

declines; but this certainly does not generally hold good with respect to emetic tartar, as will be mentioned hereafter. Dr. Marshall Hall (*Researches relative to the Morbid and Curative Effects of Loss of Blood*, 1830, also, *Introductory Lecture*, 1834,) maintains, that while a man in health can lose a given quantity of blood (say $\bar{x}xv.$) without fainting, the same individual, affected with congestion of the brain or inflammation, can bear a much larger quantity (as from $\bar{x}xxx.$ to $\bar{x}l.$) before incipient syncope,—while in fever, intestinal irritation, dyspepsia, or cholera, a smaller quantity (as from $\bar{x}vi.$ to $\bar{x}xii.$) will occasion fainting:—so that congestion and inflammation augment, while fever, cholera, &c. diminish the tolerance of blood-letting; he therefore makes use of this circumstance as a diagnostic to enable him to distinguish irritation from inflammation.

9. *Circumstances which modify the effects of Medicines.*

The circumstances which modify the effects of medicines may be arranged under two heads; those relating to the medicine, and those relating to the organism.

I. RELATING TO THE MEDICINE.—Under this head are included,—

a. *State of Aggregation.*—The state of aggregation of a medicine modifies the effect. Thus morphia is more active in solution than in the solid state.

b. *Chemical combination.*—The soluble salts of the vegetable alkalis are more active than the uncombined alkalis, and *vice versa*, the insoluble salts are less active. Lead and baryta are rendered inert by combination with sulphuric acid.

c. *Pharmaceutical mixture.*—The modifications produced by medicinal combinations have been very ably described by Dr. Paris.—(*Pharmacologia*, 6th ed. vol. i. p. 267.) The objects to be obtained, he observes, by mixing and combining medicinal substances, are the following:—

I. *To promote the action of the basis or principal medicine:—*

- A. By combining together several forms or preparations of the same substance: as when we conjoin the tincture, decoction, and extract of cinchona in one formula.
- B. By combining the basis with substances which are of the same nature, that is, which are individually capable of producing the same effect, but with less energy than when in combination with each other: as when we prescribe a compound of cassia pulp and manna.
- C. By combining the basis with substances of a different value, and which do not exert any chemical influence upon it, but are found, by experience, to be capable of rendering the stomach, or system, or any particular organ, more susceptible of its action: as when we combine mercury with antimony and opium, to increase the activity of the former.

II. *To correct the operation of the basis, by obviating any unpleasant effects it might be likely to occasion, and which would pervert its intended action, and defeat the objects of its exhibition.*

- A. By mechanically separating, or chemically neutralizing, the offending ingredient; as by digesting *Cetraria Islandica* in an alkaline solution, in order to remove the bitter principle, and to enable us to obtain a tasteless, but highly nutritious fecula.
- B. By adding some substance capable of guarding the stomach or system against its deleterious effects; as when we combine aromatics with drastic purgatives, to correct the griping qualities of the latter;—or opium with mercurials, to prevent the latter affecting the bowels.

III. *To obtain the joint operation of two or more medicines.*

- A. By uniting those substances which are calculated to produce the same ultimate results, although by totally different modes of operation: as when we combine

digitalis and potash to produce diuresis,—the first acting on the absorbents, the second on the secreting vessels of the kidneys.

B. By combining medicines which have entirely different powers, and which are required to obviate different symptoms, or to answer different indications: as when we combine opium and purgatives in painter's colic,—the first to relieve the spasm, the second to evacuate the contents of the intestinal canal.

IV. *To obtain a new and active remedy not afforded by any single substance.*

A. By combining medicines which excite different actions in the stomach and system, in consequence of which new or modified results are produced: as when we combine opium (a narcotic) with ipecacuanha (an emetic) to obtain a sudorific compound.

B. By combining substances which have the property of acting chemically upon each other; the result of which is, the formation of new compounds, or the decomposition of the original ingredients, and the developement of their more active elements: as when solutions of acetate of lead and sulphate of zinc are mixed to procure a solution of the acetate of zinc; and when the compound iron mixture of the Pharmacopœia is prepared.

