AN INQUIRY INTO THE *MODUS OPERANDI* OF THERAPEUTIC AGENTS UPON THE HUMAN FRAME.

By R. HUTCHINSON POWELL, M.D.Lond., etc.

(Concluded from p. 549 of June number.)

REMEDIAL agents influencing the *excretions* hold, perhaps, the most important place in the entire field of therapeutics, as morbid action, especially slight functional derangement, mostly arises from the retention of some effete matter, or from the presence of some extraneous toxic agent in the circulation. During the incomplete combustion effected in the system, water, carbonic acid, and urea, are not directly formed; but the morbid elements enter into intermediate combinations more or less nearly approaching them in degree of oxidation, according to the comparative perfection or integrity of the functional power of the organism; more or less disorder occurring from imperfect elimination. The presence or absence of these agents in the urine would seem to depend upon the degree of solubility of the compounds formed in their transit through the system. Salts of silver, and others, are excreted by the skin; those of less solubility, or those forming insoluble compounds with the albuminous constituents, are probably ejected with the bile in the *fæces*.

Saline diuretics seems to act in two ways; first, by causing *increased* repletion and tension of the capillaries, generally and locally, coupled with *diminished* retentive power in their walls for the displacing saline fluid; and, secondly, by a solvent effect upon effete tissues.

In the action of those of the first class, or *purely physical diuretics*, the constriction ensuing, together with the lessened absorbing function, effects the diuretic operation. Amongst the latter, or *chemical diuretics*, nitrate of potass deserves special notice. It would seem to exert a solvent effect on tissues of low vitality, though in a less degree than alkaline carbonates; the textures more rapidly being metamorphosed, and thus rendered soluble in the blood, and removeable by the glandular apparatus. The principal action, however, of nitre seems to be exerted locally on the kidneys. This salt, in common with other neutral salts, exercises a liquifying power upon the blood, preventive of the coagulation of its fibrin, which is probably held dissolved, in part, through the agency of the saline constituents. We have thus a clue to the *modus operandi* of nitre in rheumatism and other phlegmasiæ. The sulphate of bebeerine, according to Dr. Golding Bird's researches, (who has very ably worked out this department of science,) powerfully influences the excretion of effete or superfluous matters from the circulation; the extractive matters in the urine being considerably increased under its use. Salts of mineral acids, in small doses, appear to exert a preservative power over the blood-corpuscles; salts of soda being more effective than potass salts. Schmidt, however, found that in the fluid of the corpuscles of the blood, salts of potass predominated; while, in the plasma, salts of soda existed in greater relative amount. Mineral acids seldom or never enter the circulation, as such, but, after exciting a local action more or less astringent, are converted into salts, and present new pro-

perties. The wasting influence observed to follow their protracted use,—under which head *refrigerants* may be comprised,—appears to depend upon the indirect effect exerted over primary assimilation by their neutralising the alkaline agents contained in the digestive tube, and thus interfering with the elementary process of nutrition. The tartrate of potass and soda, and other vegetable acid salts, when given in small doses, render the urine alkaline in about seven cases out of ten; in the remaining instances, the urine is either acid or neutral; and these results are independent of the normal reaction in the daily amount of urine secreted. Alkaline tartrates, citrates, and acetates, suffer decomposition during their transit through the organism, carrying away in their excretion, as carbonates or oxalates, those effete matters normally eliminated through chemical agency, which is thus assisted by their presence. In connexion with this effect, it may be stated, that citrate of potass was found, by analyses of the blood of subjects while under its use, not to alter its fibrine or buffy coat; the inflammatory state progressing in the face of the alkaline carbonates resulting, and capable of being detected in the urine. Alkalies, however, when given in large doses, being converted into carbonates and albuminates, for the most part, powerfully modify the blood and other fluids, in most abnormal conditions of the body, diminishing the blood-corpuscles, and exerting a refrigerant or sedative action on the system. The urine is rendered either alkaline or neutral under their use, for the most part depending upon the quantity taken, and the time of exhibition in relation with the digestive process. Magnesia and lime act similarly, but with lessened energy, probably in consequence of their slower solubility. The mode in which the soluble forms of magnesia operate in arthritic affections, may depend upon the liberation of the alkaline earth from the blood. Citric acid, and others taken from the organic kingdom, would appear, according to Dr. Rees's researches, to promote oxidation of the tissues; a conclusion which is rendered highly probable by the increased excretion of urea following their exhibition. More stable acids probably act indirectly in checking the excretion of alkaline urine, by preventing the decomposition of urea into an ammoniacal carbonate, as suggested by Dr. Hassall.

