5. *Absorption of Medicines.*

Proofs.—The particles of most medicinal substances, when applied to the living body, become absorbed and pass into the circulation. Two facts prove this, viz., the disappearance of certain substances from a shut cavity into which they had been introduced,—and the detection of medicinal particles in the blood, secretions, or solids of the body.

a. Disappearance from a shut cavity.—Drs. Christison and Coindet found that four ounces of a solution of oxalic acid injected into the peritoneal sac of a cat, killed the animal in fourteen minutes. On a post-mortem examination, although none of the fluid had escaped by the wound, they found scarcely a drachm remaining.—(*Edin. Med. and Surg. Journ.* xix. 335).

b. Detection in other parts of the body.—Tiedemann and Gmelin (*Versuche über d. Wege auf welchen Substanzen aus dem Magen u. Darmkanal ins Blut gelangen.* 1820) have detected the following substances in the *blood* of animals to whom those agents had been administered: camphor, Dippel's oil, musk, indigo, rhubarb, lead, cyanuret of potassium, sulphocyanuret of potassium, iron, mercury, baryta, and alcohol. By other experimenters, asafœtida, sal ammoniac, iodine, hydrocyanic, and sulphocyanic acids, &c. have been found. (For authorities consult Magendie's *Elementary Compendium of Physiology*, and Christison's *Treatise on Poisons*).

In the *solids* of the body several substances have been recognized: for example, madder in the bones, silver in the skin, copper in the liver, lead in the liver, spinal cord, and muscles, mercury in various parts, &c.

In the *secretions* various medicinal agents have been recognized.—Thus, *in the cutaneous secretions*, mercury, iodine, sulphur, the odorous matter of musk, of garlic, and of onions, and other substances, have been detected;—*in the breath*, several substances have been recognized by their odour; for example, camphor, alcohol, ether, phosphorus, asafœtida, sulphur, the odorous matter of garlic, and of onions, &c. The *milk* sometimes acquires purgative properties, in consequence of the employment of purgatives (senna, for example) by the nurse. Bitters, indigo, iodine, and madder, have also been distinctly recognized in it. *In the urine* so many substances have been discovered, that it will be most convenient to exhibit them in a tabular form. The following is taken principally from the experiments of Drs. Wöhler and Stehberger, as mentioned by the late Dr. Duncan (*Supplement to Edinburgh Dispensatory*, 1829.)

SUBSTANCES WHICH PASS OFF BY THE URINE.

(A) Unchanged, or nearly so.

Salts.

Carbonate of potash.	Sulphuret of potassium.	Tartrate of nickel and potash.
Nitrate of potash.	Ferro-cyanuret of potassium (in 66 minutes.)	Borax.
Chlorate of potash.	Silicate of potash.	Chloruret of barium.
Sulpho-cyanuret of potassium.		

Colouring Principles.

Indigo } (in 15 minutes.)	Red radishes.
Madder }	Mulberry.
Rhubarb (in 20 minutes.)	Black cherry (in 45 minutes.)
Gamboge.	Cassia Fistula (in 55 minutes.)
Logwood (in 25 minutes)	Elder rob (in 75 minutes.)

Odorous Principles somewhat altered.

Oil of turpentine.	Asafœtida.	Narcotic principle of Amanita muscaria
—— juniper.	Garlic.	Asparagus (*Cullen.*)
Valerian.	Castoreum.	
Saffron.	Opium.	

Other Matters.

Astringency of Uva ursi (in 45 minutes.) Oil of almonds (*Bachetoni.*)

(B) In a state of combination.

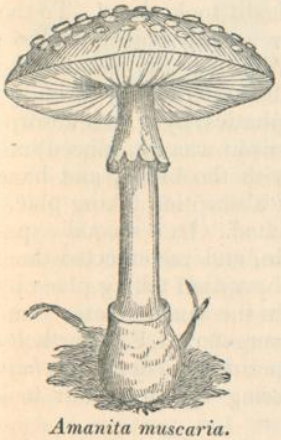
Sulphur, as sulphuric acid and sulphuretted hydrogen.
Iodine, as hydriodic acid or ioduret.
Oxalic
Tartaric
Gallic (in 20 minutes) } Acids, appear in combination
Succinic
Benzoic

(C) In a Decomposed state.

Tartrate
Citrate
Malate } of potash, or soda, are changed into the carbonate of the same alkali.
Acetate

Sulphuret of potassium changed, in a great measure, into the sulphate of potash.

Fig. 7.



Amanita muscaria.

If the accounts published respecting the *Amanita muscaria* (fig. 7) be correct, its effects are most extraordinary. A variety of this fungus has a powerful narcotic or rather inebriating effect; and that the active molecules get into the blood is proved by the fact of the urinary secretion being impregnated with them, and thus possessing an intoxicating property; and we are told that the inhabitants of the north-eastern parts of Asia use it for this property. A man, for example, may have intoxicated himself to-day by eating some of the fungus; by the next morning he will have slept himself sober; but by drinking a tea-cupful of his urine he will become as powerfully intoxicated as on the preceding day. "Thus," says Dr. Greville, on the authority of Dr. Langsdorf, "with a very few *Amanitæ*, a party of drunkards may keep up their debauch for a week;" and "by means of a second person taking the urine of the first, a third of the second, and so on, the intoxication may be propagated through five individuals."