C. By combining substances, between which no other chemical change is induced, than a diminution, or an increase, in the solubilities of the principles, which are the repositories of their medicinal virtues: as when we combine aloes with soap, or an alkaline salt, to quicken their operation, and remove their tendency to irritate the rectum.

V. *To afford an eligible form.*

A. By which the efficacy of the remedy is enhanced; as in the preparation of decoctions, infusions, tinctures, &c.

B. By which its aspect or flavour is rendered more agreeable; as when we exhibit medicines in a pilular form, or when we exhibit them in a state of effervescence.

C. By which it is preserved from the spontaneous decomposition to which it is liable; as when we add some spirituous tincture to an infusion.

d. Organic peculiarities.—Vegetables have their medicinal properties considerably modified by the nature of the soil in which they grow, by climate, by cultivation, by age, and by the season of the year when gathered.

e. Dose.—The modifications produced in the effects of medicines by differences of dose, are well seen in the case of opium, mercurials, and turpentine.

2. RELATING TO THE ORGANISM.—Under this head are included several circumstances, of which the most important are the following:—

a. Age.—One of the most distinctive characters of organised beings is that of undergoing perpetual mutation during the whole period of their existence; thus constituting the phenomena of age. In order the better to appreciate these changes, the life of man has been portioned out into certain periods or ages, as they have been termed, though as these pass imperceptibly into each other, there is no absolute or fixed distinction; and, consequently, the number of these periods has not been generally agreed on; some admitting only three, others four, five, six, seven, or even eight; the most popular number being seven.

Each period of life is characterised by certain conditions of the solids, by particular states of the functions, by a tendency to certain diseases, and by a different susceptibility to the influence of medicines.

The effects of medicines are modified both quantitatively and qualitatively, by the influence of age. Hufeland (*Lehrbuch der allgemeinen Heilkunde*, 2^{te} Aufl. 1830, p. 84) has drawn up the following scale for different ages:—

| | | | | | | | | | | | | | | | | | |
|---------|----|----|----|----|----|----|----|----|----|----|----|----|----|---------------|----|----|----|
| Years. | 25 | 20 | 15 | 14 | 13 | 12 | 11 | 10 | 9 | 8 | 7 | 6 | 5 | 4 | 3 | 2 | 1 |
| Doses. | 40 | 35 | 30 | 29 | 28 | 27 | 26 | 25 | 24 | 23 | 22 | 21 | 20 | 18 | 16 | 13 | 10 |
| Months. | | | 11 | 10 | 9 | 8 | 7 | 6 | 5 | 4 | 3 | 2 | 1 | $\frac{1}{2}$ | | | |
| Doses. | | | 9 | | 8 | | 7 | | 6 | | 5 | | 4 | | 2 | | 1 |

Suppose the dose at the end of the first year to be 1, then at the fifth it will be 2, at the fifteenth 3, and at the twenty-fifth 4. In the above table the dose for an adult is supposed to be 40 grains. Dr. Young (*Introduction to Medical Literature*, 2nd ed. p. 453) gives the following rule for determining the doses for children under twelve years of age:—"The doses of most medicines must be diminished in the proportion of the age to the age increased by 12. For example, at two years old, to $\frac{1}{7} = \frac{2}{2+12}$. At twenty-one, the full dose may be given." But no rule is of much value, as the degree of development is very unequal in different children of the same age. Moreover, the rule that applies to one medicine will not hold good with respect to others. This is particularly obvious in the cases of opium and calomel: the first must be given to children with the greatest caution, and in excessively small doses, whereas the second may be given to them almost as freely as to adults. Acetate of lead, nitrate of silver, arsenious acid, and some other metallic compounds, ought, perhaps, never to be prescribed for infants.

b. Sex.—The sex has an influence in the operation of medicines. Females differ from males in greater susceptibility of the nervous system, more excitability of the vascular system, and less energy or power in all parts. In these respects, indeed, they approach children. Women, therefore, require, for the most part, smaller doses of medicinal agents than men.

