.

Such have been the suggestions and resolutions to make experiments with drugs upon *healthy* persons, up to the present hour. The subject is now in the hands of Dr. Acland, whose good commencement reflects upon him high praise, and I trust he will prosecute his undertaking with vigour. Let it not be supposed that I wish to hinder, or in any way to interfere with

his work; on the contrary, the motive which has urged me to read this paper is the hope of offering some assistance. Having myself been deeply interested in this subject for many years, I could not be altogether silent now that it has been formally and officially brought before the British Association;—a society of which I have been an attached member almost from its origin; a society which has so many claims to the gratitude of England, for the helping hand which it has held out to all lovers of science; a society which, if it now inaugurate a new investigation into the properties and uses of drugs as medicines, will add another claim to this gratitude, the magnitude of which cannot easily be exaggerated.

Thus experiments to ascertain the physiological action of medicines have been suggested; a question now arises, have they been attempted? They have, by several hands; and before a fresh series of experiments is commenced, it will be well to examine the labours of our predecessors.

Haller, as I have remarked, was the first to make the proposal; but he did not attempt the work. Probably the first who did so was Stoerk, of Vienna, physician to the Emperor. Just a hundred years ago, he undertook to investigate the action of several powerful drugs upon himself; for example, *conium*, *colchicum*, *aconite*, *stramonium*. His experiments attracted wide attention; the subjects of them were rapidly introduced into extensive use as medicines; unfortunately, they were too highly praised, and healing powers beyond the truth were attributed to them; as a natural consequence they, and the worthy author of the experiments upon them, passed into neglect and almost into oblivion.

Some thirty years later, another German physician took up the subject with great energy and perseverance; and, after having devoted to it many years of untiring labour, produced a whole *Materia Medica* of drugs, with which he had experimented upon himself, and upon numerous friends, whom he had induced to share with him the trouble, the suffering and the risk.

These volumes have now been studied, day and night, by

some thousands of medical practitioners, and have been their almost solitary guide through a successful practice of their profession, for nearly seventy years, and in every region of the civilised world.

This is an undeniable fact, and of itself gives the experiments of Samuel Hahnemann a claim to respectful consideration.

In support of these experiments it may be stated :—

1. That they were made by a considerable number of intelligent persons, of different ages and temperaments, and of both sexes.

2. That they were made by these persons in *health*. Haller's first requirement.

3. That each drug was experimented upon *by itself*, without any foreign substance being mixed with it. Haller's second requirement.

4. That the doses made use of were generally small ones. Haller's third requirement.

5. That the results of the experiments were diligently and conscientiously observed, and written down. Haller's fourth requirement. This was carried so far that even details apparently insignificant were inserted, lest any real effect of the medicine should be omitted.

6. That the mental and moral conditions, as well as the bodily symptoms, were carefully noted.

7. That a novel, and, I think, an excellent method of preparing the drugs for experiments was adopted. Plants were bruised while fresh and in perfection, and the sap, obtained by straining, was mixed with alcohol, (to prevent fermentation and decomposition), and used in this condition. Infusions, decoctions, dried powders, extracts, and other complicated preparations being rejected. Minerals, and other insoluble substances, were reduced to a state of minute division by being triturated with an inert material. In this way, I may remark, an admirable reform was introduced into pharmacy.

8. That, lastly, a strict regimen was adhered to by each person, during the time the experiments were being made.

These are conditions which, as it appears to me, must be observed in any future experiments upon the physiological action of medicines. It will be possible to add to their completeness by availing ourselves of mechanical inventions such as the stethoscope, and of the processes of modern chemistry.

I will now point out what I think are defects, not in Hahnemann's experiments, but in the record he has given us of them, and which it will be necessary and quite possible to avoid in reporting further investigation. It is to be regretted that those who have followed Hahnemann, and who have repeated and greatly increased his observations, have, for the most part, repeated his defects.

The defects I venture to mention consist:—

1. In, commonly, not stating the doses of the drugs which were taken in the experiments.

2. In not recording the daily progress, so that a case of experiment might be reported in the same way as a case of disease.

3. In breaking up the connection of morbid phenomena, in order to arrange the symptoms under headings made of the different parts of the body, as the eyes, ears, nose, mouth, throat, chest, stomach, arms, &c. &c.