Vessels effecting absorption.—The particles of medicinal and poisonous substances are absorbed by the veins principally, but also by the lymphatics and lacteals.

1. *Absorption by the Veins.*—The circumstances which seem to prove venous absorption are the following:—

a. Detection of substances in the venous blood.—Tiedemann and Gmelin (*op. cit.*) administered a variety of colouring, odorous, and saline substances to animals, mixed with their food, and afterwards examined the state of the chyle, and of the blood of the (splenic, mesenteric, and portal) veins. The *colouring* substances employed were—indigo, madder, rhubarb, cochineal, litmus, alkanet, gamboge, and sap-green; none of them could

be detected in the chyle, but some were found in the blood and urine. The *odorous* substances used were—camphor, musk, spirits of wine, oil of turpentine, Dippel's oil, asafœtida, and garlic: they were for the most part detected in the blood and urine, but none were found in the chyle. The *saline* substances tried were—acetate of lead, acetate and cyanuret of mercury, chloruret and sulphate of iron, chloruret of barium, and ferrocyanuret and sulpho-cyanuret of potassium. A few of these were detected in the chyle, and most of them in the venous blood and urine. From these experiments we may conclude, that although saline substances occasionally pass into the chyle, odorous and colouring matters do not; all the three classes of substances, however, are found in the venous blood. These results, observe Tiedemann and Gmelin, are opposed to those of Lister, Musgrave, J. Hunter, Haller, Viridet, and Mattei, but agree with those of Hallé, Dumas, Magendie, and Flandrin.

b. Magendie's experiment.—Magendie and Delille *(Elem. Comp. Physiol.)* performed a striking experiment, with the view of settling, if possible, the question of venous or lymphatic absorption of medicines and poisons. They divided all the parts of one of the posterior extremities of a dog, except the artery and vein, the former being left entire, for the purpose of preserving the life of the limb. A portion of the *Upas Tieuté* was then applied to a wound in the foot: in the short space of four minutes the effects of the poison were evident, and in ten minutes death took place. To the inferences drawn from this experiment, however, several objections have been stated: first, the exhibition of opium, to diminish the pain of the operation, has been said to vitiate the whole of the experiment; secondly, the coats of the arteries and veins contain lymphatics, by which absorption might be carried on; and thirdly, as the poison was introduced into a wound, the poison might have combined with the blood, and have rendered it deleterious, without the process of absorption taking place. The first two of these objections have been obviated. In a second experiment, Magendie severed the artery and the vein, and reconnected them by quills, so as to preclude the possibility of absorption taking place by the lymphatics of these vessels: the effects were the same. Some years since I assisted my friend Mr. Lloyd, assistant-surgeon of St. Bartholomew's Hospital, in performing an analogous experiment, using *Strychnia* instead of *Upas Tieuté*, and without administering opium: death took place in twelve minutes.

c. Lacteals tied: effects of poisons still produced.—Magendie says that symptoms of poisoning were observed in six minutes, when nux vomica was applied to the intestine, though the lacteals had been tied.

d. Blood-vessels tied: poisons do not act.—Segalas tied the veins of a portion of intestine, and applied poison, but no effects were produced. Emmert observed, that when the abdominal aorta was tied, hydrocyanic acid was applied to the foot without producing any effect, but when the ligature was removed, symptoms of poisoning came on. *(Müller.)*

e. Rapidity of absorption.—Mayer found that ferrocyanuret of potassium could be detected in the blood, in from two to five minutes after its injection into the lungs. The rapidity with which this salt enters the blood, says Müller, is too great for it to be explained by means of the slow circulation of the lymph.

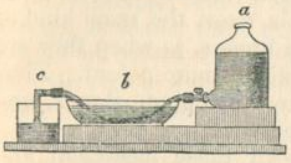
These circumstances appear to me to establish the fact of venous absorption.

2. *Absorption by the lacteals and lymphatics.*—The particles of medicinal and poisonous substances are probably absorbed by the lacteal and lymphatic vessels, as well as by the veins. But the process seems to be slow, and, moreover, is confined to certain agents. Tiedemann and Gmelin, whose experiments I have above referred to, were unable to recognize either colouring or odorous substances in the chyle, but occasionally detected certain salts. The absorption of saline, and non-absorption of colouring matters, have likewise been noticed by others *(Müller's Physiology.)*

Mechanism of Absorption.—The facts connected with absorption are best explained by assuming the existence of two powers or agencies by which this process is effected;—the one physical, and the other vital.