The periods of menstruation, pregnancy, and lactation, are attended with peculiarities in relation to the action of medicines. Drastic purgatives should be avoided during these states, especially the two first. Agents which become absorbed, and thereby communicate injurious qualities to the blood, are of course to be avoided during pregnancy, on account of the probable ill effects on the fœtus.

c. Mode of life: Occupation.—These circumstances affect the susceptibility of the whole organism, or of individual parts, to the influence of external agents.

d. Habit.—The habitual use of certain medicinal or poisonous agents, especially narcotics, diminishes the influence which they ordinarily possess over the body. Of the truth of this statement we have almost daily proofs in those who are confirmed drunkards, chewers and smokers of tobacco, and opium-eaters. Instances of the use of enormous doses of opium, with comparatively slight effects, will be found in every work on pharmacology. One of the most remarkable I have met with, is that related by G. V. Zeviani (*Sopra un vomito Urinoso*, in the "*Memorie di Matematica e Fisica della Societa italiana*." Verona, t. vi. 1792-4, p. 93). A woman of the name of Galvani, during a period of thirty-four years, took more than *two cwt.* of solid opium!! When nineteen years old she fell down stairs, and divided her urethra by a knife. Although the wound healed, she was unable to pass her urine in the usual way, but vomited it up daily with excruciating pain, to relieve which, she resorted to the use of opium, the doses of which were gradually increased to 200 grains daily.

The influence of acrid or irritating substances is but little diminished by repetition,—a remark which applies especially to bodies derived from the mineral kingdom. There are, indeed, a few instances illustrative of the effect of habit in lessening the sensible influence of inorganic agents,

but their number is small. The most common is the tolerance obtained by the repeated use of tartar emetic in peripneumonia.

Several attempts have been made to account for the effect of habit. Some ascribe it to an increased power acquired by the stomach of decomposing the medicinal agent,—an explanation adopted, in the case of poisons, by Dr. Christison, and which he illustrates by reference to the increased facility acquired by the stomach of digesting substances which had at first resisted its assimilative powers. If this explanation were correct, we ought to observe the effect of habit principally when substances are swallowed, and little, or not at all, when they are applied to a wound, to the cutis vera, or other parts unendowed with digestive powers, and opium ought to have its usual effects in ordinary doses, on application to any part of the body of an opium-eater, except to his stomach. Müller (*op. cit.* p. 60), as I have before noticed (p. 11), ascribes a great number of the instances of habituation to the substance affecting the composition of an organ, and losing its influence by saturation, while the part may still be susceptible of the action of another agent. But a strong objection to this hypothesis is, that the effect of habit is observed principally in the case of narcotic vegetables, and is scarcely perceived in inorganic substances which evince the most powerful affinities for organic principles. The same physiologist ascribes part of the phenomena observed in the effects of habit to the excitability of the organ being deadened by the stimulus being too often repeated.

e. Diseased conditions of the body.—Diseases of various kinds sometimes have a remarkable influence in modifying the effects of medicines; a fact of considerable importance in practice. One of the most striking instances is that of opium in tetanus. A scruple of this substance has been given at one dose, and repeated every two or three hours for several days, without any remarkable effects being produced. The late Mr. Abernethy mentions in his lectures (*Lancet*, vol. v. 1824, p. 71) a patient who had tetanus from a wound which he received at the time of the riots in the year 1780, to whom a scruple of opium was given every day, besides a dose of a drachm at night: when his body was opened, thirty drachms of opium were found undissolved in his stomach. It might perhaps be inferred, that the diminished effect arose from the want of solution of the medicine; and that this was Mr. Abernethy's opinion seems presumable from his advice as to the mode of using it in this disease. "Give it," says he, "repeatedly in small doses, so that it may liquefy." However, that the want of liquefaction or solution is not the sole cause of this diminished influence, is proved from the fact that the tincture is also less effective in tetanus than in health.

