IX. *A physical Inquiry into the Powers and Operation of Medicines.* By Thomas Percival, M. D. F. R. S. and S. A. Lond. F. R. S. and R. M. S. Edinb. &c. — *From the Memoirs of the Literary and Philosophical Society at Manchester, Volume the Third.*

Causa latet, vis est notissima.

OVID.

To the Literary and Philosophical Society.

Manchester, Nov. 25, 1786.

MEDICINES are the instruments employed for the preservation of health, or the cure of diseases: it must, therefore, be an object of interesting speculation to the philosopher, and of practical importance to the physician, to investigate the rationale of their action on the human body. But there is no branch of the healing art which is in itself more intricate and obscure; nor any one that has undergone so many doctrinal vicissitudes. It would trespass too much on the time allotted for such discussions, in this Society, to enumerate the multifarious hypotheses which have been

been supported by the successive sectaries in physic since the days of Hippocrates. On many of these I have animadverted in a work published near twenty years ago*: and I shall now only request your candid attention to a few observations on the opinions which are beginning to prevail in our schools; and your permission to offer some hints towards the extension of our views, and the methodising of our experience, relative to this curious and philosophical subject.

Anatomy has now revealed the exquisite structure of our corporeal frame; and physiology has taught us that, in its animated state, the organs of which it is composed are reciprocally connected with, and delicately adjusted to, each other. The minutest agent, therefore, may excite a movement capable of being propagated to any part of the system, or even through the whole of it, by a sympathetic energy, independent and far beyond the power of the primary instrument of motion. From these premises it is inferred, agreeably to the simplicity which subsists in all the operations of nature, that a medicine is only the *cause of a*

* Essays Medical and Experimental, Vol. I.

cause, to adopt a phrase of the logicians ; and that its proper action is confined to the nerves or fibres to which it is immediately applied. When received into the stomach, after the first impression on the very sensible coats of that organ, the nature of it is gradually changed by the solvent powers of the gastric juices ; or, if incapable of being digested into a mild and nutritious chyle, it is carried through the intestinal canal, and ejected as useless and noxious to the body.

Error may be built on the basis of acknowledged, if only partial, truth, and is then most specious in its form, and most authoritative in its influence on the understanding ; but the imposition ceases when we extend our views : and I shall endeavour to shew that the operation of medicines is to be measured by a more enlarged scale than the foregoing hypothesis applies to it, or any other which now occurs to my recollection.

I. Medicines may act on the human body by an immediate and peculiar impression on the stomach and bowels, either in their proper form ; in a state of decomposition ; or by new powers acquired from combination, or a change in the arrangement of their parts. The sym-

pathy of the stomach with the whole animated system is so obvious to our daily experience, that it cannot require much illustration. After fasting and fatigue, we feel that a moderate quantity of wine instantly exhilarates the spirits, and gives energy to all the muscular fibres of the body. It has been known even to produce a sudden and large augmentation of weight, after much depletion, by rousing the absorbent system to vigorous action. Such power is peculiar to living mechanism, and is properly denominated by physicians the *Vis medicatrix naturæ*. But apparent as is the sympathy of the stomach, the laws by which it is governed are very insufficiently understood; and we have hitherto learned only from a loose induction of facts, that the nerves of this delicate organ seem to be endued with diversified sensibilities; that impressions, made by the same or different substances, have their appropriate influence on different and distant parts; and that the stomach itself undergoes frequent variations in its states of irritability. A few grains of blue vitriol, taken internally, excite instantly the most violent contractions in the abdominal and other muscles concerned in vomiting. A dose of ipecacuanha, as soon as it produces
nausea,

nausea, abates both the force and velocity of the heart in its vital motions, and affects the whole series of blood vessels from their origin to their minutest ramifications, as is evident by the paleness of the skin under such circumstances, and by the efficacy of emetics in stopping hæmorrhages. The head, when disordered with vertigo, sometimes derives sudden relief from a tea-spoonful or two of æther, administered in a glass of water : and I have known an incessant cough to attack the lungs in consequence of the stimulus of a pin which had been unwarily swallowed. Of the action of medicines on the stomach, under decomposition or recomposition, we have an example, familiar to every one, in magnesia ; for this absorbent earth, by neutralising the acid in the primæ viæ, acquires a purgative quality, and at the same time yields a gas of great salubrity, as an anti-emetic, tonic, and antiseptic.

