

On the difficulty of estimating the therapeutical value of medicinal agents, being the address delivered to the Harveian Society at their annual meeting on the 13th April 1857 / by Archibald Inglis.

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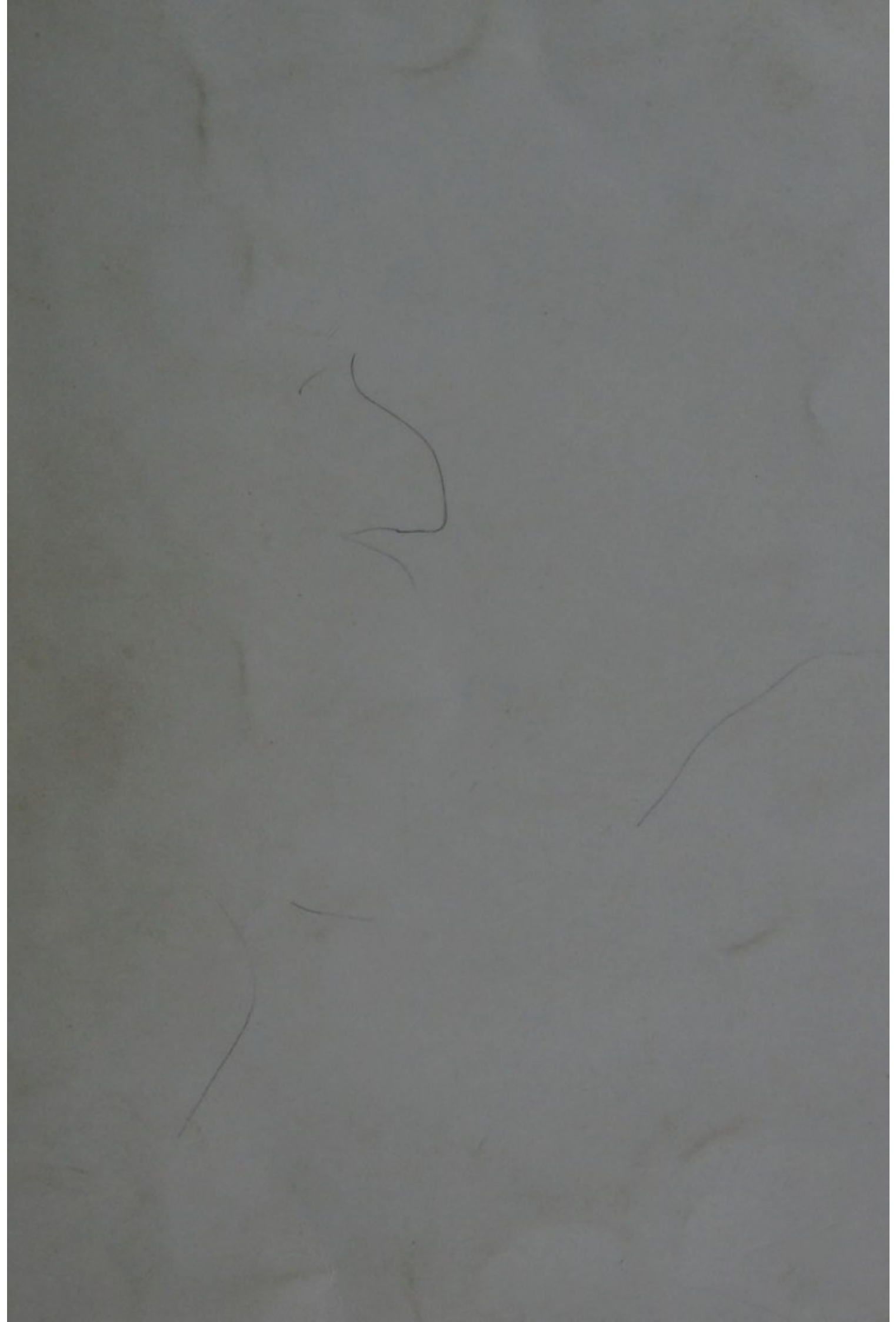
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ON
THE DIFFICULTY
OF
ESTIMATING THE THERAPEUTICAL VALUE
OF
MEDICINAL AGENTS,

BEING
THE ADDRESS DELIVERED TO THE HARVEIAN SOCIETY AT
THEIR ANNUAL MEETING ON THE 13TH APRIL 1857.

BY
ARCHIBALD INGLIS, M.D., F.R.C.S.,
PRESIDENT OF THE SOCIETY.

“Ὁ βίος βραχύς, ἡ δὲ τέχνη μακρὴ, ὁ δὲ καιρὸς ὀξύς, ἡ δὲ πείρα σφαλὲς,
ἡ δὲ κρίσις χαλεπή.”—ΙΠΠΟΚΡΑΤΗΣ.

EDINBURGH: PRINTED BY MURRAY AND GIBB.

MDCCCLVII.

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PREFACE.

IN submitting the observations contained in the following pages to my professional friends, I beg to remind them that, although it has not been unusual to give to those addresses, the reading of which forms part of the proceedings at the annual meetings of the Harveian Society, a wider circulation than that occasion affords, the form in which such essays are drawn up is necessarily more circumscribed as to the limits which they occupy, and more restricted as to the manner of treating the subjects contained in them, than if they were originally intended for publication.

When engaged in preparing for this part of the duties allotted to me for the current year by the usages of the Society, it soon became apparent that I could not do sufficient justice to the subject I had chosen as a suitable one for the occasion, without being led much beyond the limits within which it was necessary that I should confine myself; and it may therefore be thought that, before preparing these pages for the press, I should have so extended them as to supply what seemed necessary for its fuller development. As, however, it was at the request of the Members of the Society, who heard it, that this "Address" has now been printed, I have not considered it advisable to make any material alteration in the form in which it was laid before them, except by the addition of a few supplementary notes.

In the introductory remarks prefixed to the "Address," I have stated that some of the topics embraced in it had recently engaged the attention of other medical writers, alluding more especially to the valuable summary of professional experience contained in the work of Sir John Forbes on "Nature and Art in the Cure of Disease." The appearance of such a work, proceeding from the pen of a member of the profession so deservedly eminent, and whose experience has been so extensive, had it been published somewhat earlier, would probably have deterred me from my present undertaking, and may well excuse my not having enlarged my observations on those branches of my subject which are of a kindred nature

to those treated of by him. It will be readily observed, however, that, though some of the matters touched upon in the "Address" are closely allied to those which form the subject of Sir John Forbes's publication, the object which I have kept in view is quite a distinct one.