Begin (*Traité de Thérapeutique*, t. ii. p. 701) tells us, that M. Blaise, in a case of tetanus, administered in ten days, four pounds, seven ounces, and six drachms of laudanum, and six ounces, four drachms, and forty-five grains of solid opium! Begin (*op. cit.* t. i. p. 113) endeavours to explain these facts by assuming that the stomach acquires an increase of assimilative power, so that it is capable of digesting these enormous quantities of opium, in consequence of which their usual narcotic effects do not take place. He supports this hypothesis by stating, that if, during tetanus, opium be injected into the veins in much smaller quantities, it produces its usual effects. But if this latter assertion be correct, it does not at all warrant Begin's assumption; and bearing in mind that opium

administered by clysters during tetanus is less powerful than usual, and also taking into consideration the case related by Mr. Abernethy, I think we have evidence sufficient to warrant our non-admission of this hypothesis. All, therefore, that can be said in the way of explanation, is, that in tetanus the nervous system has undergone some change by which its susceptibility to the influence of opium is considerably diminished.

Another example of the influence of disease in modifying the effects of medicines is seen in the difficulty of causing salivation in fever by the use of mercury. I have repeatedly seen large quantities of mercurials exhibited internally during this disease, and in some cases accompanied with mercurial frictions, without affecting the mouth, and in general such cases terminated fatally. I never saw a fatal case of fever in which salivation was established; but whether the recovery was the consequence of the mercurial action, or the salivation of the recovery, I will not pretend to decide, though the first is the more plausible view.

e. Climate—The well-known influence of climate in modifying the structure and functions of the animal economy, and in promoting or alleviating certain morbid conditions, necessarily induce us to ascribe to it a power of modifying the effects of medicines. But it is difficult to obtain pure and unequivocal examples of it, in consequence of the simultaneous presence and influence of other powerful agents.

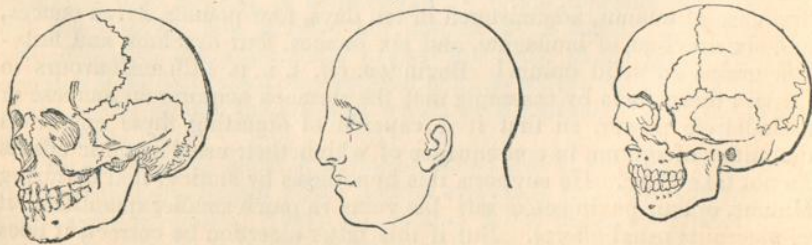
f. Mind.—The effects of medicines are very much modified by the influence of the mind. Hufeland (*op. cit.* p. 80.) knew a lady who, having conceived a violent aversion to clysters, was thrown into convulsions by the injection of a mixture of oil and milk. I have heard the most violent effects attributed to bread pills, which pills the patients had been previously informed exercised a powerful influence over the system. Much of the success obtained by empirical practitioners depends on the confidence which patients have in the medicines administered.

g. Race or species.—The effects of some medicines are not uniform on the different races or species of man.

The genus *Homo* is considered by most naturalists (among which may be mentioned the names of Blumenbach, Cuvier, Lawrence, and Pritchard,) to be made up of but one species: the differences which are observed between the inhabitants of certain regions of the world being regarded as sufficient to constitute varieties or races only, and not distinct species. Bory de St. Vincent, (*Essai Zoologique sur le Genre Humain*, 2nd edit. 1827,) however, admits no less than fifteen species.

The *races*, according to Cuvier, (*Le Règne Animal*, nouv. ed. 1824,) are three: the white, or *Caucasian*; the yellow, or *Mongolian*; the negro, or *Æthiopian*.

Fig. 22.



Head and skulls of the Caucasian Race — (*Homo Japeticus*, Bory.)