II. Medicines may pass into the course of circulation in one or other of the states above described ; and, being conveyed to different and distant parts, may exert certain appropriate energies. Chemistry furnishes numberless cases wherein substances undergo changes, and put on new forms more remarkable than can be ef-

fected by the digestion of the stomach, retaining still the *materia prima*, and being capable of resuming the original arrangement of their particles, and consequently their original qualities. Now, a body altered in its texture by the digestive organs, and carried into the system with the aliment, may, by such alteration, acquire specific powers on particular sound or diseased parts. Thus if we suppose cantharides to be changed in form and texture, when mixed with the chyle, the lymph, or blood, yet in that form and texture they may be peculiarly adapted to excite strangury in the urinary passages; or we may conceive that this new modification of their corpuscles may again be altered, and their original composition restored by a subsequent chemical change in the kidneys — an event not more singular than the separation of urine from the blood, than the revival of a metal, or the precipitation of a solvend from its menstruum by elective attraction. The urinary excretion seems to be designed by nature to carry off the recrementitious parts of the circulating fluids: and it clearly shews what compositions and decompositions take place in the body; for it varies almost every hour both in the state of health and of disease, and the lateritious,

ritious, pinky, mucous, and other appearances it exhibits, are the result of chemical changes, either in itself, or in the fluids from which it is derived.

The sensible qualities of any body are no certain criteria of its medicinal action. Peruvian bark owes not its efficacy to bitterness; for stronger bitters are not possessed of its febrifuge powers. Antimony, though insipid, is violent in its operation on the nerves of the stomach; and yet, if applied to the eye, an organ endued with equal sensibility, it is entirely inert. To what property in opium, capable of affecting the external senses, are we to ascribe its narcotic powers? or is there in the grateful taste of *saccharum saturni* any indication of a deadly poison? But the instances are numberless which may be adduced to prove the uncertainty of reasoning, otherwise than from observation, concerning the action of medicines, and the peculiar sensibility of different parts of our system to their impression. Following, therefore, experience as our guide, let us notice such facts as may elucidate the subject before us. It is well known that madder root carries its tinging quality to the bones, affecting neither the skin, the muscles, the ligaments, nor fat. Digestion consequently

consequently leaves this tinging quality unchanged ; or perhaps it is again recovered, when arrived at the bones, by some new arrangement of parts produced by the chemistry of nature. Extract of logwood, taken internally, sometimes gives a bloody hue to the urine ; but the astringency of it does not, according to my trials, accompany its colouring matter *. I recollect no instance wherein the milk either of a nurse, or of an animal, was tinged with madder or logwood. This affords some presumption that the pigment does not subsist, in its proper form, in the blood ; but that it is recovered by a subsequent change in the disposition of its constituent particles : and if one substance stain the

* It is said the fruit of the Nopal, or Indian fig, on which the cochineal is propagated, tinges the urine of those who eat it with a deep blood colour. The leaves of this shrub are of a permanent and lively green ; and it is remarkable that their juices are converted, by the concoctive organs of the insect which feeds on them, into a dye exactly similar to that produced by the powers of vegetation in the pulp of the fruit. Cartheuser obtained from the cochineal a moderately astringent spirituous extract, amounting, in weight, nearly to three fourths of the substance from which it was prepared. These facts exhibit a striking analogy between digestion and vegetation, as the products appear to be the same both in colour and quality.

bones,

bones, by being carried into contact with them, another may, in a way analogous, produce in them fragility or dissolution. In the disease termed, by the French, *ergot*, and which, with apparent reason, is ascribed to the use of a species of unsound corn, the bones lose the earthy matter that enters into their texture, and become soft and easy to be broken. This effect is gradual, and probably arises from some unknown quality of the corn, which is either not subdued by digestion, or resumed in the juices that circulate through the osseous vessels. A change in the process of vegetation may communicate a dissolvent power to an esculent feed. Mustard acquires it by its natural growth, and is capable of rendering even ivory itself soft and fragile. How far it would produce such an effect on the bones of a living body, if used as the chief article of diet, we have no experience on which to ground any satisfactory conclusion. The peasantry, in the mountainous part of this country, who live on oatmeal, are peculiarly liable to the itch, and to other cutaneous eruptions. These have sometimes been ascribed to obstructed perspiration; but such obstruction is itself only a concomitant effect of some quality in the oatmeal injurious to the skin.