The *simple diuretic drugs of vegetable extraction*, (comprising squill, copaiba, broom, juniper, guiacum, digitalis, turpentine, etc.), remove little more than the aqueous contents of the organism through the kidneys; their excessive use being followed by arrest of secretion, from the capillary congestion ensuing. The blood is rendered of higher specific gravity from the subtraction of its watery constituent, and the solids become relatively greater in amount. Hence their office would seem to be that of a merely mechanical or indirectly chemical agency, analogous to that of diaphoretics.

The therapeutic class of remedies termed *alteratives* have a close affinity with the preceding medicaments, which, indeed, insensibly merge and are resolvable into agents, exerting a slow but constant effect upon the economy. The preparations of mercury and iodine take a prominent position under this head. M. Mialhe has instituted numerous experiments upon the former, and other metallic salts, from which he concludes that they owe their efficacy to their conversion into bichlorides in the intestinal canal, and to their forming soluble compounds with albumen and alkaline chlorides; the plasticity of the

blood being diminished on their gaining access to the circulation. From an analysis of the blood of a patient suffering from ophthalmia, made by Dr. Ayres, *before* and *after* salivation, it would appear that the fibrin is diminished, the albumen but slightly affected, the solid constituents generally being increased, especially the red blood-discs. Mercury exerts a manifest influence upon morbid nutrition, stimulating that function to increased activity, and further aiding in the restoration of the normal action, probably by some species of catalytic operation, with the intimate nature of which we are but little acquainted.

Mr. Simon ingeniously suggests, that mercury, and other metallic salts, act by moderating and regulating a previously masked but impending explosion in cacoemic disorders; and thus hastening the expulsion of the products of retrogressive metamorphoses in the organism. Mercury has been detected in the saliva by Lehmann; it has also been found in other secretions, as well as in the solids. Mercury must be presented either in minute division, or in a soluble form, prior to its admission into the circulation, into which a large quantity cannot penetrate at one time.

The tartrate of antimony, the most potent salt of this metal, has experimentally been found by Boecker to increase the urea and combustible salts in the urine; promoting the waste of the blood-globules in an especial manner, and diminishing the "melanotic globules". Introduced into the stomach of animals (in four-grain doses), it was found, by MM. Duméril, Demarquay, and Lecoq, to produce very slight elevation of the thermometer; and an increase of the dose (to seven grains) rapidly lowered the animal heat. The oxy-sulphuret (in doses of one scruple daily) was found by Boecker to increase the consumption of fibrin, albumen, and red globules of the blood. The *modus operandi* of salts of antimony (more especially of the emetic preparations) has evidently a close relation with the function presiding over the animal heat of the body, whether this be effected through chemical reactions, under the control of nervous influence, or otherwise. According to Mialhe, all antimonial preparations are converted into an antimonial chloride; their degree of activity being in proportion to their solubility in the alimentary fluids. Their primary effects are dependent upon their local action, the systemic or general operation occurring subsequently to their reception into the blood, where they are decomposed into an oxide, which, according to Mialhe, mechanically obstructs the smaller capillaries. These views, though perhaps partially correct, are, however, too purely physical, and do not comport with the whole train of effects proper to these potent agents.

Numerous experiments have been undertaken, to determine the properties and probable mode of action of iodine. This metalloid and its analogues would seem to owe their peculiar effects to a liquefying power exerted over the blood, resembling that of the nitrate of potass. The organs through which they are excreted are stimulated to increased activity, probably in consequence of a conservative function, set up for the removal of agents foreign to the economy. That certain drugs select special organs for their exit, seems to be an ultimate fact, mostly incapable of explanation. These metalloid bodies, before gaining admission into the circulation, must be rendered soluble by their combining with alkalies, as haloid, or oxy-salts. Sulphur, given