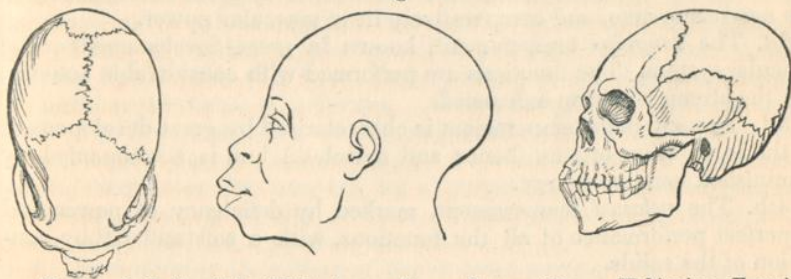
The *Caucasian race* is characterised "by a white skin; red cheeks; copious, soft, flowing hair, generally curled or waving; ample beard; small, oval, and straight face, with the features very distinct; expanded forehead; large and elevated cranium; narrow nose; and small mouth." It includes all the Europeans, the Laplanders excepted, the western Asiatics, and northern Africans.

Fig. 23.

*Head and skulls of the Mongolian race.*

The *Mongolian race* is characterised by "an olive yellow-coloured skin; hair thin, coarse, and straight; little or no beard; broad flattened face, with the features running together; small and low forehead; square-shaped cranium; wide and small nose; very oblique eyes; and thick lips. Stature inferior to the Caucasian." This race includes the eastern Asiatics, the Laplanders in Europe, and the Esquimaux in North America.

Fig. 24.

*Head and skulls of the Æthiopian or Negro Race.—(Homo Æthiopicus, Bory.)*

The *Æthiopian race* is characterised by "a black skin; hair short, black, woolly; skull compressed on the sides, and elongated towards the point; forehead low, narrow, and slanting; cheekbones very prominent; jaws projecting, so as to render the upper front teeth oblique; eyes prominent; nose broad and flat; lips (especially the upper one) particularly thick." It comprehends the Africans to the south of the Atlas chain.

Differences of race have been supposed to give rise, in some cases, to differences in the action of medicines on the body. Thus Charvet (*De l'Action comparée de l'Opium*, p. 59,) ascribes to this circumstance the different effects of opium on the Javanese and Malays (both belonging to the Mongolian race) as compared with those produced on Europeans, Turks, and Persians (the Caucasian race.) "The Javanese," says Lord Macartney, (*Embassy to China*, vol. i. p. 263-4,) "under the influence of an extraordinary dose of opium, becoming frantic as well as desperate, not only stab the objects of their hate, but sally forth to attack, in like man-

ner, every person they meet, till self-preservation renders it necessary to destroy them." A very similar account is given by Raynal (*Histoire Philosophique et Politique des Deux Indes*, t. 1^{er}, p. 359,) of the effects of opium on the Malays.

h. Temperaments.—Under the denomination of temperaments are included peculiarities affecting certain individuals, independent of race, and which consist in disproportions in the development or activity of certain organs, by which the whole animal economy is influenced. The term temperament is derived from the Latin verb *tempero*, to mix together, or to temper, and is applied to certain conditions of the body formerly supposed to arise from variations in the proportions of the fluids of the body. Thus, when the fluids were thought to be in proper relative proportions, they were said to temper each other, and by so doing, to produce a perfect temperament. When the yellow bile was supposed to be in excess it produced the choleric or bilious temperament; when black bile, the atrabillious or melancholic; when blood, the sanguineous; and lastly, when pituita or phlegm, the pituitous or phlegmatic. Although in modern times physiologists do not admit these notions, yet we cannot but acknowledge that individuals do present certain physical and functional peculiarities: and thus the existence of temperaments has been generally admitted, while the theory or explanation of them has varied with the prevailing medical doctrines of the day.

The number of temperaments has not been agreed on; Hippocrates admitted four, Boerhaave eight, others five. Under five heads, I think, we may include the leading varieties, which will then stand as follows:—

1st. The *nervous* temperament, characterised by great susceptibility of the nervous system, and comparatively little muscular power.