In reference to other writings on the same subject, I take this opportunity of pointing out that, when I wrote the remarks I have made at page 15, on the impossibility of expressing our present physiological, pathological, and therapeutical knowledge by *formulae* as exact as those applicable to physical and chemical phenomena, I of course could not be aware that the author of a review of Sir John Forbes's work, in the *British and Foreign Medico-Chirurgical Review*, since published, had been in the habit of making use of mathematical symbols for the illustration of the morbid processes taking place in the body, with a view "to facilitate the *rationale* of our therapeutical applications." The example given by the reviewer appears to me to present a very good symbolical illustration of a form of calculation of the adaptation of therapeutical agents to remedial purposes, which I have alluded to as probably not unfrequently passing through the minds of medical men when engaged in determining the mode of treatment most suitable to each individual case presented to them; and I believe it might be found advantageous to carry much further the principle of expressing symbolically the mental processes through which practical medical conclusions are often arrived at. It must, however, be kept in mind, that such expressions are only to be regarded as auxiliaries to the mental operations which they represent; and, although they may be extremely useful in conveying to others the ideas entertained by those making use of them, both as regards the arrangement of the constituents of the body in healthy and morbid states, and the order of succession of the *phenomena* that occurs during the progress of diseases and of recovery from them, they are not to be confounded with true mathematical or chemical *formulae*.

As some ideas, very similar to my own upon these and other practical subjects, seem to have occurred, apparently almost simultaneously, to the author of the review in question, the remarks I have now made seemed to me necessary for the more perfect elucidation of the views I have expressed in the text of the "Address."

EDINBURGH, October 1857.

HARVEIAN ADDRESS—1857.

GENTLEMEN,—Before entering on the consideration of the subject on which I am now to address you, I feel it necessary to premise that I had fixed upon it for this occasion before I could be aware that several of the topics, falling within the scope of it, would, before I had the opportunity of laying it before you, become the subject of discussion both in published lectures and papers, and also in a more extended form. Had I foreseen that these would thus fall into abler and more experienced hands, I would have abandoned the subject for some other; but the period of your meeting was too near at hand to permit me to change it. Not only has the interest attached to some of the matters to be brought under your notice been thus, in some measure, forestalled, but I have felt restrained from using others also, so freely as their aptness for the purpose of illustration would otherwise have induced me to do, from the consideration that, being still the subjects of undecided controversy, it would be foreign to the objects of a meeting intended to promote harmony among the members of the profession, were I to enter into a discussion regarding them, which might be more suitably conducted elsewhere. The very general manner in which I have thus been compelled to handle some portions of my subject, will, I fear, impart to them a degree of vagueness and want of precision, inseparable from such a mode of treating them. If I should, however, from this cause fail to engage your attention to the extent I would desire, I trust you will accept these preliminary remarks as an explanation of my reasons for the course I have adopted, and allow me now to proceed to the proper subject of this essay, namely—

THE DIFFICULTY OF ESTIMATING THE THERAPEUTICAL VALUE OF MEDICINAL AGENTS.

The rapid progress of scientific discovery, which forms one of the most distinguishing features of the two last centuries, bears testimony to the correctness of those methods of investigation which have led to the establishment of such important results; while the extent to which, more especially in our own times, the knowledge thus acquired has been successfully applied to purposes calculated, not merely to gratify the intellectual tastes of the learned, but also

to promote the health, the comfort, the social and commercial intercourse, and the rational enjoyment and general happiness of all classes, proves that the pursuits of the votaries of science are no longer of that visionary and unproductive character which, in earlier days, exposed them, often not unjustly, to the ridicule of the unlearned.

We are now met to do honour to the memory of one of our own profession, who lived near the commencement of the era I have now indicated, and who was the professional adviser of the great philosopher to whose writings we are accustomed mainly to attribute so remarkable a revolution in the manner of cultivating and extending scientific knowledge. But, although Harvey enjoyed the friendship, and must, to a certain extent, have shared the confidence of the celebrated Chancellor of James I., it seems to have been the originality of his own genius that impelled him to enter the field of inquiry, in the department of science most congenial to him, by that pathway of observation and experiment, the practical value of which it was his lot to exemplify, whilst his more profound contemporary was engaged in pointing it out, and inculcating its adoption as that which was alone likely to lead to successful discovery in every branch of human knowledge.¹ In pursuing this career, Harvey was rewarded by obtaining results which, by establishing on an incontrovertible basis the discovery we are this day met to commemorate, have conferred on him immortal fame, and have produced an influence both on the science and the art of medicine, which will endure as long as their importance to the welfare of the human race continues to be appreciated.

The value of the discovery of the circulation of the blood, whether viewed in the relation it bears to the practice of our profession, or as one of the most important advances made in physiological research, cannot be over-estimated; but it is only when, by contemplating the successive steps by which the illustrious Harvey brought that discovery to its completion, we are led to acknowledge that in medicine, as in all other departments of science, there is but one method of investigation through which great discoveries are likely to be accomplished, that we can truly recognise his claims to the homage we are this day met to accord to him. It is then that we come to regard him not merely as the discoverer of a great physio-

¹ If Harvey was at all indebted to extraneous sources for the method adopted by him in conducting his investigations, a reference to the writings of his more immediate predecessors in anatomical and physiological research, shows that it was much more likely that he derived the impulse by which he was guided from the spirit then abroad in the schools in which he was educated, than that he imbibed his ideas from his intercourse with his illustrious contemporary. Sayings of his have been recorded by his biographers, showing that he did not appreciate, so highly as has been done in more recent times, the labours of his learned friend; and still more conclusive evidence on this subject is afforded by the fact, that he began to promulgate his views on the circulation of the blood in public lectures, some years before the appearance of the first part of Lord Bacon's *Instauratio Magno*.

logical fact, but as having made a mighty advance in releasing physiological inquiry from those trammels by which its cultivators had felt themselves tied down to explain observed phenomena only in accordance with preconceived and generally visionary theories.