Sulphur,

Sulphur, whether externally or internally used, produces a cure in the itch. In each way, therefore, we may presume its operation to be similar. But when taken into the stomach there can be no doubt that it undergoes a change in the modification of its parts, and that it does not circulate through the blood vessels either in the form, or with the properties of sulphur; yet when conveyed to the surface of the body it appears evidently to recover its original powers, communicating its peculiar odour to the perspiration, tinging silver, and curing cutaneous defœdations*. The same holds true of the vitriolic acid, when administered in large doses. It seems to acquire phlogiston in the animal body, and to pass off by the pores, as hepatic air, or as volatilised sulphur. Even when given to nurses, it proves an effectual remedy for the itch both in them and the children whom they suckle. Mercury, combined

* Bishop Watson, in his Chemical Essays, warns those who use cosmetic lotions, containing cerusse, to forbear from them at Harrowgate, Moffat, or other places where they drink sulphurated waters, "lest they should be in the state of
"the unlucky fair one, whose face, neck, and arms, were
"suddenly despoiled of all their beauties, and changed quite
"black." Vol. III. p. 365.

with

with sulphur into an æthiops, has been generally regarded as inert : but instances have occurred in which, under this form, though accurately prepared, it has produced salivation—an evident proof of a chemical change in the æthiops, by which the mercury was restored to its pristine powers. Indeed the same reasoning may be applied to the specific action of mercury on the salival glands, in whatever mode it be administered*. A ptyalism is sometimes produced by antimony. Dr. James assured my friend, Sir George Baker, that he knew six instances of it occasioned by his fever powder, although he had left mercury out of its composition long before they occurred ; but the patients thus affected had neither their teeth loosened nor their breath made offensive.

Most persons have experienced the effects of asparagus on the urine†. This takes place
very

* We have the concurrent testimony of many authors, that mercury has been found, restored to its original form, in the carious bones of their patients.—Vide Joan. Fernel. cap. 7 ; Gabriel. Fallop. cap. 78 ; Joan. Lang. lib. i. epist. 43 ; Alex. Petron. cap. 1. lib. vi. &c. &c.

† Cabbage, especially that of the winter's growth, impregnates water with a disagreeable smell, somewhat similar

very speedily, and strongly too, even though a small quantity only has been eaten. The smell is much more disagreeable than that of asparagus itself: and as the odorous particles conveyed to the kidneys must be greatly diluted in their passage, (even on the supposition of the retrograde motion of the lymphatics, which does not seem probable in a case so invariable and uniform) I should conceive that a new combination of particles takes place in the urinary organs, and that the odorous part of the secretion differs in its form and quality, both from what subsisted in the chyle and in the blood.

There are certain medicines which, when swallowed, quickly manifest themselves in the discharges with some of their original qualities. Soap lees, when taken in large quantities, render the urine alkaline and lithonthriptic; and the same excretion becomes impregnated with fixed air, if mephitic water be drank freely. A patient, whom I visit at this time, has six grains of the balsam of tolu administered to him thrice every day, and his urine is strongly

to that which is communicated by asparagus: yet, I believe, cabbage is never known to taint the urine; perhaps from its having no chemical affinity with it.

scented

scented even by this small quantity. Fuller asserts of the balsam of copaiba, *Urinam odore violaceo minime inficit; illam vero sapore amaro imbuat*. Garlick affects the breath, though applied only around the wrists. The milk of a nurse is likewise easily tainted with it. A purgative given to one who suckles will sometimes produce no operation on her bowels, if she be costive, but a powerful one on the child at her breast. But a still more convincing proof that there may be a renovation of the original qualities of a body, after it has undergone the process of digestion and other subsequent changes, is deducible from these facts — that butter is often impregnated with the taste and smell of certain vegetables on which the cows have pastured; that the milk of such cows discovers no disagreeable flavour; neither does the whey nor cheese prepared from it. Now butter is formed first by a spontaneous separation of cream; and secondly by a fermentation of it, that is, by a two-fold and successive new arrangement of its elementary parts. By these changes the original offensive materials in the food of the cow seem to reassume their proper form and nature.

After venæsection the serum of the blood has sometimes appeared as white as milk, whilst

the crassamentum retained its natural colour. This whiteness hath been shewn to arise from oleaginous particles (not unassimilated chyle) floating in the circulating fluids*; and may serve to explain a fact, recorded by a writer of good authority, on the natural history of Aleppo, that “in certain seasons, when oil is plentifully taken, the people become disposed to fevers and infarctions of the lungs; which symptoms wear off by retrenching this indulgence †.” Some years ago cod-liver oil was annually dispensed amongst the sick in our hospital, to the amount of fifty or sixty gallons. The taste and smell are extremely nauseous; and it leaves upon the palate a flavour like that of putrid fish. This remedy is most salutary when it operates by perspiration; and the sweat of those to whom it is administered always becomes strongly tainted with it. An oil of the same kind forms no inconsiderable part of the food of many northern nations; and it is said to penetrate and imbue the deepest recesses of the body ‡.