1. *Absorption by physical agency (Imbibition*, Magendie; *Exosmose* and *Endosmose*, Dutrochet.)—Two fluids separated by an interposed dead membrane, mutually, though not equally, permeate the membrane, so as to become intermixed with each other. If a current of water, coloured by litmus, be allowed to pass from a bottle (*fig.* 8, *a*), through a vein immersed in diluted sulphuric acid contained in a glass dish (*b*), into a reservoir (*c*), the litmus liquor is soon observed to become reddened by its passage through the vein, in consequence of the acid permeating the venous coats. If the relative position of the fluids be altered,—that is, the litmus put in the dish (*b*) and the acid passed from the bottle (*a*) through the vein, the litmus will still become reddened, shewing that the acid has passed in this case from within outwards.

Fig. 8.



But it may be said this effect is cadaveric only; that is, it occurs in the dead but not in the living vessels:—and in support of this view may be urged, the transudation of blood within the blood-vessels, and of bile within the gall-bladder, both of which phenomena are observed after death. Magendie has endeavoured to meet this difficulty with respect to the imbibition of poisons. He exposed and isolated the jugular vein of a dog, placed it on a card, and dropped some aqueous solution of the extract of nux vomica on its surface, taking care that the poison touched nothing but the vein and the card. In four minutes the effects of the substance became manifest, and the dog died.—*(Magendie's Lectures* in the *Lancet*, Oct. 4, 1834.) It must be admitted, however, that the result of this experiment does not absolutely prove, though it strongly supports, the opinion of the imbibing power of the living vessels; for it might be objected, that the nerves of the venous coats propagated the impression of the poison, and that death took place without absorption; or, that the small veins of the venous coat had taken up the poison. The proof, therefore, should consist in the detection of the poison within the vessel. Now this has been obtained by Magendie: a solution of nux vomica was placed on the carotid artery of a rabbit; but as the tissue of arteries is firmer and less spongy, and their parietes thicker than those of veins, a longer time elapsed before the poison traversed the vessel. In fifteen minutes, however, it had passed, and on dividing the vessel the blood adherent to its inner wall was found to possess the bitter taste of the poison.

With these results before us, we can hardly refuse to admit the imbi-

bition of living tissues, though I think we may fairly question whether this process can be effected so readily in the living as in the dead tissue.

2. *Absorption by a vital agency.*—The physical and chemical agencies with which we are at present acquainted are totally inadequate to explain all the phenomena of absorption. We are constrained, therefore, to admit another agency, which we may denominate vital or organic.

IS THE ABSORPTION OF A MEDICINE, OR POISON, ESSENTIAL TO THE PRODUCTION OF ITS REMOTE EFFECTS?—Magendie and Müller (*Physiol.* p. 246, *et seq.*) seem to consider the passage of poisons into the circulation essential to their operation on the system: while Messrs. Morgan and Addison (*Essay on the Operation of Poisonous Agents*, 1829,) deny that in any case absorption is absolutely necessary for the operation of a poison. "We are not opposed," observe the latter gentlemen, "to the theory of venous absorption, but to that theory which would associate with it the *absolute necessity* for the admission of a poison into a vein." The following facts will be of considerable assistance to us in forming an opinion on this controverted point:—

1. *Activity of substances injected into the blood-vessels.*—Medicinal or poisonous agents injected into the blood-vessels, exert the same kind of specific influence over the functions of certain organs, as when they are administered in the usual way; but that influence is more potent. Thus tartar emetic causes vomiting, castor oil purging, opium stupor, and strychnia convulsions, when thrown into the veins.

2. *Detection of substances in the blood.*—All those medicinal and poisonous agents whose sensible or chemical properties enable them to be readily recognised, have been detected in the blood, or in the secretions which are formed from the blood, after their ordinary modes of administration; as by the stomach.

3. *Activity of medicines promoted by the means which promote absorption, and vice versâ.*—The remote effects of many medicinal and poisonous agents are influenced by the same circumstances that influence absorption; and we are therefore naturally led to presume a mutual relation. Now these circumstances are principally three in number, viz. the nature of the tissue to which the agent is applied—the properties, (physical or chemical) of the medicine itself—and the condition of the system.

a. Nature of the tissue.—Nux vomica acts with the greatest energy when applied to the pulmonary surface,—with less when introduced into the stomach,—and with the least of all, when applied to the skin. The same order of gradation is observed with respect to opium. Now the faculty of absorption, or of imbibition, as Magendie calls it, does not take place with equal intensity in all tissues. Certain physical conditions, (viz., a fine and delicate structure, and great vascularity) enable the pulmonary surface to absorb or imbibe with extreme rapidity: in this respect, indeed, it is not equalled by any tissue of the body. Hence, then, if we assume that nux vomica and opium act by becoming absorbed, we can easily comprehend why they are so energetic when applied to this part. The membrane lining the alimentary canal absorbs with less facility than the pulmonary membrane, which may be accounted for by its less vascularity, and by its being covered, in some parts at least, by an epidermoid layer, and in all its parts by mucus, which, to a certain extent, checks absorption. The cutaneous surface, lastly, being covered by an inorganic

membrane (the epidermis,) does not possess the same physical faculties for absorption met with in either of the foregoing tissues; and hence the comparative inertness of medicines when applied to it. In fact, it is only by the long-continued application of these agents to the skin, that we are enabled to affect the general system; and that the obstructing cause is the epidermis, is shewn by the facility with which the system may be influenced when this layer is removed, as has been proposed and practised by Lembert and Lesieur, constituting what has been denominated the *endermic* or *emplastro-endermic* method of treating diseases; of which method I shall have occasion to speak hereafter.

