

p. 164,) observes, that from this inferior developement, the brain of the dog "is not so liable to sanguineous congestion, and when this condition is observed, it is not very intense—stupor is the only symptom of it; never coma, loss of consciousness, nor profound sleep." I have observed that the root of monkshood does not act precisely alike on rabbits and dogs. In the latter, one of the most remarkable symptoms of its operation is diminution of feeling; in the former, the function of feeling is much less obviously affected, but we observe more evident paralysis of the hind extremities. Differences of this kind are to be expected, since they are connected with unequal developement of the nervous system. As rabbits and horses cannot vomit, irritant poisons when administered to them cannot act as emetics. The skin of horses is more susceptible than the human integument of the action of turpentine. On the other hand, certain agents, whose operation on the human body is most energetic, have, comparatively, very little effect on the horse—as colocynth, briony, and jalap.—(*Moiroud, Pharmacologie Vétérinaire*, pp. 269 and 274.)

On man.—The action of medicines on the *dead* human body, or on parts separated from it, as the blood recently drawn from the veins, has been examined, with the view of learning the operation of these agents on the living body. It may be of assistance to us in ascertaining either the mechanical or chemical action of substances; but as the greater number of medicines act only on the living body, and quite independently of any known mechanical or chemical influences, this mode of investigation is of very limited value.

In ascertaining the action of remedial agents on the *living* body, it is necessary that we examine their influence both in healthy and diseased conditions. For, by the first we learn the positive or actual power of a medicine over the body; while by the second, we see how that power is modified by the presence of disease. Moreover, in the latter condition we sometimes discover remedial influences which our knowledge of the effects of medicines on the healthy body could not have led us to anticipate. The beneficial operation of arsenious acid in agues, or in lepra, could never have been inferred from any experiments made with this substance in health merely; nor could we have formed a correct estimate of the effects and proper dose of opium by employing it in tetanus, nor by using mercurials in fever. The homœopathists assert, and with truth, that the study of the effects of medicines in the healthy state is the only way of ascertaining the *pure* or *pathogenetic* effects of medicines—since when we administer our remedies to invalids "the symptoms of the natural disease, then existing, mingling with those which the medicinal agents are capable of producing, the latter can rarely be distinguished with any clearness or precision."—(*Hahnemann's Organon*, translated by C. H. Devrient, p. 190.)

3. Mode of Action of Medicines.

The production of effects by the application of medicines to the living body, depends on the existence of two classes of powers or forces; the one in the medicine, the other in the organism.

1. *Active forces of Medicines.*—Bodies act on each other in one or more of three ways, viz.: *mechanically*, by their weight, cohesion, external form, and motion; *chemically*, by their mutual affinities; and *dynami-*

cally, by agencies which are neither mechanical, nor chemical merely. Hence we may examine the actions of medicines under the three heads of mechanical, chemical, and dynamical.

a. Mechanical.—The alterations of cohesion, of form, of relative position, &c. caused by medicines, are denominated their mechanical effects. They are frequently attended or followed by organic changes; consequently, a medicine, whose action is simply mechanical, may produce two classes of effects—the one mechanical, the other vital; and the whole of its operation may be denominated *mechanico-vital*.

Müller (*Elements of Physiology*, translated by Baly, p. 59) considers that mechanical agents may give rise to chemical changes in the tissues. "Mechanical influence in frictions," he observes, "acts under certain circumstances as a vivifying stimulus; it has this effect, probably, by inducing in the composition of the tissues, slight chemical changes, as a consequence of which the affinity of the tissues for the general vital stimuli already in the organism is increased."