In the present day, nothing short of a rigid adherence to the inductive method of inquiry satisfies us as to the correctness of any doctrine in physiology, or in most of the other branches of medical knowledge; but, within the period of time during which so much has been done for the advancement of its more scientific departments, if we turn to the most practically important of all, namely, the treatment of disease, we find that theory has succeeded theory in rapid succession, and that the ranks of the profession have often been divided against each other in support of the most opposite views. At one time we find that not only individual ailments, but whole classes of diseases, have been treated on the most opposite principles, and yet success claimed by the advocates of each; at another, theories of therapeutical action resting on the insecure basis of a hasty generalization, instead of that of sober induction, have obtained unbounded sway; nor, even in the most recent times, do we need to look far for instances of such theories being grounded even on gratuitous assumption, and yet moulded into such a plausible form, as to find an acceptance, not alone confined to persons unconnected with the profession, and therefore not supposed to be qualified to exercise much discrimination in such matters, nor yet to that section of those engaged in its practice who have been least favoured in respect of education, or ability to form a sound judgment on what falls under their observation, but extending to individuals possessed of no small share of natural talents, and enjoying ample opportunities of improving them in the field of medical practice. Yet, if we compare medicine as an art with those branches of human industry or human occupation in which, in the present day, practical skill under the guidance of scientific knowledge has achieved so many triumphs, we cannot feel otherwise than assured, even on a superficial examination, that, in order either to establish fixed principles for the treatment of disease, or to extend our knowledge of the application of individual medicines, or classes of medicines, to the cure of particular maladies, the same methods of investigation must be followed which have been successful in other departments.

If we select, as an example upon which such a comparison may be founded, the art of navigation, we see that the extension and correction of our knowledge of astronomical and of meteorological *phenomena*—the continually increasing accumulation of facts and observations connected with geography and hydrography—the study of the laws of terrestrial magnetism—the multiplication and improvement of instruments, by means of which the knowledge acquired in these sciences can be applied to practical purposes—above all, the introduction of a new propelling power, of great intensity, yet easily controlled and regulated, have given to the operations of

the mariner a celerity, a safety, and a certainty as to the course he is pursuing, which, fifty years ago, would have been thought almost fabulous. The steps by which each of the branches of knowledge just named has been made to contribute its complement of information to the general result, are the following:—First, a careful observation of phenomena in each; secondly, the collection of these phenomena into groups, the bond of connection in each of which is conformable to laws inductively inferred from the observations made; thirdly, the application of those laws, by deductive inferences, to the various circumstances and situations in which those having to make a practical use of them are likely to be placed; fourthly, the application of the information thus supplied to the purpose of testing experimentally, as opportunities occur, the correctness of the principles that have been assumed, so as either to confirm their truth, or demonstrate their fallacy; and, lastly, the discovery, during this experimental process, of new applications of the principles already adopted, or of new facts, which serve as the foundation of fresh inductions; so that, in the example we have chosen for illustration, every vessel that speeds over the surface of the ocean can be made, not only to bear its testimony to the accuracy of previous observations, and the inferences drawn from them, but also to furnish materials for a more perfect or more extended generalization. In like manner, the discoveries that are daily being made in physical and chemical science find their appropriate application in our numerous manufactories, and our great works of construction, in which the correctness of the principles furnished to them is tested, and fresh materials are provided, suggestive of new discoveries.

Nor does the mode in which we may expect to advance practical medicine differ materially in its aspect from these. All the sciences dependent on observation may be pressed into its service. Natural History, in the usual acceptation of the term; Physical and Chemical Science, both as regards their relation to the phenomena and processes going on in the living body, and in their application to the recognition and the relief of disease; Anatomy, Physiology, and Psychology; and, still narrowing our circle to its more immediate object, the observation of the phenomena of disease during life—of the mode in which a return to health seems to be accomplished—of the changes of structure that take place in fatal cases—and of the effects of medicinal agents both in health and disease—are not only made each to fulfil its part in making up the sum of knowledge required for medical practice, but also to furnish new facts, which may assist in giving greater certainty or facility to our curative efforts, or enable us to extend their application to morbid states in which they have been hitherto untried.

But, though the comparison we have instituted between medicine and other branches of practical science shows an analogy sufficiently close to inform us as to the direction our efforts for improving and

extending it ought to take, a closer examination makes us acquainted with important differences, which account, in a great measure, for the former making less rapid progress than that by which the latter have been distinguished.

Many of the preliminary investigations which have brought to their high perfection the art of navigation, and that of the engineer, are dependent on principles admitting of all the accuracy of mathematical demonstration; whilst others of a more variable character—*e.g.*, the strength of different kinds of material—are reducible to the test of experiment, rendered all the more easy from inanimate matter being the subject of it. The chemical changes, too, which are brought into activity in many of our manufacturing processes, are of a simpler nature than those occurring in living organisms; and their recurrence, under similar circumstances, may not only be predicted, but, by means of the ascertained laws of chemical affinity and combination in definite proportions, they may be reduced to *formulæ* almost as certain in their application as those of mathematics. So large, indeed, is the *ratio* of the certain to the uncertain in all these pursuits, that success may be considered the rule, danger or failure the rare exception. Highly, therefore, as we ought to value the talent, and estimate the skill which, by making scientific research go hand in hand with its practical application, has brought various branches of industry to their present position, it is evident that he who wishes to advance medical science, and to lay down precise rules for its practice, has a range of far more intricate subjects to investigate, and far greater difficulties to overcome, before he can render the results of experimental inquiry subservient to his purpose.

It is plain that a comparatively small proportion of the phenomena which the medical man has to deal with falls directly under the cognizance of the senses. By the use of these he may, indeed, become acquainted with the external characters of the medicinal agents he is called upon to employ, and with the anatomical structure of the dead body. By the same means, also, especially when aided by optical or acoustic contrivances, or when the products of either healthy or morbid actions can be made the subject of chemical analysis, he may become acquainted, to a certain extent, with some of the *phenomena* which accompany or result from the processes going on during life; but the processes themselves are, in most instances, not the objects of sense, and it is only by inference that we can throw any light on their nature. The laws, also, of physical science may serve to elucidate some of the *phenomena* of the living body; and chemistry makes us acquainted with both the proximate and ultimate constituents of the solids and fluids which compose it; yet we find that, during life, both chemical and physical forces act in subordination to a power, the operations of which it is much more difficult to trace, and which either modifies or supersedes their action in a manner not exemplified in the inorganic kingdom of

nature; while the mutual action and reaction of mind and body on each other form a still more subtle subject of investigation, yet intimately connected with successful medical practice.