internally, was found by Boecker to increase the proportion of urea and uric acid in the urine; the other constituents being either augmented or diminished. The exhalation of carbonic acid from the lungs becomes remarkably increased from small doses of sulphur. In large doses, it is diminished simultaneously with increased action from the liver; the dark (melanotic) globules diminished in (inverse) ratio to the increased pulmonary exhalation of carbonic acid gas; a proportionate decrease in the other blood-constituents likewise resulting. From MM. Millon and Laveran's researches, upon the effect of the administration of several saline bodies on the urine, it would appear that sulphur is never detected therein; being either ejected from the body in union with some organic constituent, as with tauro-cholic acid in bile, or else becoming oxidised in its transit through the system. We have here some elucidation of the effects of sulphurous mineral springs. Salts of ammonia, in like manner, exercise a well-marked modifying power over the digestive organs, and over the crasis of the blood. The muriate, administered internally, has been found by Boecker to diminish the blood-plasma and red corpuscles, though it subsequently increases the latter; promoting secretion from the mucous membranes generally. The acetate of ammonia appears to divide its acid and base between the skin and kidneys respectively. It has been conclusively shown by Dr. Bence Jones, that when the former salt is exhibited, nitrous acid is found in the urine, resulting from oxidation of its nitrogenous element. This salt is well known to possess cholagogue properties, and probably acts in virtue of this evolution of nitrous acid in the circulation; removeable compounds resulting by its facilitating the destruction of combustible matter, to the manifest relief of the system. The other salts of ammonia are less efficacious, not being sufficiently stable to gain access to the blood before entering into new combinations; to these, however, some of its properties are due. Its nitrogenous element brings ammonia into relation with neurotic agents. All its salts, according to Dr. Delieux, appear to act more or less as alteratives and antizymotics, by their neutralising powers in toxæmic states of the blood, and as sedatives in chest affections; thus connecting ammoniacal agents with those specially affecting the nervous system. Dr. Teissier, of the Hôtel Dieu of Lyons, arrives at the following conclusions, which are here quoted as being both recent, and confirmatory of the foregoing statements. "Solution of ammonia may be usefully given in disorders connected with smoking tobacco. It is equally useful in the injurious effects attending the abuse of alcoholic potations, especially nervous derangements. It is incorrect to consider ammonia as efficacious only in slighter cases of inebriation, as it is capable of rendering signal services in permanent lesions. Ammonia has not stimulating and sudorific properties alone; if thus restricted in its circle of operation, it would be impossible to furnish an explanation of its happy effects in a crowd of maladies,—in certain nervous disorders, in venomous wounds, in cases of internal poisoning. It possesses anti-poisonous properties more than is generally supposed; being justly regarded as a potent alexipharmic. The doses usually prescribed are too strong, from ten to fifteen drops daily being sufficient, if we do not wish to induce hæmorrhage or a cachectic state."

All the medicinal *agents promotive of free alvine evacuations* have the effect in common of removing out of the system effete or toxic matters, whose presence would impede or depress the organic functions. This indication forms the basis of our treatment of most diseases in the first instance, just as a similar depurative process is beneficially applied, by means of other agents, through the various secreting and excreting organs. Their action severally is either stimulant or depressant; the preponderance of either effect marking the character of the individual purgative. Local hyperæmia, quickly followed by secretion, constitute their normal action. There exists a marked sympathy between all parts of the intestinal canal, acting from above downwards; its extremities being the most sensitive. Certain drugs have special affinities for the several anatomical divisions of the digestive tube, for which it would be difficult to assign a satisfactory explanation; as it would also be for their quicker or slower operation. All these agents have a derivative effect upon the circulation, which materially contributes to their remedial powers. Most cathartics exert a stimulant effect upon the muscular coat of the intestines; thus it happens that some drugs not directly cathartic, as *nux vomica*, produce this effect by their restoring the motive ganglionic function. Purgatives which are insoluble in the intestinal fluids, act as such by the mechanical irritation set up. The *modus operandi* of these severally is suggested by their peculiar effects on the organism. Oleaginous purgatives act chiefly by endosmosis, inducing an increased flow of serous fluid from the intestinal capillaries, and consequently augmented fæcal excretion. Strong saline solutions exert a similar effect, and in a like mode; sulphate of soda was found to act much as the double tartrate of potass and soda. Mercurial preparations, taraxacum, and other evacuants, for the most part act by inducing an increased discharge of bile; but the stimulant or irritant operation of the former agents is imparted to the intestinal excrements, in common with the secretions of the system generally, whereby exaltation of function ensues. Purgatives of the hydragogue subdivision, as elaterium, gamboge, croton oil, etc., operate in removing abnormal serous accumulations, through some special agency, which, for want of a more explicit term, is called *vital*; the animal heat being at first depressed, but subsequently raised, under their use. Resinous drugs, as colocynth, aloes, etc., having purgative properties, are dissolved by the intestinal alkaline fluids, and then are absorbed; the lower portion of the intestinal canal coming more particularly under their operation, and the evacuant action arising from their acrid or irritant qualities. Rhubarb acts as a purgative and diuretic; its resinous constituent being determined to the bowels, and its saline matter to the kidneys.