Formerly most of the articles of the *Materia Medica* were supposed to act on the organism mechanically merely. "I doubt not," says Locke, "but if we could discover the figure, size, texture, and motion of the minute constituent parts of any two bodies, we should know, without trial, several of their operations one upon another, as we do now the properties of the square or a triangle. Did we know the mechanical affections of the particles of rhubarb, hemlock, opium, and a man, as a watchmaker does those of a watch, whereby it performs its operations, and of a file, which, by rubbing on them, will alter the figure of any of the wheels, we should be able to tell before-hand that rhubarb will purge, hemlock kill, and opium make a man sleep."—(*Essay concerning Human Understanding*, book iv. chap. 3.) These mechanical notions of Locke harmonized well with those of the *iatromechanical* or *iatromathematical* sect of the age in which he lived; a sect which ranked amongst its supporters Borelli (its founder,) Bellini, and others, in Italy; Sauvages, in France; and Pitcairn, Keill, Mead, and Freind, in England. The functions of the body, the production of diseases, and the operation of medicines, were explained on mechanical principles. The action of stimulants, for example, was supposed to depend on the pointed and needle-like form of their particles, and the operation of emollients on their globular form.—(*Sprengel, Hist. Médec. by Jourdan*, t. 5, p. 131, *et seq.*) I need hardly say, the existence of particles with the peculiar shapes assumed, is quite imaginary; and, indeed, if, for the sake of argument, we assume their existence, the action of medicines is, notwithstanding, quite inexplicable. We can, indeed, easily believe that a ball of glass may be swallowed with impunity, and that the same substance, reduced to the form of a coarse powder, might cause irritation by the mechanical action of the angular particles on the tender alimentary tube; but we could not, on this hypothesis, explain why one medicine acts on one part of the body, and a second on another part.

There are very few medicinal agents now in use whose remedial efficacy can be solely referred to their mechanical influence. Indeed, several of the processes to which medicines are subjected before they are administered, have for their principal object the prevention or diminution of this influence. Among the medicines still employed, on account of their mechanical action, are the hairs of the pods of *Mucuna pruriens*, quick-

silver, and, perhaps, powdered tin; the first and the last are used as anthelmintics—the second, to overcome intus-susception, or intestinal invagination.

b. Chemical.—If substances, having powerful affinities for organic matter, be applied to the living tissues, they first destroy the life of the part, and then enter into combination with one or more constituents of the tissues: such substances are termed caustics. But the destruction of life in one part is attended with alterations in the vital actions, and the production of inflammation in surrounding parts; so that the chemical action of caustics is attended by both chemical and vital effects, and the whole of their operation may be denominated a *chemico-vital process*.

If the energy of the affinity of caustics for organic matter be diminished, as by diluting them, the vital powers are sometimes enabled to resist the production of any immediate chemical change, and the life of the part is consequently preserved. The caustic, then, operates at first as a mere irritant, and causes alterations of vital action only. In this case the active force is still supposed to be affinity; that is, the particles of the caustic are presumed to have a tendency to unite with those of the organised tissues; but the union being resisted by the vital powers, a new action is set up which constitutes the changes or effects before referred to. The long-continued application, however, of these weak chemical agents, will gradually effect slight changes in the composition of the tissues without producing the death of the altered parts. These organic alterations of a living part are of course attended by the production of morbid actions.

Chemical changes are sometimes produced in the secretions of distant parts by the internal use of certain agents. Thus the qualities of the urine are modified by the administration of acids or alkalis. Do these modifications or changes depend on the chemical influence of the substances swallowed? or on some other kind of influence which these agents exert, either directly or indirectly, over the secreting organs? Neither explanation is without difficulties; but I conceive the first to present the fewest. It cannot be denied that when either alkalis or acids are swallowed, they pass out of the system, in part at least, by the kidneys; and that in the urine they possess their usual chemical properties, modified by the presence of any substances with which they may have united. Moreover, the qualities which they impress on the urine are similar to those which they produce when added to this secretion after its evacuation from the bladder. Thus, by the internal use of alkalis, it has been found that the natural acidity of the urine may be destroyed, and an alkaline quality substituted for it: the same condition of urine is produced by the addition of alkalis to this fluid out of the body. Again, the internal use of soda or magnesia may give rise to the appearance of white sand (phosphates) in the urine: now the same kind of deposit may be produced in healthy urine by the addition of a few drops of an alkaline solution to it. Furthermore, by the administration of acids (sulphuric or hydrochloric), phosphatic deposits are diminished or entirely prevented, while the employment of alkalis promotes them. Now this influence of acids is probably, in part at least, chemical, since we find that a few drops added to urine which contains these deposits, dissolves them. In other words, as the modifications which acids and alkalis produce in the condition of the urine are precisely those which we might expect from the known

chemical properties of these bodies, it is more rational to refer these modifications to influences the nature of which we can understand, than to those which are incomprehensible.