But, to enter a little more minutely into our subject, let us consider what are the grounds on which a medical man may consider himself warranted to place confidence in particular medicines, or classes of medicines, as being the most adapted to the treatment of particular diseases, or as likely to afford tolerably uniform results from their use. If the art of medicine consisted merely, in the first place, in discriminating diseases by means of those groups of characters which form the *bases* of systems of nosology, and, secondly, in applying to their cure those remedies which bear the reputation of being most successful in the treatment of each, his task would not be a very difficult one. A tolerably accurate observation of the *phenomena* presented to him at the bedside, and a ready memory as to the supposed curative effects of individual remedies, would be all that would be required at the outset; and the frequent repetition of the exercise of those faculties of observation and memory would tend to their improvement, but, at the same time, would constitute the whole of that experience, the possession of which is so often regarded, by non-professional people at least, as the chief qualification required for constituting an accomplished physician. If the characteristic phenomena of diseases were equally well defined with those which enable us to classify objects of natural history, and if the evidence on which one article after another has been added to our list of therapeutic agents had been always trustworthy, profound investigations into their mode of action would, indeed, have been unnecessary; and, though these might have been undertaken from the natural desire of extending the boundaries of scientific knowledge, the successful cultivation of the art of medicine would have still continued to rest on a *basis*, which, though being, to a certain extent, the result of observation and experience, and therefore correct in principle, would, nevertheless, have been confined within very narrow limits.

He who has been justly called the father of medicine was almost restricted to these sources of information for his guidance, yet the amount of knowledge he acquired, and the practical utility of the directions he has founded upon them, continue to excite our admiration even to the present day; and, while human anatomy was almost unstudied, and the notions entertained both of the functions of the healthy body and of the causes of disease rested almost wholly on conjecture, and were often of the most fantastic description, it is no wonder that empiricism (an appellation not formerly employed in the opprobrious sense now generally attached to it) should for so long a period have had numerous adherents, who gave it a preference over the so-called rational systems which emanated, from time to time, from the various schools of philosophy. We have now, however, learned from a more extended and continually increasing knowledge both of healthy and morbid anatomy, from a more ac-

curate acquaintance with the functions of the various organs of the body, and a more careful study of the deviations from the normal state to which those functions are liable, from more correct ideas of the causes which tend to develop diseased states of the body, and from the information which our improved means of diagnosis give us of the succession of internal changes taking place during the progress of diseases, that the external *phenomena* which are most striking to our senses when called to the bedside, are not always to be depended upon as the most correct *indices* of the morbid processes going on in the body, and that the classification founded upon them, though not without its uses, neither necessarily brings into proximity diseases requiring the same remedies or even similar modes of treatment, nor indicates for each a plan of treatment to be undeviatingly followed under every variety of circumstance, and throughout the whole of its progress. In like manner, we are now well aware that, though numerous valuable remedies have, from very early times, been justly held in high repute for their medicinal virtues, and others equally important have since been added to them in consequence of the extension of commerce and the discovery of new countries, the application to the treatment of disease, both of these, and of many of much more doubtful efficacy, has been much influenced by the medical theories prevalent at different periods. The searching scrutiny of a more practical era has consequently expunged from our lists many substances which were only held in estimation on account of fanciful notions entertained of their supposed occult qualities, or on other grounds equally frivolous or untenable, and has considerably modified opinions formerly prevalent as to the therapeutic actions of others.

But, while the necessity of determining by experiment the real remedial value of different medicinal agents has been generally acknowledged, it is obvious that many difficulties have to be overcome in prosecuting such investigations. Rapid as the advancement has been of the sciences of physiology and pathology, a knowledge of which sheds so much light both on the nature of morbid changes and of therapeutic action, they are but in a state of progression, and in the latter especially, the unexplained or undetermined still probably far exceeds what can be considered as established; and microscopical investigation and chemical analysis, while adding largely to our acquired knowledge, have opened up new fields of observation, and indicated new directions for research, some of which are as yet scarcely more than entered upon.

The discoveries made through means of these valuable auxiliaries, by making us acquainted with many of the molecular changes produced both by diseased action and by the continued use of remedial agents on the blood, on the organic structures which it nourishes, and the secreted fluids which are derived from it, appear at first sight, indeed, to place almost within our grasp the altered conditions which require to be rectified, and the means of their restoration; but when,

in order to discover a starting point for our curative efforts, we attempt to trace back a diseased state of the constitution through these molecular changes to the first departure from health, or, with a view to ascertain the *modus operandi* of remedies, we try to trace forward their action through a similar series of changes until restoration to health is effected, we find ourselves constrained to pass over many links in the chain of causation, or to supply them *pro tempore* by conjectures, which more extended observation, instead of confirming, may lead us afterwards to reject. Nor is it probable, even if we could correctly fill up what appeared to be wanting in such a course of inquiry, that we would find that remedial measures, except such as are of a hygienic description, produce their results by a directly counteracting power exercising its influence on those functions in the deranged state of which the first departure from health consisted, or even on the morbid changes more immediately resulting from a disordered state of these functions. On the contrary, it would appear to be more frequently the case that remedies, strictly medicinal, produce their effect by acting on some one or more of the functions not primarily implicated in the disease, but which have been more or less affected during its progress, and in which a change of action may be excited, and the chain of morbid *phenomena* may be thereby so broken that the disease can no longer maintain its onward course, and a condition tending to returning health is thence produced.

In watching such a process, moreover, for the purpose of determining the remedial value either of a medicine or of a plan of treatment, there are several sources of fallacy which require to be guarded against.