4. In mixing, in this arrangement, the symptoms which had been experienced by a dozen or more separate persons.

5. In adding to the symptoms of the experimenters those of accidental, and even of fatal cases of poisoning, without indicating which symptoms belong to these, nor the doses by which they were produced.

6. In recording, without discrimination, every trivial sensation and every slight circumstance occurring after the dose of the drug had been taken. In this manner symptoms have been accumulated to such an extent, that with many drugs it is very difficult to lay hold of their characteristic effects.

Such are the deficiencies in the reports; but there is one defect, which I feel constrained to insist upon, which belongs to the experiments themselves, as well to their record—though

I am quite aware that Hahnemann himself and many of his admirers regard it as one of the great excellencies of his system—namely,—

That he limits himself to the observation of symptoms, and does not endeavour to connect them together, so as to represent a pathological condition.

But as I read a paper on this subject last year at Birmingham,* I will not enlarge upon it now.

Notwithstanding these defects, obvious and grave as I think they are, the work undertaken and accomplished by Hahnemann was a mighty work, and it was nobly done; and I trust the time will come when he will receive the grateful thanks of the profession, as well as of the world.

The time which can be reasonably claimed for this paper is so limited, that it would be impossible to give even a sketch of what has been done in this province of labour by others since Hahnemann's time. But a great deal has been accomplished, with which those who are willing to begin the work afresh should make themselves acquainted. There are upwards of three thousand medical men of this school on the North American Continent alone, and many among them are able and industrious men. I will content myself with one extract from an address delivered not long ago at New York. Dr. W. H. Watson spoke to this effect:—

“If Hahnemann had done nothing else he would be entitled to the lasting gratitude of mankind, for his suggestions in regard to acquiring a knowledge of the medicinal powers of drugs, by experimenting with them on the healthy subject. This is the glorious mission of our school. While our brethren, under the guidance of Rokitansky and his colleagues, are rendering great service to the world by elucidating the effects of disease, through their researches in the domain of pathology, to us belongs the honor of discovering and applying those remedies which will relieve the diseased conditions brought to light by

* “Medical Systems. An Address at the First Meeting of a Medical Association, by the President.” Longman & Co.

the knife of the pathologist. It is only by large numbers of persons that reliable provings of drugs can be carried on. The constant symptoms, obtained by hundreds of individuals from the administration of the same drug, must necessarily be its characteristic symptoms; whereas many of the symptoms obtained by a single prover may be purely imaginary, or the result of some accidental cause, and have no relation of cause and effect to the drug which has been administered. But when a hundred persons in good health are affected in a certain manner, after taking a particular drug, the conclusion is irresistible that the symptoms thus produced are the effects of the drug which has been administered."

I will now, with your permission, venture upon some *suggestions* which may be of use to those who shall undertake the further prosecution of this great work.

- I. On the *objects to be pursued*.
- II. On the *mode of proceeding*.
- III. On the *utilisation of the results*.

I. On the objects to be pursued.

These, I think, are the three following:—

1. To ascertain the *organs affected* by each drug.
 - (i) By careful diagnosis.
 - (ii) By chemical investigations in cases of fatal poisoning.
2. To learn the *effects produced* upon these organs, the pathology and morbid anatomy.
 - (i) By observation of symptoms.
 - (ii) By post-mortem examinations.
3. To discover, if possible, the *modus operandi*. This object, I think, must of necessity be postponed, until the two former have been considerably advanced.

In attempting to ascertain the organs affected by each drug, a great deal of care will be needed with respect to the *doses* with which the experiments are made. I may mention, as a familiar example of what I mean, tartarised antimony, which, as you

are all aware, in one dose acts on the lungs, in another on the skin, in a third on the bowels, and in a fourth on the stomach.

Another point of importance is to discover the organ which, in a given dose of the drug, is the *first* to appropriate it, and so to be acted upon by it; then that which is *second*, *third*, and so on. In this way the several organs which have an affinity for a given drug may be made out, and their relative power of attraction. As an illustration of this point I may refer to the *heart* and its strong affinity for the following drugs:—

Aconite,
Spigelia,
Bovista,
Digitalis.

The primary action of these drugs, in certain doses, is on the heart; but if we enquire after the secondary one, that is, after the organ which, in the second place, appropriates each of them, we shall find that it is different for each, *e.g.*:—

<i>Aconite,</i>	after the heart,	affects	the brain and nerves.
<i>Spigelia,</i>	„	„	the eyes.
<i>Bovista,</i>	„	„	the skin.
<i>Digitalis,</i>	„	„	the kidneys.