Do substances (such as acids, alkalis, and metallic salts) which are known to possess affinities for the constituents of the blood and of the tissues, exercise those affinities in their passage through the system? and are the constitutional effects of those substances referrible to chemical influences? It is impossible to give satisfactory answers to either of these questions. We cannot deny the chemical influence of these agents; but we are hardly authorised to ascribe the whole of their effects to it. The truth is, that the facts on which we are required to form our opinion are too few to enable us to draw any accurate or precise conclusions. By the internal use of madder, the bones and some other parts become coloured; and the long continued employment of the nitrate of silver gives rise occasionally to a deposit of silver under the skin. But with two or three exceptions of this kind, no chemical changes in the living tissues or organs are obvious, and we have no right, therefore, to assume that any exist. For when external agents are taken into the system, they become subject to a superior power, and are no longer at full liberty to obey the ordinary laws of affinity. It must be some power superior to that recognized in chemical operations which prevents the action of the gastric juice on the stomach during life.

Müller, (*Elem. Phys.* p. 58, *et seq.*) however, ascribes the operation of most external agents to their chemical influence. Vital stimuli, (a certain degree of external heat, atmospheric air, water, and nutriment,) he observes, "do not merely produce a change in the composition of the organic structures, and stimulate by disturbing the balance in the system, but renovate the tissues by entering, in a manner indispensable to life, into their composition." On the other hand, all agents of this kind, as well medicinal substances as caloric, electricity, and mechanical influences, "may, when their action is excessive, have the very opposite of a vivifying effect, by producing such a violent change in the organic matter, that the combinations necessary to life cannot be maintained." "A great number of substances are important as medicaments, from producing a chemical change in the organic matter, of which the result is, not an immediate renovation of material and increase of vital force, but the removal of that state of combination of the elements which prevented healthy action, or excited diseased action; or the chemical change produced is such as to render the organ no longer sensible to a morbid stimulus; or it is such that certain apprehended destructive changes in its composition are no longer possible, as in the antiphlogistic plan of treatment; or, lastly, these substances produce a change in the nutritive fluids. Such substances are alteratives. By these remedies an organ morbidly changed in composition cannot be rendered sound by, as it were, a chemical process, but such a slight chemical change can be produced as shall render it possible for nature to restore the healthy constitution of the part by the process of nutrition. These remedies, again, may be divided into two principal kinds, according as they act chiefly on the nervous system, or on the other organs dependent on that system. Among those of the first kind, the most important are the so-called narcotics; those of the latter kind comprehend the numerous medicines which exercise their action on diseases in other organs. These remedies

also, by removing the obstacles to cure, become indirectly vivifying or renovating stimuli ; and they may themselves, by disturbing the balance in a part, produce symptoms of irritation. If used in excess, they either give rise to the injurious effects of the heterogeneous stimulants, or, by inducing a sudden change of composition, annihilate the vital force, as is the case with the narcotics. Since, however, such alterative medicines affect the composition of an organ each in its own way, one alterative may, after a time, lose its influence, as it were, by saturation, while the organ may still be susceptible of the influence of another. A great number of the instances of habituation are referrible to this cause."

Such are the statements, as to the operation of medicines, made by one of the first physiologists of the age. They deserve careful and attentive examination. But however plausible they may appear, the student is not to be unmindful that, for the most part, they are opinions merely, and that the chemical changes in the tissues, so frequently referred to, have not been as yet demonstrated by chemical analysis. Furthermore, I would refer those who are desirous of becoming acquainted with the arguments which have been adduced against the chemical action of medicines on the system, to Vogt's *Pharmakodynamik*, bd. i. p. 9, *et seq.* The only chemical change which this author will admit medicines to be capable of producing, is that which takes place in the parts to which they are applied.

c. Dynamical.—The above-mentioned mechanical and chemical influences are considered by many writers insufficient to explain the effects caused by the greater number of the articles composing our *Materia Medica*; principally on the ground that substances which exercise a most potent influence over the organism, frequently do so without producing any obviously mechanical or chemical changes in the condition of the body. A third mode of operation has, therefore, been admitted, which is unattended with any recognizable changes of form or of composition.