All *astringents*, acting chemically, appear to impart their property to the blood through which the capillaries become acted upon; the effect being probably dependent on their combination with the more fluid portions of the blood, exudation being thus checked.

Under this head are comprised gallic and tannic acids, salts of alumina, lead, and iron. The two former astringents may be considered identical in their action as in their composition; tannic acid being made up of the elements of gallic acid, *plus* sugar and water, and, moreover, as tannic acid has been shown by Frerichs to be converted into gallic acid in the circulation. Tannic acid acts more

as a local astringent, thus contrasting with gallic acid, the effects of which are more apparent upon the system at large. Salts of alumina and lime seem to constringe by being deposited as insoluble compounds, either in the capillaries or tissues, or on the mucous surfaces. This absorbent property is especially marked in the phosphate of lime, which, at first rendered soluble by the gastric acids, is immediately precipitated on being absorbed, and thus sheaths the organic pores by the insoluble gelatinous salt resulting. A greater degree of astringency, or a styptic action, results from a chemical union with the more solid portions of the blood or tissues, an insoluble or soluble compound being formed; the vitality of the tissues being, however, preserved. Creasote has the former effect; and its antiseptic properties are probably due, in common with other remedies of this denomination, to its counteracting the tendency to decay (*eremacausis*) in the solids and fluids. Salts of lead, bismuth, and zinc, act as astringents, according to Mialhe, by being first absorbed as chlorides in union with chloride of sodium, forming double salts, which are decomposed by the contents of the intestinal capillaries into insoluble metallic salts; this deposition obstructing their circulation, and checking secretion. Salts of copper, acting as astringents, are, according to the above authority, divisible into a soluble and an insoluble group; the former, united with an organic acid, are directly absorbed, the albuminous salt first formed being re-dissolved in an excess of the salt of copper; salts of the mineral acid group forming albuminous salts of difficult solution.

The *emetic* effect of the tartrate of antimony, as of ipecacuan, in inducing vomiting, is exerted when introduced either into the stomach or veins; with its nature or mode of production we are imperfectly acquainted. Ipecacuan, topically applied, has an irritant operation, but modified according to the tissues with which it is brought in relation; the dynamic (proper) effect being exerted independently of the local, which is, moreover, counteractive of the former, and must be avoided in its exhibition; the therapeutic action being essentially sedative and alterative. The temperature of the body is less affected (lowered) than by emetic tartar (in $3\frac{1}{2}$ gr. doses); large doses even raising the animal heat, thus contrasting with the latter drug. Sulphates of zinc and copper rapidly induce vomiting; the latter being found, by M. Dumeril and colleagues, to produce a marked and lasting depression of temperature, when injected into the stomach (in $3\frac{1}{2}$ gr. doses), and the œsophagus being tied. The action of *expectorants* is partly dependent upon their control over disease manifested locally; nauseating remedies relaxing the pulmonary exhalants, stimulating drugs increasing and modifying pulmonary secretion. Senega, *ex. gr.* was found by Boecker to increase the several constituents of the urine, as well as carbonic acid from the lungs and kidneys respectively.

The *modus operandi* of expectorants inductive of vomiting, is manifestly that of mechanically dislodging abnormal accumulation.