2d. The *sanguine* temperament, known by great development of the vascular system. The functions are performed with considerable activity, but the strength is soon exhausted.

3d. The *muscular* temperament is characterised by great development of the locomotive organs (bones and muscles;) but is accompanied by diminished nervous energy.

4th. The *relaxed* temperament, marked by deficiency of power and imperfect performance of all the functions, with a soft and flabby condition of the solids.

5th. The most *perfect* temperament is that in which all the organs and functions are properly balanced, and in which we have the greatest strength.

Each of these temperaments varies in regard to its susceptibility to the influence of medicinal agents. In the sanguine temperament stimulants are to be employed very cautiously: in the nervous and relaxed temperaments, evacuants are to be used with great care.

i. Idiosyncrasy.—Under this denomination are included these peculiarities which affect the functions of organs, without having any obvious relation to development, and which are not common to a number of individuals. Its effect in modifying the effects of medicines and poisons is, in general, to increase their activity. Thus, some individuals are peculiarly susceptible of the action of opium, some of mercury, and others of alcohol. The odour of ipecacuanha will, in certain persons, produce short and difficult respiration, approaching almost to a paroxysm of asthma. The late Mr. Haden (*Dr. Dunglison's translation of Magendie's Formulary, with notes*

by C. T. Haden, Esq. 1825,) has related a case in which two drachms and a half of tincture of colchicum produced death: the mother of the patient was also exceedingly susceptible of the action of colchicum even in very small doses. In some instances the effect of idiosyncrasy is to diminish the activity of medicines. Thus some persons are exceedingly insusceptible of the action of mercury.

k. *Tissue or organ*.—The nature of the part to which a medicine is applied, has an important influence over the effect produced. The stomach, for example, is much more susceptible of medicinal impressions than the skin. Opium acts more powerfully on the system when applied to the serous than to the mucous tissues. Carbonic acid acts as a positive poison when taken into the lungs, but as a grateful stimulant when applied to the stomach. The modifications effected by the nature of the tissue will be more fully noticed hereafter.

8. Therapeutical Effects of Medicines.

The effects produced on diseases by the influence of medicines are denominated *therapeutical*. They are sometimes termed *secondary*, because, in a great majority of instances they are subordinate to those already described under the name of physiological.

MODE OF PRODUCTION.—Therapeutical effects are produced in two ways:—

1. *By the influence of a medicine over the causes of diseases*.—This may be *direct* or *indirect*. Medicines which act directly are termed by Hufeland (*Lehrbuch*, p. 194) *specifica qualitativa*. As examples, the chemical antidotes may be referred to. Those anthelmintics (as oil of turpentine), which poison intestinal worms, also belong to this division. If the efficacy of sulphur in the cure of itch depend on its destroying the *Acarus Scabiei*, this will be another instance of the direct operation of an agent on the cause of a disease. As an example of a medicine acting *indirectly*, I may mention the dislodgement of a biliary calculus, contained in the ductus choledochus, by the administration of ipecacuanha as an emetic: or the removal, by a purgative, of a morbid condition of system, kept up by the presence of some depraved secretion in the bowels, the result of a previous disease.

2. *By modifying the actions of one or more parts of the system*.—In a large majority of instances the causes of disease are either not known, or they are not of a material nature. In all such cases we administer medicines with the view of producing certain changes in the actions of one or more parts of the system, and thereby of so altering the diseased action as to dispose it to terminate in health. Thus inflammation of the lungs frequently subsides under the employment of nauseating doses of tartarized antimony; and emetics will sometimes put a stop to the progress of hernia humoralis.

The medicines belonging to this division may be arranged in two classes; those which are applied to the diseased part, and, secondly, those which are applied to other parts.

a. *Topical agents*.—Under this head we include unguents or lotions used in cutaneous diseases, ulcers, &c.; gargles in affections of the mouth and throat; collyria in ophthalmic diseases; and injections into the vagina and uterus in affections of the urino-genital organs. In all such cases we can explain the therapeutic effect in no other way than by assuming