In the inorganic kingdom we have also evidence of an influence which cannot be denominated either mechanical or chemical. The communication of magnetical and electrical properties to iron by mere contact with another body, without the production of any change of form or of composition, either of the iron itself or of the imparting body, is an example of this. Now to influences of this kind the term *dynamical* has been applied; and in several pharmacological works, (among which are Burdach's *System der Arzneimittellehre*, C. H. E. Bischoff's *Handbuch der Arzneimittellehre*, and Vogt's *Lehrbuch der Pharmakodynamik*), it is employed to indicate those influences of medicines over the organism which are ascribable to neither mechanical nor chemical causes.

Some have attempted to account for the action of medicines on electrical principles. All bodies, says Bischoff, (*op. cit.* bd. i. p. 158,) by contact with each other, act as electrics, without, however, necessarily undergoing any chemical changes. Therefore, when a medicine is applied to the organism, its action is electrical (p. 162.) But though, says this writer, a medicine may produce electrical without chemical changes, yet the reverse of this does not hold good, for no chemical changes can occur without the production of alterations in the electrical condition of bodies (p. 163); and, consequently, the operation of caustics is an electro-chemical process.

In some few instances the effects of medicines are analogous to those of electricity. Thus the instantaneous death caused by hydrocyanic acid is something like an electrical phenomenon. "A drop of acid, mixed with a few drops of alcohol," says Magendie, "when injected into the jugular vein, kills the animal instantly, as if he had been struck by lightning."—(*Formulaire*, 8^{me} ed. p. 174.) The same physiologist has compared the convulsive shock, caused by the *Upas Tieuté*, "to that which takes place when a current of galvanic fluid is directed along the spinal marrow of an animal recently killed."—(See *Orfila's Toxicologie Générale*.) Again, "If an animal be touched whilst under the action of this substance [extract of *nux vomica*,] it experiences a commotion similar to that of a strong electrical shock; and this takes place every time the contact is renewed."—(*Formul.* p. 5.) These phenomena deserve especial notice in relation to the suggestion of Dr. Faraday, (*British Annals of Medicine*, for Feb. 24, 1837,) that the agent or source of the animal portion of the nervous system may be electricity.

2. *Vital force of the Organism*.—The peculiar properties possessed by living beings are two in number; namely, a capability of receiving impressions, and a capability of contracting—that is, of executing certain motions when the requisite impression has been made. The first has been denominated *latent* or *organic sensibility*; while the second has been termed *insensible* or *organic contractility*. These two properties, observes Adelon (*Physiologie de l'Homme*, 2^e ed. t. iv. p. 565,) are reducible to one (*sensibility*;) for to feel is to change the mode of existence, in consequence of an impression—that is, it is to move in a way that is neither physical nor chemical. But as Mr. Grainger (*Observations on the Structure and Functions of the Spinal Cord*, p. 105,) has justly observed, "Organic sensibility is not sensibility of any kind; but a capability possessed by certain nerves (the incident) of receiving and transmitting the impressions of physical agents to the true spinal cord; which organ, by its peculiar power, excites muscular contraction through the medium of the reflex nerves." He proposes, therefore, to call it *excitability* (p. 127;) and suggests "that the contraction required for the nourishment and support of plants is the result of an excited action, effected by a structure analogous in its office, though differing in its physical character, to the true spinal (and, I believe, sympathetic) system of the animal kingdom."—(P. 131.)

Vital properties have by some been ascribed to organic structure, by others to a distinct internal principle called *Life* or the *Vital Force*. For an account of the opinions of writers on this subject I must refer to *Barclay's "Inquiry concerning Life and Organization,"*—as the subject hardly falls within the scope of a work on Pharmacology.

4. *Physiological Effects of Medicines.*

The *primary* or *physiological effects* of medicines may for convenience be divided into such as are *local*, or those that occur in the part to which the agent is applied;—and into those that take place in distant organs, and which by way of distinction we denominate *remote effects*.

1. *TOPICAL* or *LOCAL EFFECTS*.—These are of three kinds:—

a. Mechanical or Mechanico-vital effects, as those caused by the hairs of the pods of *Mucuna pruriens*,—by demulcents,—by adhesive plaster, &c.