Numerous remedies act in virtue of sympathies existing with neighbouring or remote organs; such as some of those comprised in the *emmenagogue* class,—*ex. gr.* aloes, oil of turpentine, etc.; the former influencing the uterine system through the bowels, the latter through the urinary organs. The kind of influence thus brought into operation, compels us to view the human organism as something over and

above a reducing or transforming apparatus; its numerous vital affinities being modified or controlled by agents whose mode of action is indirect, and in their turn dependent upon the connexion subsisting between, and the reactions of, the several components of the body.

Having rapidly passed in review those medicaments whose mode of action has a close connexion with *mechanical* or *chemical* changes thereby affected, other agents, more or less referred to under previous heads, may be here noticed; as, although not divested of their physical affinities (as we shall find), they evince peculiar *dynamical* properties, for which we are for the most part unable to assign a satisfactory explanation. These are, stimulants, tonics, narcotics, and sedatives, whose action, though evinced elsewhere, is principally through and upon the nervous system. They have all a close relation in common with the nervous tissue and its functions; some of them acting upon special divisions of this system. Most of them contain nitrogen; viz. hydrocyanic acid, morphia, and codeia, acting on the cerebral and ganglionic centres; strychnia, brucia, and conia, acting on or paralyzing the spinal cord; veratria and colchica, nicotina and digitaline, specially affecting the ganglionic system; cinchonia and quinia, acting on the nervous system generally. Hydrocyanic acid furnishes one of the most potent toxic agents in relation with the vital functions, quickly arresting or annihilating them; probably by a catalytic action, of a kind which interferes with the process of hæmotosis. Alcoholic and etherial bodies come under this head, impeding as they do more or less the respiratory function, by the ensuing increase of extractive matter, which appropriates the oxygen introduced for the purposes of the economy. Chloroform, when inhaled, was found by Grouby to increase the bright colour of arterial blood, and to impart the same to venous blood. A different result, however, has been arrived at by other experimentalists, who found venosity of the blood to be induced and increased under its use. When injected into the veins by M. Flourens, it immediately induced paralysis of the muscles, with tetanic rigidity, as did volatile oils of turpentine, mint, rosemary, and fennel. Sulphuric ether, and other ordinary ethers, (also fixed oils, oil of naphtha, sulphuric acid, ammonia, and camphor), were found to produce muscular paralysis, with *relaxation of fibre*. Thus the former agent seems to *partially suspend*, while the latter *entirely exhaust* the motive nervous influence, manifested respectively through the ganglionic and spinal systems. Chloroform, and related agents, inhaled, induce, as is now well known, general anæsthesia; the sciatic nerve being found to retain its motive power, although insensible. They induce a state of the spinal cord, which renders it insusceptible of the transmission of impressions. Dr. Abeille, of Corsica, has recently used electrical currents, passed through needles introduced into the cervical, spinal, and other muscles, with success, in removing the insensibility consequent upon the inhalation of chloroform, which state he believes to depend upon a short and temporary disturbance of the cerebro-spinal nervous system, removeable in this way, even after asphyxia has set in. We here may remark that merging of properties of neurotic agents severally, which will be shortly referred to.

Phosphorus, in an unoxidised state, forms an essential constituent

of the nervous tissue, and especially affects the nervous system, being analogous to iron in its relation with hæmatosine. Nearly similar effects ensue from arsenical, antimonial, and ammoniacal preparations; these bodies respectively seeming capable of replacing each other (isomorphically) in the combinations making up the nervous structure. The former agents, of exclusively vegetable extraction, approach nearer to the composition of nervous matter than any other class of remedies, and probably exert a direct influence over its production, any excess being discharged through the urine, unchanged in composition. Of the latter bodies, arsenic and antimony act in any state of combination, when gaining access to the blood; phosphorus and ammonia require to be presented in special forms, as being normal constituents of the organism; and azotised bodies evince different effects, varying with the amount and state of combination of the nitrogenous element. Here we have an illustration of the analogous action of quina and arsenic. The well-known effects of tea and coffee upon the nervous system, both moreover retarding the oxidation of tissue, come under this head, as do antimonials and digitalis, in respectively subduing vascular excitement. The special affinity of these agents severally, for particular divisions of the nervous system, appears to be at present quite incapable of any satisfactory explanation. This election, no doubt, has a close dependence upon the proximate changes and operations going on in the blood and tissues, as well as on minute peculiarities of structure in the parts most concerned, as before referred to.