The first of these which I shall mention is, the difficulty of finding in a number of individuals, even when the essential symptoms are sufficiently marked to determine that they are labouring under the same disease, such a similarity of condition in other respects as to afford a fair opportunity of judging of the effects of the remedies applied. Differences of constitution, whether original, as those arising from peculiarity of race, from hereditary predisposition, or difference of sex; or afterwards developed at various periods of life, from differences of climate, of early training as to food and exercise, and of exposure to various degrees of temperature; differences between town and country life, varieties of occupation, and in habit and mode of living; constitutional tendencies peculiar to different ages, and the number, kind, and severity of previous attacks of disease,—are all circumstances which exercise an influence in modifying the aspect and progress of a disease, and in varying the effects which medicines are likely to produce on it.¹ Besides the modifying in-

¹ It is well known that some peculiarities of constitution exist, termed idiosyncracies, of such an unusual character, as to baffle all calculation as to what is likely to be the result of administering to them certain medicines or classes of medicines; and, if there are some such extreme cases, many others probably

fluences which exist in the constitutional state of the individuals attacked by disease, the intensity also of its exciting causes, and the length of time during which they have been in operation, have each their effect in determining its severity; and the varying states of the atmosphere occurring at different seasons of the year, and in different years, and probably extending over more lengthened periods, impress upon many complaints those peculiarities of form which we are accustomed to designate as their epidemic character. Hence the difference of the results, whether favourable or unfavourable, attendant upon and attributed to different plans of treatment, may in reality owe their origin to some of the circumstances above enumerated; and it is only by a comparison of results obtained under circumstances as nearly similar as possible, by extending our observations to a large number of cases, and by, at the same time, carefully excluding those where any considerable modifying circumstance is supposed to exist, that we can hope to acquire *data* for forming a legitimate conclusion.

A second source of fallacy may arise from the action of medicines which have been administered previously to those whose curative powers we wish to ascertain. In some instances, if the mode of administration of these has been such, that they have not been eliminated from the system before the new medicine has been given, the effects of the former may be mistaken for those of the latter; in other instances the action of the previous medicine may exercise a very considerable modifying influence over that of the succeeding one, either by accelerating or retarding its effects, or by combining the action of both so as to produce a result that neither separately would have occasioned; while, in a third case, the effects of the one medicine may just neutralize those of the other. It is obvious, then, that cases where several medicines have been given in succession are not favourable for drawing correct inferences as to the remedial powers possessed by each; yet, in many instances, the urgency of the symptoms, or the progress of the disease through several successive stages, may have imperatively required such treatment; thus narrowing the limits within which we can exercise that method of exclusion which is essential to the accurate determination of the results.

A third source of fallacy in estimating the virtue of remedies is, the existence of the so-called *vis medicatrix naturæ*, or tendency by means of which the constitution makes an effort to obviate the effects of those morbid agencies which exercise a disturbing or deleterious influence on any of its functions, and which thus, in many instances, enables it to bring about a restoration to health, even where no medicine has been given nor remedial treatment used.

Although the ignorance that exists in regard to the restorative

partake of the same character to an extent more limited, yet sufficient to modify materially the action of remedial agents.

power inherent in the constitution, and the facility with which its effects may be mistaken for those of the medicine which a patient may happen to have been using at the time he has begun to perceive signs of returning health, have often rendered non-professional persons the dupes of unprincipled practitioners, and have even led conscientious medical men, from want of sufficient attention to its influence, to become the unconscious promoters of delusive notions, it is not in the present day that enlightened physicians are disposed to overlook it, or to underrate its importance. It is far more easy, however, to admit the potency of such an agent, than to discriminate between its effects and those of the remedies employed.

It is not always possible, in the first place, to determine to what extent the *phenomena* attendant upon a disease are to be viewed as of a morbid nature, or to be classed among the restorative efforts of the constitution; and, in the second place, in endeavouring to discriminate between the action of remedies and the restorative powers of the constitution, although a disease may sometimes be the subject of observation while running its natural course, if it be thought safe to allow it to do so, and thus the inherent powers of the constitution may, in some degree, be ascertained, the reverse process is impossible, because the physiological effects of a medicine, when administered during health, do not necessarily furnish a criterion of its power in the cure of disease, and when administered while a morbid process is going on, its effects cannot be viewed unmingled with those of constitutional reaction.

No doubt, the difficulty of viewing them separately depends in part on the impossibility, already noticed, of selecting cases sufficiently similar in all respects to make them the objects of an exact comparison; but a still greater impediment is the want of any analogy subsisting between the combined operation of medicinal agency and the constitutional restorative powers, such as we have now been considering, and the combined operation of any of the physical or chemical forces acting on inanimate matter; for it cannot be said that the light recently thrown on the extent to which these latter forces operate in living bodies is sufficient, as yet, to enable us to explain wholly by means of them the *phenomena* of diseased action, of returning health, or of medicinal agency. That any analogy, drawn from the operation of forces acting on inanimate matter, is still insufficient to aid us in such an investigation, will be made more apparent by stating, that even if it were possible to submit to comparison two cases in all respects similar, so that we should have the constitutional restorative powers acting alone in the one, and along with a medicinal agent in the other, we could in no way say, as we would do in estimating the operation of physical forces, that the difference between the effect produced by the combined agency in the one case and the more simple one in the other, would represent the exact amount of curative influence possessed by the remedy which could be made available for application to other cases, or to other allied forms of

disease, and far less to those which, possessing less resemblance to them in their characteristic symptoms, might yet, from some of their *phenomena*, seem to require the use of the remedy we are testing. Nor would we arrive at a more correct conclusion were we to attempt to take the converse way of conducting our researches, and, having first ascertained the physiological effects of a remedy, were to expect that a certain amount of these, superadded to the restorative powers of the constitution, would, together, put at our disposal a known quantity of curative influence, to or from which we could, by varying our doses, add or subtract what was necessary to adapt it to the intensity of the disease in each individual case. It is possible that some valuable results might be obtained, in regard to the curative effects of medicines, by endeavouring to a certain extent to conduct our researches in one or other, or in both together, of the methods just described. It is possible that even some calculation of this kind takes place, almost unperceived, in our minds, when we are endeavouring to determine what is the best remedy or treatment for each case as it presents itself to us, and to proportion our doses, not merely to the age and strength of our patients and to the violence of the disease, but also to the probable efforts that the constitution will make to bring about a restoration to health. We cannot, however, in the present state of our knowledge, reduce the result of our observations, as in the physical sciences, to anything approaching to a mathematical *formula*, according to which, by setting on the one hand the sum of the morbid influences and effects with which we have to contend, and on the other, the results that can be produced by the combined action of the restorative influences and curative agencies we have at our disposal, we could ascertain the exact amount of the latter necessary to counteract the former.¹