In

* See Hewson on the Blood, p. 146.

† See Ruffel's History of Aleppo. X

‡ Oil was formerly administered in pregnancy, by Sir Da-

vid

X. From the inserted commas used here, one would conclude this to be a literal transcript of the original passage; which, however, is considerably different, and is as follows—“The Christians from the great quantity of oil they use in their Lent, and that too mostly burnt, as frying is their favourite manner of dressing that kind of victuals, are at such seasons subject to a feverish disorder attended with a cough. The skin over the whole body feels hot, parched, & dry; but it is most violent in the palms of the hands and soles of the feet. They wheeze much in breathing, and labour by coughing to expectorate, but without effect. Bleeding, a gentle laxative, with the plentiful use of pectoral vapouraceous diluents, soon remove the complaint. *Hist. of Aleppo. p. 141. 1st ed.*”

In the Philosophical Transactions for 1750, (Vol. I. part ii. p. 295) Dr. Wright relates an experiment to prove that chalybeates do not enter the blood. He forced a dog, which had fasted thirty-six hours, to swallow a pound of bread and milk, with which an ounce and a half of green vitriol were mixed. An hour afterwards he opened the dog, and collected from the thoracic duct near half an ounce of chyle, which assumed no change of colour when the tincture of galls was dropped into it, though it acquired a deep purple from the same tincture when one fourth of a grain of sal martis had been dissolved in it. This experiment is usually deemed decisive in support of the theory, that chalybeates exert their operations solely on the stomach, and that the vigour they communicate to the system arises exclusively from their tonic powers on the alimentary canal, and on the sympathy of the stomach with various other parts of the body. I am not inclined to doubt either the tonic action or the sympathy supposed; but I see not that they preclude the im-

vid Hamilton, and other experienced physicians, to promote easy delivery: but modern theory has superseded their observation and experience.

mediate

mediate agency of steel on remote parts of the human frame; for this remedy, in other forms capable of being introduced into the circulation, may exert considerable energy, as deobstruent, stimulant, or astringent: and the experiment adduced only evinces that it did not subsist in the chyle as a vitriol qualified to strike a black colour with galls. Neither does the calx of iron nor the glass of iron possess this power; yet, though changed, they are both capable of being restored to it. Perhaps, with equal reason, it might be presumed, by one ignorant of chemistry, that sal martis contains no iron, because it is not acted upon by the loadstone.

With the foregoing observation of Dr. Wright I shall contrast those made by the celebrated Dr. Musgrave, which are also recorded in the annals of the Royal Society: — “ I injected,” says he, “ into the jejunum of a dog, that had, “ for a day before, but little meat, about “ twelve ounces of a solution of indigo in “ fountain water, and after three hours, opening the dog a second time, I observed several “ of the lacteals of a bluish colour, which, on “ stretching the mesentery, did several times “ disappear, but was most easily discerned when “ the mesentery lay loose — an argument that “ the

“ the bluish liquor was not properly of the
 “ vessels, but of the liquors contained in it.
 “ A few days after this, repeating the experi-
 “ ment in another company, with the solution
 “ of stone blue in fountain water, and on a
 “ dog that had been kept fasting thirty-six
 “ hours, I saw several of the lacteals become
 “ of a perfect blue colour within very few mi-
 “ nutes after the injection; for they appeared
 “ before I could sew up the gut.

“ About the beginning of March following,
 “ having kept a spaniel fasting thirty-six hours,
 “ and then syringing a pint of deep decoction
 “ of stone blue with common water into one of
 “ the small guts, and after three hours open-
 “ ing the dog again, I saw many of the lac-
 “ teals of a deep blue colour; several of them
 “ were cut, and afforded a blue liquor, some
 “ of the decoction running forth on the me-
 “ sentery. After this I examined the ductus
 “ thoracicus, (on which, together with other
 “ vessels near it, I had, on my return, made a
 “ ligature) and saw the receptaculum chyli and
 “ that ductus of a bluish colour; not so blue
 “ indeed as the lacteals, from the solution
 “ mixing, in or near the receptaculum, with
 “ lymphæ, but much bluer than the ductus
 “ used

“ used to be, or than the lymphatics under the
 “ liver, with which I compared it, were *.”