b. The physical and chemical properties of the medicine.—Another circumstance, tending to prove some connexion between the activity of a medicine and its absorption is, that the effect of many medicines is in proportion to their solubility. Arsenic and morphia are both more energetic in solution than in the solid state. Now liquids, (particularly those miscible with the blood,) are much more readily absorbed than solids. In the treatment of many cases of poisoning, we endeavour to take advantage of this principle, and by rendering substances insoluble, diminish their activity, or render them quite inert. Thus the antidote for the salts of lead, or of baryta, is a sulphate, the acid of which forms an insoluble salt with either of the bases (lead or baryta.) Tannic acid (or astringent infusions which contain it,) is for the same reason found useful in cases of poisoning by vegetable substances whose active principle is an alkaloid; and we employ carbonate of lime as an antidote for oxalic acid, to render this substance incapable of being absorbed.

c. Condition of System.—Magendie asserts, as the result of experiments, that plethora uniformly retards, and depletion as constantly promotes, absorption. If, therefore, we wish to promote this function, we have a ready means of doing so, in blood-letting. Now every surgeon knows that one powerful means of promoting the action of mercurials on the mouth, is to abstract blood; and, therefore, we should be cautious about bleeding a patient, while a poisonous dose of some narcotic, as opium, is in the stomach. Nay, in theory, the best means of preventing the operation of poisons which act by becoming absorbed, would be to throw a quantity of warm water into the veins. Magendie tried this on animals, and found it successful.

4. *Magendie's experiment.*—The experiment of Magendie, already related, of applying the *Upas Tieuté* to the leg of a dog, connected to the body only by two quills, is another argument in favour of the operation of medicines by absorption: for in this case the action of the poison could have taken place only after it had passed into the blood.

5. *Division of the spinal cord.*—Some poisons, as hydrocyanic acid, are equally active when applied to the legs of an animal in whom the spinal marrow has been divided. In this case, the effect of the poison could not be the result of its action on the nerves of sensation and voluntary motion. But it may be said the division of the lumbar spine does not prevent the action of poisons by the nervous system, because it does not destroy the action of the excito-motory or sympathetic systems, the nervous branches of which are distributed to the lining membrane of the blood-vessels. I am aware that it is an experiment liable to objection; but, on the whole, it is certainly favourable to the opinion of the operation of poisons by absorption; more particularly when we bear in mind that the motion of the blood is

necessary to the action of the poison; for if the circulation of a part be obstructed, the poison will no longer act. These reasons are, to my mind, conclusive, that in a large number of instances at least, if not in all, the operation of a medicine on remote parts of the system depends on its absorption. Nor can I admit that this opinion is at all invalidated by the arguments and experiments of Messrs. Morgan and Addison.

The principal objections which have been raised to the theory of the operation of medicines by absorption, are the following:—

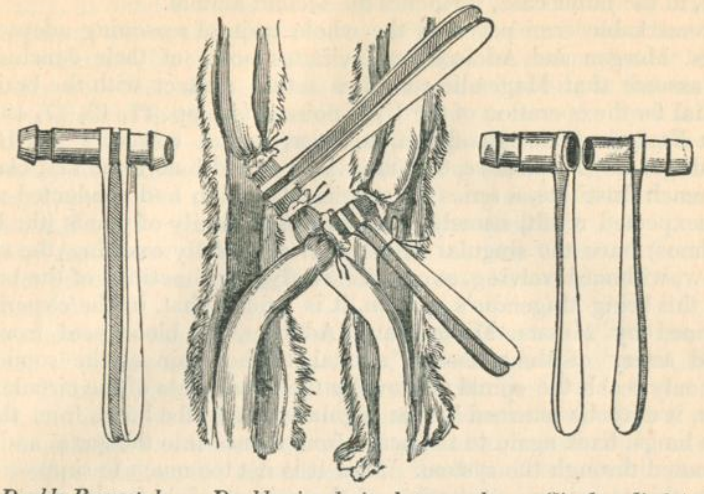
a. The experiments of Magendie and others, it has been observed, only show that a poison may get into the veins, and do not prove that absorption is essential to the effect. "We must strongly protest," say Messrs. Morgan and Addison, "against the assumption that, because a poison has been found to enter and pass through a vein, it is thence to be inferred that such a process is, under all circumstances, absolutely necessary to its operation." But it has been proved that the more absorption is facilitated the more energetic do poisons act, and *vice versâ*.