The numerical method, lately adopted with a view to ascertain

¹ In writing the above passage, it almost appeared to me a stretch of imagination, to assume, even hypothetically, the possibility of expressing the whole of the knowledge that is required at the bedside of our patients, in *formulae* similar to and equally precise with those which physical and chemical science furnishes for practical application to so many other arts and employments; but so strong a tendency exists in the present day to reduce, at least, our physiological knowledge to an exactitude of this nature, that I considered it not altogether superfluous, by a supposition such as I have there made, to mark the distinction which, notwithstanding the recent researches and inferences of physical physiologists, is still required to be made whenever the vital element has to be taken into account. The following remarks of a distinguished continental author, quoted in the *British and Foreign Medico-Chirurgical Review* (April, 1857, p. 346), will show that I am not overstating the tendency just alluded to. Speaking of a chemical or chemico-physical theory, to which he thinks the explanation of "all animal phenomena" can be reduced, Ludwig says, "This theory will be undeniable, if it is possible to show with mathematical exactitude, that the elements in the animal body are so arranged, as to time, place, and quantity, as to render it possible to deduce from their reaction all the functions of the living and dead organism." The "if" introduced in this passage implies an important admission, the want of attention to which, in many similar modern theories, has led the unwary into

the relative value of various modes of treatment, though pursued on a different plan from the hypothetical one just suggested, may also be considered as in some respects an attempt to introduce an approach to mathematical accuracy into our researches; but, with a few notable exceptions, it has hitherto been conducted on too narrow a *basis*, and with too little regard to the number of modifying influences which ought to be taken into account, and the many sources of fallacy which beset such inquiries. Hence, the results obtained from this method of investigation have as yet fallen far short of the expectations that were raised by the introduction into medical reasoning of a process apparently so strictly philosophical.

Again, although many of the changes, excited both by morbid agents and the remedies employed to counteract them, partake of the nature of chemical combinations or decompositions, these are so modified by the powers peculiar to living organized beings, and, moreover, take place among organic substances and tissues of such complex chemical constitution, that it is only possible, as yet, to represent them to a very limited extent by chemical *formulae*.

Seeing, then, that scientifically conducted investigations into the curative effects of medicines are attended with so many difficulties,¹ and liable to be influenced by so many sources of fallacy, it is not to be wondered at that some medical men—especially those whose practice has met with a considerable amount of success—without availing themselves of much of the results of modern dis-

the adoption of conclusions which the hypothetical character of the premises did not warrant. In the instance just quoted, it will probably be long before the fundamental theorem, assumed as the conditional *basis* of the argument, can be demonstrated as a reality; and what is so far off from accomplishment in regard to physiology, is necessarily still more distant when we require to take into account the complications arising from the changes produced in the relations existing between the elements composing the body by the introduction into it of the results of diseased action and of the administration of active remedial agents.

¹ In addition to the difficulties enumerated in the text, there should have been noticed the scruples that every conscientious medical man must entertain in regard to the propriety, in the majority of instances, of making experiments on the patients entrusted to his care and relying on his skill. There is a natural reluctance in all men to be made the subject of experiment, where life or health are at stake, and, either when a medical man feels that the method of treatment which he has been taught chiefly to rely on has sufficient evidence in its favour to enable him to use it with confidence in its success, under favourable circumstances, or when a patient applies to him, in the full belief that he will apply the best ascertained means of cure, derived either from his own experience or his knowledge of the experience of others, it would be unjustifiable to incur the hazard of neglecting known means of relief, and of having recourse to untried remedies. I cannot here enter into a detail of the circumstances that would justify a medical man in entering on a purely experimental method of treating a disease, or of the cautions that ought to be observed in conducting it; my purpose, at present, being only to point out that the comparative rarity of the occasions on which it should be had recourse to, contributes still further to limit the means at our disposal for advancing by experiment the knowledge of practical medicine.

covery, should be inclined to despise theoretical inquiries, and, contenting themselves with the improved means of *diagnosis* of the present day, and a *materia medica* purified from many excrescences, and at the same time augmented by useful additions, should chiefly trust to their own experience and discrimination in the application of the materials placed at their disposal. On the other hand, considering the tendency of the human mind to theorize, it is not surprising that others, partly repelled by the complex nature of the investigations required, and partly induced by the extent to which, of late years, the investigation of laws connecting a limited number of phenomena has led to the discovery of more general laws, and to the facility of applying our knowledge to practical ends to which such generalizations give rise, should, passing over the laborious processes through which these laws have been established, have adopted, upon insufficient *data*, theories of great apparent simplicity, by which they have imagined that all the phenomena of disease could be accounted for, and the operation of all medicines explained by referring their mode of action to one or two simple principles.

That both these methods of proceeding are unphilosophical, is pretty obvious; but of the two, that which is analogous to the empiricism of ancient times has generally led to the most useful results, or, at all events, has been the least obstructive to the true progress of scientific medicine. That it has been so, however, has chiefly arisen from the impossibility of any method of practice being empirical, in the strict acceptation of the term. The practitioner who attempts to follow such a method, is obliged to assume, in the first place, that there is a certain degree of conclusiveness in the evidence that has led his predecessors to make use of particular medicines or plans of treatment in various diseases; he must assume also that there is a certain amount of resemblance in the cases he attempts to treat by them to those in which they have been already successfully applied; and, if his experience is of any real value to him, it is so by his assuming, that what he has found successful in certain cases, may be applied with advantage to others similar to, though not exactly identical with, them. Nor is this all; for, if he be an acute observer, he will scarcely fail to find out some of the modifying circumstances which occasionally render the results of his practice different from what he might have anticipated, and to seek for some means of adapting his treatment to those circumstances. In all this he is a theorizer, and not an empiric; and the defects in his system consist not in the complete absence of theory, but in his making no attempt to account for the phenomena he observes, nor to connect them together in such a way that any very general rules of practice could be founded on them. Nevertheless, many important facts may be recorded, and even discoveries made, by such observers; and the accumulation of these furnishes to others the materials from which more general principles can be elicited.