Phosphorus exhibited internally, in combination with vegetable oils, in cases of phthisis, was found by Dr. Theophilus Thompson, productive of benefit. This ingenious and philosophical observer suggests that it probably acts by facilitating the evolution of the phosphoric salts from the blood necessary to its healthy constitution; and, further, by appropriating superfluous oxygen, tending to prevent destructive suppuration taking place in the pulmonary tissue.

Strychnia, and other remedial agents specially exciting the spinal nervous system, were found by Boecker—to whom we are indebted for many exact experiments on this subject—constantly to induce a liquefied condition of the fibrine of the blood, which is usually found fluid after death from poisonous doses, just as from the effects of lightning. The suspension and loss of nervous influence may possibly induce this state of the blood in an indirect manner, viz., in consequence of the motor lesion of the respiratory and circulatory systems. Recent experiments by Lepelletier upon brucine, throw some light upon its mode of action, as well as upon all remedial agents, ranked under the head of *dynamical* agents. He found its physiological operation especially evinced upon the nervous system, its action being momentary or permanent. In the former case, it acts at separate intervals, and upon isolated portions of the economy, the action being partial and passing away. In the latter instance, its effects are manifested at a given moment, becoming universal, and constituting general attacks. The evanescent effects are a pricking sensation in the extremities, and in the head. In doses beyond $1\frac{1}{2}$ gr., shocks resembling electrical succussions ensue, becoming greater in proportion to the increase of dose, and being exerted chiefly upon paralysed limbs; the muscles engaged in the process of mastication and deglutition being but little affected, contrasting with the

effects of strychnia in this respect. Loss of sleep subsequently ensues, also headache, and impaired vision. The more permanent or veritable effects are, first, yawning, stretching; subsequently, convulsive movements of the extremities, desire to vomit, and bitter taste in the fauces, shivering, followed by general feebleness, preceding the subsidence of the attack. Secondly, spasmodic movements of the extremities, lasting from five to ten minutes. Thirdly, feebleness and oppression, some pain in the limbs, which become feeble and much relaxed, headache, disturbed sight and hearing, with thirst, restlessness, heat, and subsequent sweating of skin ensue. The therapeutic effects of brucine were favourable in cases *not dependent* upon inflammation of the lining membrane of the spinal cord.

Premising these remarks as to the general relationship of remedies peculiarly affecting the nervous system, we may glance at the distinctive phenomena evinced by each subdivision. *Stimulants* produce an excitement of a transient character, dependent upon their power of arousing the nervous energy and play of the vascular system. The ensuing depression is a *secondary* consequence of the previous excitation, and not a *direct* result, as from sedatives.

Tonics exert a more moderate effect of a like kind, directly regenerating nervous power, whether administered in health or disease. Many remedies, previously referred to, may be arranged under this head, their roborant effects being due to very different sources and modes of action; thus, an astringent acts as a tonic, by arresting wasting discharges. Roborant agents have, indeed, a close relation with astringents, with which the former are often met in natural combination. However, it is apparent that roborant and constringent properties differ in kind, from the fact of their properties being respectively more marked in remedies possessing one quality nearly to the exclusion of the other—quina being a pure tonic, catechu an astringent, Peruvian bark a compound of remedies uniting the effects of both. Again, an alterative medicine may, by removing some noxious matters from the blood, exert a roborant effect; as may a plastic agent, nitrate of silver, *ex. gr.*, by combining with albumen, and thus modifying nutrition. Iron pre-eminently typifies the tonic property of drugs. Some recent experiments of Mialhe would appear to show the pertartrate to be the most active preparation of iron. The red globules of the blood are greatly increased under its use, the fibrin being little affected, and the albumen slightly increased. According to the above authority, iron is received into the circulation in every instance, as a per-salt united with an organic acid; an interchange then ensuing with the albuminate of soda contained in the blood, an albuminate of iron resulting.¹

Narcotics, like stimulants, produce, primarily, excitement, followed by repression of nervous and vascular energy, according to the dose. Opium, being a composite drug, possesses a mixed operation: narcotine being its stimulant portion, morphia its true narcotic principle; sleep directly following its ingestion without previous excitement, un-