b. Mr. Travers, in his *Further Inquiry concerning Constitutional Irritation*, points out very forcibly the analogy to be observed between the effects of severe injuries and of poisons which operate rapidly on the system. Thus both strychnia and punctured wounds cause tetanus, and he, therefore, concludes their *modus operandi* must be identical: consequently, as there is nothing to absorb in the one case, so absorption cannot be essential in the other. But although the symptoms caused by the above poison are very analogous to those of traumatic tetanus, yet we are not to conclude that the effects of strychnia and of a puncture are precisely alike. "The fact of two substances producing similar symptoms in one organ," observes Müller (*op. cit.* p. 56) "does not prove that these substances produce exactly the same effects, but merely that they act on the same organ, while the essential actions of the two may be very different." And I confess I see nothing unphilosophical in supposing that the same morbid condition of a part may be induced in more than one way: for as every part of the organism depends for the performance of its proper functions on the receipt of arterial blood and of nervous influence, so alterations in the supply of either of these essentials may modify or even suspend the functions of a part.

c. Messrs. Morgan and Addison tell us that the blood circulating in the carotid artery of a dog poisoned by strychnia is not poisonous to a second dog, and they therefore infer that this poison does not act on the brain by absorption, but by an impression upon the sentient extremities of the nerves.

By the aid of a double brass tube, (fig. 9,) consisting of two short brass cylindrical tubes to each of which a long handle is attached (fig. 11), they established a complete circulation between the carotids of a poisoned and of a sound dog, by connecting the lower and upper ends of the divided arteries in both animals, so that each supplied the brain of the other with the portion of blood which had previously passed through the carotid artery to his own, and, consequently, the poisoned dog in this case received from the unpoisoned animal a supply of arterial blood equal to that with which he was parting. (Fig. 10.) One of the dogs was then inoculated with a concentrated preparation of strychnia, which had been found upon other occasions to produce death in these animals in about three minutes and a half. In three minutes and a half the inoculated

Fig. 9. Fig. 10. Fig. 11.



Double Brass tube. *Double circulation between the Carotids of a poisoned and a sound dog.* *Single cylindrical Brass tubes.*

animal exhibited the usual tetanic symptoms which result from the action of this poison, and died in little less than four minutes afterwards, viz. about seven minutes from the time at which the poison was inserted, during the whole of which period a free and mutual interchange of blood between the two was clearly indicated by the strong pulsation of the denuded vessels throughout their whole course. The arteries were next secured by ligature, and the living was separated from the dead animal; but neither during the operation, nor subsequently, did the survivor shew the slightest symptom of the action of the poison upon the system.

The inference which has been drawn from this experiment is, that the arterial blood of an animal under the influence of poison is not poisonous. But it appears to me that this is not a necessary inference, and as it is opposed to the result of other experiments, it requires careful investigation ere we admit it. Vernière has proved that if the extract of nux vomica "be thrust into the paw of an animal after a ligature has been tightened round the leg, so as to stop the venous, but not the arterial circulation of the limb, blood drawn from an orifice in a vein between the wound and ligature, and transfused into the vein of another animal, will excite in the latter the usual effects of the poison, so as even to cause death; while, on the contrary, the animal from which the blood has been taken will not be affected at all, if a sufficient quantity is withdrawn before the removal of the ligature."—(*Christison's Treatise on Poisons*, 3d ed. p. 10.)

Mr. Travers, (*op. cit.*) in noticing the different results obtained by Vernière and Messrs. Morgan and Addison, observes, that "if it be inquired why the poisoned blood concentrated below a ligature, and transferred into the vein of a healthy animal, proves destructive, while the blood of their common circulation affects only the one of the two animals which is the subject of the inoculation, the answer is obvious—that either

the mechanical impulse fails, or the activity of the poison is exhausted before, in the latter case, it reaches the second animal."

A remarkable error pervades the whole train of reasoning adopted by Messrs. Morgan and Addison, and vitiates some of their conclusions. They assume that Magendie considers actual contact with the brain as essential for the operation of the Upas poison, (see pp. 42, 43, 47, 49, &c. of the *Essay.)* This assumption, however, is not correct. "In 1809," says Magendie (*Formulaire*, 8me éd. p. i.) "I laid before the first class of the French Institute, a series of experiments which had conducted me to an unexpected result, namely, that an entire family of plants (the bitter Strychnos) have the singular property of powerfully exciting the spinal marrow, without involving, except indirectly, the functions of the brain." Now, this being Magendie's opinion, it is evident that, in the experiment performed by Messrs. Morgan and Addison, the blood sent from the carotid artery of the poisoned animal to the brain of the sound one could only reach the spinal marrow by the usual route of the circulation; that is, it must be returned by the jugular veins to the heart, from thence to the lungs, back again to the heart, from thence into the aorta, and then distributed through the system. Now it is not too much to suppose that, during this transit, some portion of the poison might be decomposed or thrown out of the system before it could arrive at the spinal marrow; and even if this were not the case, this organ could only receive a small quantity of the poison contained in the system, namely, that sent by the vertebral to the spinal arteries. Hence we ought to expect that a poison thrown into the arteries will operate less powerfully than when thrown into the veins, unless it be into the arteries supplying the parts on which the poison acts. Moreover, as an anonymous reviewer has observed (*Lond. Med. and Phys. Jour.* vol. lxiii.) it is to be recollected that as the carotid artery, in its healthy state, is little more than one-fourth of the calibre of the vessels carrying blood directly to the brain, consequently the dog not inoculated was subject to the influence of one-fourth only of the quantity of the poison which was conveyed to the *brain alone* of the inoculated animal. Furthermore I would add, that it is not too much to suppose that the circulation of the blood through the tube would not be so free as through the artery.