It would be easy to enumerate a large number of drugs, whose affinities with certain organs have been already ascertained with some precision; but enough has been said to indicate the direction the investigation should take, and to show how attractive and useful it must necessarily become to those who are disposed to give to it their time and attention.

II. On the mode of proceeding.

1. The experimenters should be intelligent men, and the more of them the better, especially of medical men.

2. The best known drugs should be experimented upon first; next I would recommend the commonest wild plants of our native country: as the daisy, buttercup, dandelion, furze, white and black thorn, &c. &c.

3. The committee of experimenters should agree to try, at one time, one and the same drug.

4. The doses should be agreed upon. Three classes have been recommended—

- (i) Poisonous.
- (ii) Medicinal.
- (iii) Infinitesimal.

The first to be used only upon animals. These experiments I beg leave to protest against; any advantages to be derived from them do not compensate for the cruelty; the effects of poisonous or semi-poisonous doses may be learned from cases in which they have been accidentally or wilfully taken.

The second, (medicinal doses), which may vary considerably as to magnitude, are those which should be taken by the experimenters.

The third, (infinitesimal doses), should, I think, be postponed till sufficient positive information regarding the second has been obtained.

It is a question whether the experimenters should know what they are taking, and it has been recommended that they should not know. I think they should sometimes know, and sometimes not. When the drug is a poison, and the doses considerable, then, I think, the person taking them should always know.

5. The experimenters should be in health; a moderately careful regimen should be observed; the drug should be unmixed with others; and the mental and moral state should be recorded, as well as the bodily condition.

6. The reports should be drawn up just as cases of natural disease have been reported by physicians since the days of Hippocrates; the symptoms conscientiously written down day by day; and a careful diagnosis and pathology attempted.

7. An analysis should be made of all the cases thus reported of experiments with the same drug, and conclusions drawn—

- (i) As to the organs which have shown an affinity for the drug; the degrees of this affinity; and the doses required for each organ.

(ii) As to the changes produced in the several organs
—the pathology.

If an earnest investigation be undertaken, with these objects in view, and pursued in the manner proposed, information will be gradually accumulated, which may be drawn up in *tables*; showing the several organs and tissues of the body, and the drugs, and their doses which each can appropriate; the physiological or pathological changes occasioned in consequence; and the characteristic symptoms, mental, moral, and physical.

III. On the utilisation of the results.

No doubt the love of truth for its own sake should be the strongest stimulus to the efforts of the experimental philosopher; still the question of usefulness, how to turn the discovery of truth to practical advantage, is a lawful one, and, in the case before us, one of pressing interest and importance to the well being of mankind. What then is the practical end of these investigations into the action of drugs in health? Suppose the tables just now mentioned were completed, (would that they were!) how are they to be utilised? It seems to me that this would be by a comparison being instituted between the *physiological* and the *therapeutical* action of medicines; a comparison between the effects of drugs in health, and the effects of the same drugs in disease. When this comparison has been made, the further question will arise how far, and in what manner can the physiological action guide the therapeutic use? How can these experiments in health be made use of to direct the employment of the same drugs in disease? It is in the highest degree probable that the result of this aggregate of experiments and enquiry will be the establishment of a *principle* which shall be, for all time coming, a settled rule in therapeutics,—the compass, the guiding star to the medical practitioner.

I will add one concluding observation.

Diseases are more or less local; the action of drugs is also local; it follows that there are two ways in which drugs may be used as remedies: they may be given, in any case of illness, so that the action shall be upon those organs which remain

healthy, or upon those which are affected by disease. The former of these methods has been longest in use; the latter, in my judgment, presents the most successful results. Both these methods rest upon the same fact, namely, the local action of medicines; both may be theoretically explained; both have observation to justify them; and there cannot be a more interesting, or a more useful problem for the younger medical men of the present generation to seek to solve, than this:—the investigation of the physiological action of medicines, with the view to determine their therapeutic use.

HORTON HOUSE, RUGBY,
July 27th, 1866.

The reading of this paper was followed by an interesting discussion, in which several medical men took part, and which was closed by the President, Professor Humphreys, who observed that the paper had been well characterised as a suggestive one, for that, in reality, our knowledge upon the subject was as yet small.

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James ...
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