Stone blue is a preparation of cobalt, pot-ash, and white lead, which, being converted into glass, is ground into a fine powder; and if such a substance can pervade the lacteals, we may conclude that they are permeable to other bodies besides those designed for nutrition, and capable of assimilation with the blood. This argument, from analogy, receives great additional force from the known fact that mercury, and various other active remedies, may be conveyed into the body through the absorbents of the skin, a system of vessels similar to those above mentioned in their structure, uses, and termination. In a case of hydrocephalus internus, on which I have lately been consulted, a child under one year of age received, by successive frictions, four ounces, six drachms, and two scruples of the unguentum cœruleum fortius between the 8th of February and the 7th of April, 1786. One scruple was administered each time; the operation took up more than half an hour; and the part to which the oint-

* See Philosophical Transactions abridged by Motte, chap. iv. part ii. p. 76.

ment was applied was always previously bathed with warm water—precautions which seemed to secure the full absorption of the mercury*. I should not omit to mention that the child recovered without any symptoms of salivation, and continues perfectly well. Indeed I have repeatedly observed that very large quantities of the unguentum cœruleum may be used in infancy and childhood without affecting the gums, notwithstanding the predisposition to a flux of saliva at a period of life incident to dentition. The practicability of curing the hydrocephalus internus is a late and happy discovery; and perhaps the peculiar efficacy of quicksilver in this alarming disease may reflect some light on the general rationale of its action. The structure of the brain is yet very imperfectly known; but anatomists have sufficiently ascertained that it is most copiously sup-

* Thirty-seven grains of calomel were given internally during this space of time, at proper intervals, and in sixteen doses. The case referred to occurred in London, and was under the immediate direction of several physicians of eminence. The use of mercury was adopted by my advice; and the estimate of the quantity consumed, as made by the apothecary, has been transmitted to me by G. H. Esq. the father of the child.

plied with vessels of every order, so that about one tenth of the whole mass of blood circulates within it, although the weight of the encephalon does not exceed one fortieth part of the whole body *. On this large system of vessels mercury may be presumed to act with a force proportionate to its magnitude and extent; and, in the instances when no salivation takes place, it is not unusual for profuse sweatings to occur about the head. An acceleration of growth also, to an extraordinary degree, is frequently observed after the disease has been thus subdued. In one case, which fell under my direction in 1784, a young lady, nine or ten years of age, of a noble family in this county, increased in stature two inches within the space of four months succeeding her recovery.

Whence is it that a medicine, so irritating as mercury, can be conveyed into the course of circulation, when even milk, or the mildest liquors, if transfused into the blood vessels, have been found to produce convulsions and death? Is it that what passes by the lymphatics or lacteals is carried into the thoracic duct, and there

* See *Monro on the Structure of the nervous System*, p. 3; folio.

mixed with a large portion of the chyle and lymph, by which its acrimony is sheathed and diluted, or its chemical properties changed, before it enters the mass of blood? For the absorbents of the skin, and of the intestines, should seem to require a capacity to bear the stimulus of those extraneous bodies to which, in both situations, they are exposed.

III. Medicines introduced into the course of circulation may affect the general constitution of the fluids, produce changes in their particular qualities, superadd new ones, or counteract the morbid matter with which they may be occasionally charged. By observations on the hæmorrhages, which have been sustained without destruction to life; from experiments made on animals, by drawing forth all their blood, and by a computation of the bulk of the arteries and veins*; the mass of circulating fluids has been estimated at fifty pounds in a middle-sized man, of which twenty-eight pounds are supposed to be red blood. Fluids, bearing so large a proportion to the weight of the whole body, have assuredly very important offices in the animal œconomy. Endued with the com-

* Vide Halleri Prim. Lin. sect. cxlix.

mon properties of other fluids, they are subject to mechanical laws; being variously compounded, they are incident to chemical changes; and as they are contained in a living vascular system, their motions become subject to the influence of nervous energy.

But the prosecution of this subject will exceed the bounds of the present evening's discussion: and I shall reserve what I have farther to advance upon it to some future meeting of the Society.

CATALOGUE OF BOOKS.

1. **A** Dissertation on the Influence of the Passions upon the Disorders of the Body. By *William Falconer*, M. D. F. R. S. 8vo. Dilly, London, 1788.

2. Journal of a Voyage to New South Wales; with sixty-five Plates of non-descript Animals, Birds, Lizards, Serpents, curious Cones of Trees, and other natural Productions*.

By

* In this work we find an account of two new species of gum, which are said to possess valuable medicinal properties.

One