How do medicines and poisons which have entered the blood-vessels affect distant organs?—Viewing the question theoretically, we see three ways by one or more of which remote parts might be conceived to become affected after medicinal globules have passed into the blood.

1. *By modifying or altering the properties of the blood, and thereby unfitting it for carrying on the functions of the body.*—Although no facts are known which can be regarded as absolutely proving that the action of medicines or poisons is primarily on the blood, yet none I believe are inconsistent with such a notion in all cases, while several strongly favour it: and it has been justly observed by Andral (*Treatise on Pathological Anatomy*, translated by Drs. Townsend and West, vol. i. p. 642), that "as the blood nourishes the solids, and as without its presence they cannot support life, the state of the solids cannot but be influenced by the state of the blood."

In the first place, it must be admitted that in many diseases the properties of the blood are altered, and in some cases these alterations often

appear to be primary; that is, they precede alterations of the solids.—Secondly, in some diseases the blood acquires poisonous properties, and is capable of transmitting the affection of the individual from whom it was taken.—Thirdly, by the use of poisons, medicines, and particular kinds of diet, the properties of the blood become altered, while at the same time the condition of the solids is modified. Now as from the food is formed the chyle, from the chyle the blood, and from the blood the solids, a necessary connexion must exist between the quality of the ingesta and the condition of the solids. For facts and arguments relative to these positions, I must refer to Andral's work before quoted.

But if medicines or poisons introduced into the torrent of the circulation act primarily on the blood, what, it may be asked, are the effects produced?

In some cases the action is mechanical, as when air is introduced into a vein. "A very small quantity of air," says Magendie, (*Lancet*, Nov. 15, 1834) "passed slowly into a vein, mixes with the blood, traverses the lungs, and is exhaled with the pulmonary transpiration, without causing any remarkable accident; but when the quantity is increased, especially in a sudden manner, the air mixes with the blood contained in the heart, and forms with it a foamy kind of liquid, which does not pass readily through the capillary system of the pulmonary artery. In consequence of this obstacle to the passage of the blood through the lungs, the respiration and circulation become necessarily troubled, and the animal soon dies in a state of asphyxia,—not from any pernicious action of the air on nervous system." (For further information *On the Influence of Air in the Organs of Circulation*, see Dr. J. R. Cormack's *Prize Thesis* on this subject; Edin. 1837.) Water, when introduced into the circulation, probably acts merely as a diluent. For though when mixed with blood out of the body it dissolves the envelope of the red particles, we can hardly suspect that it produces a similar effect within the blood-vessels, from the circumstance that large quantities of water may be thrown into the veins without causing any remakable disorder of system; whereas if the globules were deprived of their envelope, or changed in their form, great disorder of the system might be expected. Solutions of various substances (as sal ammoniac, chloruret of sodium, carbonate of potash, sugar, &c.) produce no change in the globules out of the body; they therefore probably act mechanically on the blood.

Some substances exercise a chemical action on the blood; as the mineral acids, the alkalis, various metallic salts, alcohol, &c. The affinity of these agents is principally directed to the fibrin and albumen of the liquor sanguinis, and to the constituents of the globules. Hydrocyanic acid even would appear to be a chemical agent, since it makes the blood oily, fluid, and bluish in colour. Such substances, therefore, as exercise a chemical influence, cause speedy death when they are thrown into the veins, unless, indeed, the quantity introduced be very small. It is possible that organic substances may, as Dr. Christison supposes, be decomposed in the blood, without that fluid undergoing any apparent change. "A very striking proof of this is furnished by oxalic acid. Dr. Coindet and I, in one of our experiments, injected into the femoral vein of a dog, eight grains and a half of oxalic acid, which caused death in thirty seconds. Here it was impossible that the poison could have passed off by any of the excretions; yet we could not detect even that

large proportion in the blood of the iliac vein, and vena cava, collected immediately after death. As the blood possessed all its usual properties, we must suppose that the poison underwent decomposition in consequence of a vital process carried on within the vessels."—(*Treatise on Poisons*, 3d ed. p. 16.)

It must not, however, be assumed, that agents which effect chemical changes in the blood out of the body, or when injected into the veins, necessarily produce the same phenomena when absorbed from the intestinal or other surfaces; for the quantity taken up at any one time by this process is small in proportion to the volume of the circulating fluid, and the affinities between these agents and the constituents of the blood seem to be kept in check by the vital properties.

As the blood is a vital fluid, medicines may effect changes in it which are neither mechanical nor chemical. Strychnia and morphia produce no obvious effect on the blood, yet it is not impossible that they may cause some changes in its vital condition; and that to these, part of the symptoms caused by their use are to be referred. Here, however, all our remarks are but conjectural.