On the other hand, hasty attempts at generalization, founded

either on an insufficient number of facts, on inaccurate observation of them, or on incorrect assumptions as to their causal connection, serve only to retard the true progress of the science, and, consequently, of the art of medicine. Their apparent simplicity, and often their plausibility, may gain them advocates for a time, and the facility with which, owing to the sources of fallacy we have already pointed out, the facts passing under daily observation can be made to bend to preconceived notions as to the manner in which they can be explained, may give them powerful sway even over a considerable number of the profession, but careful observation and experiment at length succeed in pointing out their insufficiency, and producing their overthrow. In this manner the theories of Brown and of Broussais, resting in part on observed facts, which, rightly interpreted, have their significance, but the range of which was far too limited to serve as a foundation for constituting theories intended for general application, could only maintain their reputation for a limited period; and, when it was discovered that they were at variance with many easily observed facts of daily occurrence, soon ceased to be regarded as furnishing a key to the interpretation of morbid phenomena, or indicating any general rule for the treatment of disease. Nor can we doubt, when such has been the fate of theories which, to a certain extent, were constructed from acknowledged facts, that in other instances of more recent date, where they have been made to rest on principles assumed in the first instance before any facts could be adduced to support them, and more especially where hypothesis has been heaped on hypothesis, with the hope of overcoming the stubborn resistance with which facts refused to accommodate themselves to the forced and unnatural interpretations endeavoured to be put upon them, such theories, however popular for a time, will, ere long, sink into their merited insignificance.

While it is evident, then, from the abortive result of the attempts hitherto made to establish a general theory of the treatment of disease, as well as from the incomplete, and even, in some instances, almost rudimentary, state of our knowledge of some of the *phenomena* necessary for its construction, that there does not yet exist a sufficient accumulation of facts for such a purpose, it is not to be inferred that no progress has been made towards it. It may be, that, owing to the complex nature of the forces by which the living organism is acted on, no theory of general application to all cases will ever be arrived at; but we are not, therefore, to regard all we know as a collection of isolated facts. In spite of the retardation, and sometimes even retrogression, produced either by scepticism as to the reality of our progress, or by too hasty inferences from ascertained facts, we are, in the present day, beyond all former periods, advancing in two most important particulars required in the inductive process, namely, in the first place, the tracing, by observation and experiment, the chain of causation, both backwards and forwards, of the phenomena

of health and disease, and of the action of medicinal agents on both; and, in the second place, the classification of our knowledge into such a degree of order, that the principle of connection between similar phenomena may be rendered obvious, and the laws thence inferred may be more easily extended from lesser to larger groups, so as to lead towards the establishment of more general laws. If, in the legitimate pursuit of these objects, it should happen, as will almost unavoidably be the case, that differences of opinion should be for a time maintained, and that views, held at one time as sufficient to explain certain groups of *phenomena*, should be, as science advances, superseded by others, the controversies dependent on such occurrences ought not to be identified with those that have resulted from the crude or visionary speculations formerly described. If we examine the history of physical and chemical science, or even search the annals of natural history, we find parallel examples of such differences of opinion, and of controversies arising from them, often carried on with an asperity little befitting either the object of contention or the eminence of the individuals engaged in them. It is not wonderful, then, that among so large a body as that of which the medical profession is composed, including in their number many who have not been trained to habits of logical accuracy, or to the rigorous requirements of the inductive process of reasoning, yet eager to add to the gradually accumulating mass of facts, or to take part in the discussion of the leading questions of the day, differences of opinion should arise, and that, in the keenness of debate, personal feelings should occasionally be stirred up to mingle in the contest. The difficulties that beset the path of observation, and obscure the inferences that should be drawn from it, are sufficient to account for many such controversies, without either assuming, as has often hastily been done, that the medical profession consists mainly of individuals of a peculiarly irritable temperament, prone to rush into uncalled-for strife, or rashly concluding that the objects of medical investigation are so obscure as to render hopeless the expectation of any approach to unanimity in the application of the principles derived from it. Such controversies, when confined within legitimate bounds, so far from leading any part of the non-professional portion of the public to hesitate in placing confidence in medical knowledge, ought, in reality, to be regarded as signs of the eagerness of their search after truth, and earnestness of success in the pursuit of it; and the frequency of their occurrence, instead of deserving to be made a subject of ridicule, as it sometimes is, may rather be considered as a proof of the vigorous spirit of inquiry with which the profession is animated. It is desirable, no doubt, both for the purpose of eliciting truth and securing the respect of those who do not enter the *arena* of debate, and of opponents towards each other, that such controversies should be conducted with courtesy and candour, and that no selfish or unworthy motives should be allowed to mingle in them; but it may safely be asserted that

the present era will, on the whole, bear a favourable comparison, in this respect, with any that have preceded it.

Recognising, then, the earnest spirit of inquiry that is abroad among the profession in the present day, and the logical *acumen* that distinguishes the most able among those who seek its advancement, as among the most promising signs of the progress of sound medical knowledge, I would have felt inclined, had your time permitted, to have entered into some detail of other circumstances which indicate that, not only as a deeply interesting science, but also as an art of the highest importance to the community, medicine is in a state of steadily progressive advancement; but I can now but barely allude to these. Among these I would enumerate the progress that has been made by all the collateral sciences bearing upon medicine; more especially physiology, as studied in the light that microscopical investigation and minute chemical analysis have thrown upon it; pathology, as advanced by the same means, and by those improved methods of *diagnosis*, which not only enable us to distinguish one disease from another more accurately, but also to discriminate the different stages of each, and to connect the external signs by which they are accompanied with the succession of morbid changes going on internally; chemistry also, as applied to the analysis of medicinal substances, to the obtaining them in increased purity, and separating their active from their inert constituents, and to the discovery of new compounds possessing energetic properties. In addition to these, the study of the causes of disease has necessarily led to a larger amount of attention to hygienic laws, or those circumstances which, either singly or combined, exercise a beneficial or a prejudicial effect on the maintenance of health; so that, if medical men were judiciously seconded by those whose chief interest it is to do so, the adoption of many measures of a salutary tendency, and the removal of much that at present exercises a noxious influence on the health might be effected, and in many cases the very first inroads of disease might be averted. Nor is it an augmented power of preventing disease alone that is effected by our increased knowledge in this department; but, in many instances where morbid action has already made considerable progress, the removal of the external predisposing or exciting causes, or, where that cannot be accomplished, the removal of the patient from their influence, is now known to form the most important part of the treatment required.