¹ This conclusion, it may here be remarked, is not in accordance with the observations of others, as may be seen by reference to a paper by the writer of this article, published in the *Lancet*, (August 1844), "On the Comparative Medicinal Effects of the Salts of Iron"; also in a thesis presented to the University of London, when graduating.

less the brain be considerably disturbed. Opium produces a sedative effect in small doses, a stimulant effect in medium doses, and a powerfully sedative action, again, in very large doses; the system, though feeling the shock, being unable to react upon it. Codeia, another constituent of opium, appears to act as a stimulant upon the cerebro-spinal nervous system—sleep never following its exhibition—and as a sedative on the ganglionic system.

Indian hemp is a very powerful narcotic, being at first stimulating in its effects, and thus presenting a close resemblance to opium.

Henbane is also a compound remedy, containing sedative with narcotic properties. Belladonna was found by Boecker to increase all the urinary constituents, except the uric acid and non-combustible salts, which were diminished. It also promoted biliary and alvine excretion; the blood-globules and, subsequently, the plasma, were used up. Belladonna is a local stimulant to the mucous membrane, a narcotic and sedative effect subsequently ensuing. It would appear to exert its influence by deadening spinal reactivity, a contrary or exciting effect taking place in the cerebral centres; thus evincing the antagonism of these centres of nervous action respectively. Its preventive property in scarlatinal epidemics may probably arise from its obtunding the organic nervous system. Aconitine is another drug exerting an acro-narcotic and a sedative effect, the latter especially predominating. Its peculiar effect in producing a numb constrictive sensation, the development of which is necessary to its operation, is very significant of its *modus operandi*. It appears to exert its influence chiefly upon the cutaneous surface, relieving pain, and promoting exhalation charged with morbid principles. (*Teissier*.)

Conicine, or conia, has been found to resemble nicotine by M. Orfila, in its potent effects upon the system, both being absorbed, and detectable in the principal organs of the body. The poisonous symptoms produced by either are much alike, being distinguishable into three periods: respectively characterised by vertigo, convulsions, and sinking.

Nicotine exerts an irritant effect when locally applied, but its general operation is essentially that of a sedative.

All true narcotics appear to accomplish their effects by slackening the nervous currents throughout the body, by their interference with the conducting power of the nerves, probably as a result of their forming a new chemical compound, of more or less persistence, with the nerve-matter.

Sedatives directly and positively lower nervous energy,—not, like stimulants, from exhaustion consequent upon previous excitement.

Digitaline, the active principle of foxglove, typifies this order (sub-division) of neurotic agents. It acts as a direct sedative on the ganglionic system; but, like some other neurotic agents, exerts an irritant effect when locally applied. Its general action is affected by the state of the stomach, if unhealthy; the sedative operation being interfered with. Its effects are partly referrible to its controlling the circulation, and thereby diminishing the amount of blood in the lungs. In large doses, digitaline induces emeto-catharsis, more or less sudden. In still greater amount, its poisonous effects are manifested; more generally when injected into the veins, than when taken into the stomach. It occasionally acts upon the nervous centres as an excitant, according to Homolle

and Quevenne's experimental researches; and Delafond found it to raise the pulse in the phlegmasiæ. Green tea was found by the writer to exert a compound influence, acting as an irritant and sedative in severe sea-sickness; very great depression, with rapidity and irregularity of pulse, attended with præcordial anxiety, following its use, in the form of a strong infusion; symptoms which, *ceteris paribus*, were not previously experienced on like occasions. Colchicum was found by Boëcker to diminish the urinary constituents; the skin, lungs, and liver evincing increased activity at first, but the latter organ only at a later period. This agent was found to destroy the melanotic globules in the liver; the pulmonary and cutaneous secretions being subsequently diminished. So much for experiment. Its action is essentially sedative, however, and not that of an evacuant exclusively.

A significant resemblance may be traced in the effects of these several subdivisions of neurotic agents, so much so, as to suggest almost identical properties and modes of action, differing, however, in the special part of the nervous system engaged, and in their degree of influence thereupon. Their relative order, as to these effects, might stand thus: tonics mark the ascent, stimulants the culminating point, narcotics the descent, and sedatives the complete repression of nervous force. Their sphere of operation differs in some cases, but it is the same nervous element, existing as a complex apparatus, that is concerned in all, the effects of course varying with the functions of each subdivision of the nervous system.