2. *By pervading the structure of the organ acted on.*—The usual mode of explaining the action of medicines after their absorption, is, that when they have got into the blood, they are carried in the ordinary course of circulation to the heart, and from thence to the lungs. Here the blood undergoes certain chemical changes, and is probably deprived of part of the medicinal particles: at least this appears to be the case with respect to certain odorous substances. The blood still impregnated with medicinal particles being returned to the heart, is transmitted from thence to all parts of the system. In their passage through the tissues of the different organs, it is presumed that these particles act on one or more parts which are endowed with a peculiar susceptibility to their influence.

Thus the opiate particles are supposed to exert a specific influence on the cerebral tissue; strychnia is thought to act on the grey matter of the spinal marrow; mercury, on the salivary glands; diuretics, on the kidneys; and so on. Müller supposes that a change is effected on the composition of the organic matter of the part acted on. The molecules are ultimately got rid of by the excretory organs. On this supposition, then, the blood is merely the "vehicle of introduction."

It must be admitted, that this theory, plausible as it may appear, cannot be satisfactorily proved. We may adduce several arguments in favour of it, but absolute proof or demonstration cannot be offered: our facts merely show the passage of medicinal particles into the blood, and the affection of the remote organs; but the link which connects the two phenomena cannot be, or at least has not yet been, demonstrated. The strongest argument in favour of this mode of explanation is, that the molecules of certain medicines may be detected in some one or more of the excreted fluids; while, at the same time, the functions of the organs secreting or excreting these fluids, have become influenced by the medicine. Now the simplest, and therefore the most plausible explanation, is, that the molecules, in passing through the organ, acted on its tissue, and thus gave rise to a functional change. The diuretic effects of nitre, alkalis, turpentine, &c., are readily explained on this theory: but when the affected part is not a secreting organ, and especially when the medicinal agent is not readily detected by its phy-

sical or chemical properties, we have not the same evidence to offer in support of this view, which, notwithstanding, may be not the less true. Several objections present themselves to this explanation. Many medicinal substances may be detected in the secretion of an organ, though no evident influence has been exercised over the organ itself. Thus the colouring particles of rhubarb may be recognised in the urine, although the action of the kidneys does not appear to be altered; and therefore it may be said, that in those cases where the quality of the secretion is affected, we have no right to infer that it depends on the passage of medicinal particles through the secreting vessels. This objection, however, deserves but little attention, inasmuch as we know that the susceptibility of the same part is not the same to all medicines; for it is not every medicine which produces vomiting when applied to the stomach.

It has also been said that this theory of medicines "being conveyed by the circulation to particular parts, is utterly gratuitous, and no less improbable." "What intelligence," says an American writer, (Chapman's *Elements of Therapeutics*, 4th ed. vol. i. p. 73,) "directs them in this voyage of circumnavigation to the port of destination; and how, on their arrival (admitting it to happen,) are they separated from the great mass of fluids in which they are enveloped?" It is not supposed, on this theory, that medicines are *conveyed to particular parts*, but *to every part* of the body in which the blood circulates. How then, it may be replied, is it that particular parts only are affected, since medicinal molecules are in contact with every part? We do not pretend to account for this circumstance. Every one is familiar with the fact that carbonic acid may be applied to the stomach in large quantity with impunity; whereas, if taken into the lungs, it acts as a narcotic poison. The urine has very little effect on the bladder, but if introduced into the cellular tissue, gives rise to violent inflammation.

I have already alluded to another objection to this theory—namely, that injuries sometimes produce the same symptoms as poisons. But it must be recollected that in a large number of instances injuries do not produce the same symptoms; and in those cases where the effects of the two are analogous, I see no difficulty in assuming that there are two modes of affecting the nervous system.

The most important objections that have been advanced against the operation of medicines through the circulation, by local contact with the tissues, are those founded on the experiments of Messrs. Morgan and Addison. Of all their experiments, the following are, I conceive, the strongest against the theory under examination:—

The jugular vein of a full-grown dog was secured by two temporary ligatures; one of which was tied round the upper, and the other round the lower part of the exposed vein. The vessel was then divided between these two ligatures, and the truncated extremities re-connected by means of a short brass cylinder or tube (fig. 13,) within which was placed a portion of woorara, of the size of a grain of canary-seed (fig. 12.) Both the temporary ligatures were then removed (fig. 14), the accustomed circulation through the vessels was re-established, and in forty-five minutes the animal dropped on the ground, completely deprived of all power over the muscles of voluntary motion: in two minutes, convulsions and respiration had entirely ceased. This result was to be expected, whatever theory be adopted.

Fig. 12.

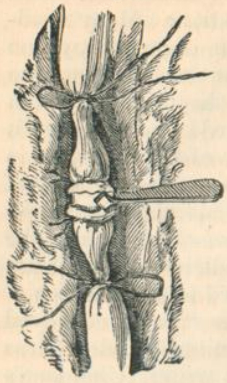


Fig. 13.

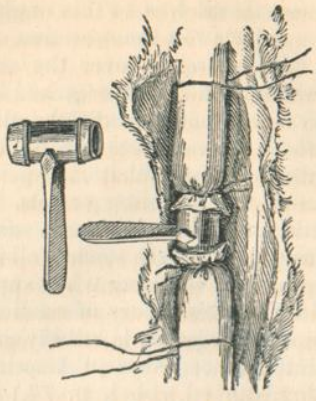


Fig. 14.