I would also have felt inclined, had I not already encroached too far on your time, to have entered into some further detail, not only of the progress already effected by the application of scientific knowledge to the advancement of practical medicine, but also of the prospective influence it may be expected to exert on it; and to have pointed out some of those branches, the cultivation of which holds out the greatest promise of future progress. Among these, I am especially disposed to indicate a more extended and minute study of the remote physiological changes produced by the long continued

use, and consequent absorption into, and accumulation within the system, of medicinal substances. Some of our most valuable medicines have been long known to act chiefly in this way; but our classification of remedies has, for the most part, been rather founded on the more immediate and most easily recognised of their physiological or therapeutical effects; but, in chronic diseases at least, it is obvious that it is not by these that a cure is most likely to be effected. It is now pretty well ascertained by chemical analysis, that not only substances derived from the inorganic kingdom of nature, such as the metals and their preparations, but that also some of the best defined, and, at the same time, most energetic organic compounds, may become for a time incorporated either with the fluids or the solids of the body, and that a considerable period of time may elapse before they are again eliminated from it; and it is extremely probable, that the same takes place in regard to substances more difficult of detection. If the substance thus admitted be foreign to the chemical constitution of the animal frame, or even if, without being so, it deranges the usual proportion existing between the constituents of the fluid or tissue with which it becomes incorporated, it cannot fail to influence the functions for which these are destined. Nor will the power, first, of modifying the chemical composition, and then influencing the function of the various component parts of the body, be found to be confined to those substances which are sufficiently elementary in their constitution, or sufficiently stable in regard to the forces by which their elements are held together, to admit of their introduction into the system unchanged; but we may also expect, in time, to become much more extensively acquainted than at present with similar effects produced by others, the chemical constitution of which is more easily subverted, and the elements of which, when introduced into the body, enter into new combinations with each other, and with those already existing there.

It is in this manner that, if the absorption of substances, either contained in medicines or in articles of diet, have the effect of modifying the composition of the blood, either by altering the relative proportion of its normal constituents or by the introduction of new ones, an influence will be exerted on the accomplishment of all the purposes which the blood serves in the animal economy. Its own power of assimilating other substances admitted into it; its action relative to the function of respiration, and the maintenance of animal heat; its capability of performing its part in separating the various secretions, and eliminating by these morbid or effete matters from the body; its fitness to act as a stimulus to the heart; its power of nourishing the tissues; and its influence on the due performance of the functions of the nervous system, will all be more or less affected. Again, the mode in which the nutrition of the various organs of the body may be affected by an abnormal state of the blood, such as has just been alluded to, may consist in its being stimulated, and thus leading to

increased growth ; in its being diminished, leading to atrophy ; in disintegration being promoted or retarded, or in the tissues being abnormally altered in their chemical and in their organic structure. All these changes, in turn, will have an effect in modifying the functions for which the organs affected by them are destined ; and the alteration of function thus produced, will have a reactive influence on the performance of other functions, and on the constitution generally.

For example, various articles of food or of medicine are found to diminish the secretion of *urea* by the kidneys, or of carbonic acid by the lungs ; and the effect thereby produced, may either be hurtful, and even poisonous, by causing an accumulation in the constitution of these principles, or of other compounds formed from their elements, or by conveying them to particular organs, on the functions of which they exert a pernicious influence ; or, at another time, it may be beneficial, by retarding the disintegration of the tissues from which the elements of these principles are derived, and thus, in states of debility, preventing the waste of important and even vital organs. The effects of the preparations of iron, on the other hand, are reconstructive, primarily, as regards the corpuscles of the blood, and secondarily, in promoting the nutrition of the tissues ; while those of mercury and of iodine promote disintegration, the one acting chiefly on the products of plastic inflammation, the other on exudations of an abnormal character. It is probable, also, that the metallic tonics, found useful in nervous affections, produce their effects by a vital chemistry exerted on the nervous tissue ; and, in a similar manner, it may in time be found, that each constituent of the body may be affected by appropriate agents, and that while some assist in eliminating from the system accidentally introduced foreign ingredients, others may act in promoting the disintegration and removal of those refractory morbid products which have hitherto been considered beyond the influence of curative agency.

As closely connected also with the processes of vital chemistry now mentioned, I can only just advert to the part which the *vis medicatrix naturæ* performs in eliminating from the body noxious constituents ; in restoring the normal chemical constitution of its component parts, after they have been altered by disease ; in providing substitutes where portions of tissue have been destroyed or removed, under circumstances that do not admit of their renewal in their original form ; and in transferring to other organs the functions of those whose natural action has become so obstructed or perverted, as to prevent their accomplishing the chemical changes usually effected by them. Whether we consider the restorative powers thus exercised by the constitution, under circumstances sufficiently favourable to enable them to accomplish alone the above objects, or as requiring the aid of medicinal agents and medical treatment to effect them, a vast field for chemico-pathological and therapeutical investigation lies before us, which, in this point of view, has hitherto been but very partially cultivated.

In conclusion, there remains one more aspect in which the subject of this essay may be placed before you, and to which I cannot refrain from drawing your attention ; namely, that while, on the one hand, a consideration of the powers possessed within certain limits by every organized being, of maintaining in each of its component parts a nearly uniform chemical constitution and physical structure adapted to the purposes for which it is destined, and of restoring, often unaided, deviations from the normal state produced by influences which, for a time, have acted more powerfully than those of a conservative description, presents us with one in addition to the many proofs of design revealed by every branch of study connected with our profession ; I see no reason to doubt, on the other hand, that the numerous array of medicinal substances to be found in the different kingdoms of nature, not adapted for food, yet exerting powerful effects on the functions of the body, were designed to act, as I do not hesitate to affirm they have been found to do, as valuable auxiliaries to the inherent powers of the animal frame, and were provided for that end by the all-wise and benevolent Creator, who has made nothing in vain, and whose own wise purposes are promoted by our endeavouring to discover the design and use of every thing He has called into existence.