As bearing upon this merging of properties, it may be called to mind, in relation with the nervous apparatus, that convulsions, numbness, and paralysis, would appear to be related phenomena, connected with, though more or less remote from, that equipoised condition of the nervous tissue, which ordinarily maintains its (galvanoid) action in a steady and unremitting operation. Impairment in the degree of this normal condition induces disturbance, in the form of tingling, numbing, etc., or even causes complete loss of nervous force, (paralysis), and its concomitant mental manifestations.

The *primary* effect marks the special relation of each neurotic agent to particular nerve-centres, the entire nervous system and organism being ultimately implicated. Brucine and digitaline may be respectively supposed to represent the extreme circuit (or opposite poles) of effects consequent upon the administration of neurotic remedies; each converging, as it were, from a reverse direction, to evince tonic effects in the former agent, and excitant in the latter; and thus completing the circuit of action here drawn from the analogous operation existing between those therapeutic agents. Beyond this general parallel, one cannot venture to suggest or point out any closer relationship; imperfectly acquainted as we are with the intrinsic action of the nervous system, and not even agreeing upon the fundamental operations of its special subdivisions. It is impossible, in the present state of our knowledge, to refer most of these neurotic agents to any mode of action other than that of dynamical bodies, calling into play or repressing nervous force diffused throughout the organism. This they probably effect in virtue of their purely physical qualities, or chemical properties, having relation with the structure and functions of the animal economy. Thus opium, *ex. gr.*, and other agents powerfully affecting the

nervous system, injuriously influence plants as well as animals, showing some effect in common upon organic life, whether manifested in the animal or vegetable kingdom of nature.

In concluding this compressed *résumé* of his subject, the writer would just remark, that the instances cited in illustration of the physiological and therapeutic effects of remedial agents, may not be deemed apt or to the point, and the explanation, (in most cases very imperfectly), attempted to be given, may be termed a *petitio principii*. But the truth is, that we are not able to dip further into the arcana of natural operations, than to express, in very general terms, the method by which changes are brought about in the system under these operations; a statement but little removed from the mere assertion of the phenomena ensuing upon their exhibition. If we may ever hope to deduce general conclusions of a more comprehensive and intelligible character, it must be by very gradual steps supported by trustworthy data, and in accordance with improvements and discoveries in other related departments of science.

21, Edward Street, Portman Square, June 1852.

ON NEAT'S-FOOT OIL, AS AN OCCASIONAL SUBSTITUTE FOR COD-LIVER OIL.

By C. RADCLYFFE HALL, M.D., L.R.C.P.L., Fellow of the Royal College of Physicians, Edinburgh; one of the Physicians to the Western Hospital for Consumption, Torquay.

Our best acknowledgments are due to Professor Hughes Bennett for bringing into general use a remedy so important as the cod-liver oil. To its efficacy, the experience of the entire profession bears testimony. No other remedy of recent introduction has so completely supported the pretensions made in its behalf, or so generally fulfilled all reasonable expectations from its administration. In every case of chronic innutrition, whether from scrofula, tubercle, rheumatism, cancer, syphilis, morbus Brightii, or other visceral disease, with the single exception, perhaps, of disease of the liver, the cod-liver oil is useful, *provided* it can be readily digested. It is not therefore with any intention of recommending a substitute for the cod-liver oil, where that can be taken with comfort, that I direct attention to the internal use of another animal oil; but with the object of showing that we are not without an allied remedy in reserve in certain cases in which the cod-liver oil cannot be made to agree.

More or less, it is usual for the cod-liver oil to disagree at first with the majority of patients, and there are few who do not find it desirable occasionally to intermit its use. But this ordinary amount of disagreement may generally be overcome by perseverance, and by attending to a few little points in the administration of the oil. These little points are,—to commence with very small quantities; to avoid the presence of much fluid in the stomach; to avoid an empty state of the stomach; to take the dose an hour, or less, after a solid meal, when the food is somewhat chymified; to try the different kinds of oil, if