In another experiment two temporary ligatures were applied to the jugular vein, as in the former case. A cylinder of quill, containing a little woorara, was then introduced into the vein between the two ligatures; another ligature was then applied (fig. 15), and the upper temporary ligature removed (fig. 16). In the space of 108 seconds after the removal of the ligature, the animal dropped in convulsions, as in the former case, and expired in 3¼ minutes. Now, in this experiment, the direct entrance of the poisoned blood into the heart, &c. was prevented by the lower ligature: hence, if this poison operated by contact with the brain, a greater length of time was necessary for its effects to be produced; inasmuch as the circulation was no longer going on through the trunk of the jugular itself, and, therefore, if the poison acted by actual contact, it must have got into the system by the vessels of the vein.

Fig. 15.

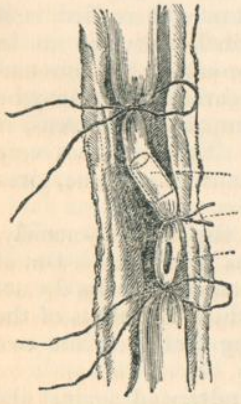
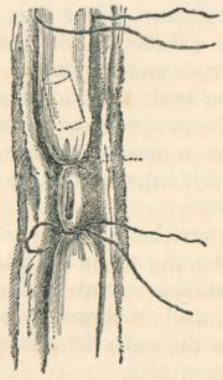


Fig. 16.



This experiment, however, cannot be regarded as conclusive. For although the "result is certainly different from what might have been anticipated, on the supposition of the circulation of the poison in the blood being essential to its action, yet we cannot regard it as a conclusion against that supposition, unless it were shown that the poison, when the ligature above it is removed, and when it mingles itself with the stream of blood in the vein, does not taint this blood as far back as the next anastomosing branches, and so make its way forward to the heart. That this is not the effect of removing the farther ligature, is not shown by these authors; and their other experiments in favour of their peculiar doctrine of the mode of action of poisons, we have no difficulty in pronouncing to be inconclusive."—(See a criticism in *The British and Foreign Medical Review*, vol. v. for Jan. 1837.)

3. *By acting on the lining membrane of the blood-vessels.*—Messrs. Morgan and Addison contend, that when poisons are "introduced into the current of the circulation in any way, their effects result from the

impression made upon the sensible structure of the blood-vessels, and not from their direct application to the brain itself."—(*Essay*, p. 60.) The proofs adduced in support of this theory are, first, "the extreme susceptibility of the inner coat of a vein, when exposed to the action of a poison," as shown by the experiment related at page 26: secondly, that woorara acts on the brain as quickly when injected into the femoral, as when thrown into the carotid artery: thirdly, that woorara, applied to the cut surface of the cerebrum, caused no symptoms of poisoning: fourthly, that by establishing a complete double circulation between the carotids of a poisoned and of a sound dog, the latter does not become affected.

Of all these "proofs," however, the only important, though not unobjectionable one, is the first. The second and third are merely negative; their object being to show that poisons do not act by pervading the structure of the part, and to the fourth I have before offered some objections.

In conclusion, then, I would observe, that while Messrs. Morgan and Addison have thrown some doubt over our previously received notions on the operation of medicines, they cannot be admitted to have established their own hypothesis; and further experiments are still required to settle this doubtful question.

6. *Operation of Medicines by Nervous Agency.*

Messrs. Morgan and Addison contend, "that all poisons, and perhaps, indeed, all agents, influence the brain and general system, through an impression made upon the sentient extremities of the nerves, and not by absorption and direct application to the brain." Müller, on the other hand, asserts, "that before narcotic poisons can exert their general effects on the nervous system, they must enter the circulation."

Difficulties are met with by exclusively adopting either of these opinions. The operation of some medicines seems to be best explained by supposing the previous absorption of these agents, while that of other substances appears to be most satisfactorily accounted for by presuming they affect the nerves independently of absorption.

Proofs that some substances act independently of absorption.—Several circumstances lead us to infer that, in some instances, substances act on the general system without necessarily undergoing absorption.

a. The instantaneous operation of some Poisons.—One drop of pure hydrocyanic acid, says Magendie, placed in the throat of the most vigorous dog, causes it to fall dead after two or three hurried inspirations. If the nose of a rabbit be introduced into a receiver filled with hydrocyanic acid vapour, the animal drops dead instantly. Sir Benjamin Brodie once happened to touch his tongue with the end of a glass rod which had been dipped in the essential oil of bitter almonds; scarcely had he done so, before he felt an uneasy, indescribable sensation at the pit of the stomach, great feebleness of limbs, and loss of power to direct the muscles, so that he could hardly keep himself from falling. These sensations were quite momentary. In the cases now quoted the rapid action of the poisons seems almost incompatible with the idea of their absorption. Müller, however, thinks otherwise, and asserts they are explicable on the theory of absorption by imbibition. "The rapid effects of prussic acid," he observes, "can only be explained by its pos-