without much benefit. The calomel which had been continued up to this time, had not affected the gums, and none of the remedies which were tried produced more than a temporary relief. She continued to get worse in spite of most careful attention, the pain in the abdomen continued severe, the head became involved, and after a week's more suffering, she died.

Post Mortem Examination.—A large quantity of whey-coloured fluid, mixed with flakes of lymph, filled the peritoneal sac, and a layer of lymph covered the intestines. The peritoneum covering the uterus was highly inflamed. The substance of the uterus exhibited marks of inflammation, and its internal surface had a gangrenous appearance at several points.

I shall conclude by mentioning, that since the establishment of the Hospital, 1012 women have been attended, of whom six have died, or rather less than 1 in 168. There have been eight cases of turning, or 1 in 121; and seven crotchet cases, or 1 in 138.

104, STEPHEN'S-GREEN.

ART. V.—*On the injurious Effects of the Pharmaceutical Treatment of Digitalis Purpurea in forming its Tincture; with a Proposal for a more efficacious Formula.* By M. DONOVAN, Esq.

THE singular control which digitalis purpurea is capable of exercising over the circulatory system has raised it to a high rank amongst therapeutic agents.

Its effects, however, are not always equally energetic, for we frequently find it to disappoint the practitioner; and hence very different opinions have been entertained concerning its powers.

Such disappointments have rendered it an object with chemists to discover and isolate the active ingredient in this plant, to ascertain its properties, and to determine the means of producing from it preparations of unvarying medicinal efficacy. With this view, the Society of Pharmacy of Paris, in 1835,

offered a prize of 500 francs for the best answer to the question, “does there exist in *digitalis purpurea*, one or more proximate principles, to which the medical properties of this plant may be attributed?” Notwithstanding the labour bestowed on the investigation at different times by several eminent persons, the subject is still involved in obscurity. In the absence of precise knowledge of the active principle of *digitalis*, it will be of use to point out some errors in the pharmaceutic management of the plant, which, I conceive, give origin to many of the disappointments above alluded to; to offer some suggestions as to the mode of prevention; and to introduce such improvements as have been suggested to me by the labours of those chemists that have investigated the constitution of this important medicine.

It is well known to all medical readers, that about fifteen years since, the existence of an alkali in this plant was announced by M. Leroyer of Geneva, to which he referred its poisonous qualities. By a process not necessary here to describe, he separated from foxglove leaves a bitter deliquescent matter, which slowly restored the blue colour of reddened litmus paper, and which Prévost found to be capable of assuming the form of minute crystals. To this substance the name of *digitaline* has been given. It possesses the properties of an active poison: a grain of it introduced into the abdomen of a rabbit, in a few minutes began to retard the respiration and circulation; at length the animal, apparently falling into a tranquil sleep, died. A solution of half a grain being injected into the circulation of a cat, the same symptoms supervened, and death ensued in fifteen minutes. A grain and a half introduced into the circulation of a dog, killed him in fifty minutes.

Thus this substance undoubtedly *contains* the active principle; but it has been proved that *digitaline* is neither a proximate principle, nor of an alkaline nature, as will appear by comparing the experiments of Leroyer, Planiava, Dulong of Astafort, Haase, Planizza, Pauguy, Welding, Brault, and Poggiale.

Dr. Graves, of Dublin, was the first who called in question the alkaline nature of digitaline, in a paper which he placed in my hands a few months after Leroyer's announcement ; and he showed that when certain precautions are taken, this substance does not manifest any alkaline reaction.

M. Dulong of Astafort, made an examination of foxglove leaves in 1827, which convinced him that they do not contain a peculiar alkali. He arrived at the following conclusions :

1. Digitalis contains a bitter matter, which possesses peculiar properties, and which ought to be regarded as the active principle of the plant.

2. This matter does not present the characters of vegetable salifiable bases.

3. Digitalis does not contain a base analogous to strychnine, although the fact has been asserted in Sweden.

M. Dulong concludes with an important fact, which, however, has attracted but little attention. He found that this bitter active principle of digitalis, forms with infusion of galls an insoluble precipitate. Hence he concludes that watery infusion of nutgalls will act as an antidote to the poison of digitalis, especially if used in conjunction with the means already known.*

In 1835, the result of the experiments of MM. Brault and Poggiale was published by these chemists. The following is the substance of their memoir :

We have often (say they) repeated all the processes to prepare this pretended digitaline, and have never yet been able to procure it. The process of M. Pauguy consists in boiling digitalis in distilled water sharpened with sulphuric acid, treating the decoction with calcined magnesia, and the dried precipitate with alcohol. The latter solution when distilled will deposit a white crystalline substance in small needles. Without fear of falsehood we affirm that this process furnishes *no product whatever*.

* Journal de Pharmacie, XIII. p. 379.

We have repeated the process of M. Leroyer different times, and, like that chemist, we have always obtained a heavy brown substance possessing an extremely acrid, bitter taste. This is the digitaline of M. Leroyer. Our examination has proved that this is an extract composed of a great quantity of chlorophylle, much resin, a fatty matter, and different salts of lime and potash.

M. Leroyer relates, that M. Prévost has seen crystals of digitaline by the aid of the microscope. We affirm, on the contrary, that these are salts of lime and potash which the digitalis contains.

After these reflections we have nothing to add on the labours of M. Planiava. His digitaline is nothing but an extract composed nearly of the same principles as that procured by the process of M. Leroyer.

It results from the preceding facts, that the pretended digitaline has never been obtained; that the digitaline of M. Leroyer is composed of chlorophylle, resin, a fatty matter, and some salts of lime and potash: and that the process of M. Pauguy furnishes absolutely no substance at all.

We may be permitted to believe that digitalis leaves are composed of chlorophylle, resin, fatty matter, amidon, vegetable fibre, gum, tannin, salts of lime and potash, volatile oil, and oxalate of potash.

We believe, (they continue,) that the purgative and diuretic effects of foxglove are attributable not to a peculiar principle, but to the union of all the substances which compose it, and especially to the resin. This resin has a bitter taste, is acrid, and almost corrosive. If one places on his tongue a very small portion of it, he experiences a very painful sensation of heat, and constriction in the throat. Two grains of this resin swallowed, powerfully irritate the stomach. It is very soluble in warm alcohol; it is soluble in ether and volatile oils; insoluble in water, but soluble in water sharpened with any acid.

In conclusion, MM. Brault and Poggiale observe, that the

fecula deposited by foxglove juice, has been very much employed in medicine, because the resin it contains communicates to it the properties of *digitalis*.*

At a meeting of the Society of Pharmacy, February, 1835, M. Pelletier stated that he had observed and confirmed the most important facts in the foregoing memoir.

From all these investigations it is plain, that in *digitalis* a principle or combination of principles exists, which in minute quantity is capable of producing the deadly effects of this medicine. Leroyer says it is an alkali ; Dulong says that it is a bitter principle of a reddish-yellow colour, and of an excessively bitter taste ; that it softens by heat, and draws into threads like resin, becoming dry and brittle when cold : that it is slightly deliquescent in the air ; and that it is soluble in water and alcohol, although insoluble in sulphuric ether. Brault and Poggiale conceive that the purgative and diuretic effects depend chiefly on a resin, but also on the united agency of all the other principles. Haase also supposes the resin to be the active ingredient.

In the present state of our knowledge of this subject, it is not in our power to determine which of these views is the correct one ; and hence in the modes of conservation and extraction which we employ, it is prudent to have regard, if possible, to all of them, and not to rely upon any one of them in particular. Thus, were we to admit of the statement of Dulong, that the active principle of foxglove is insoluble in ether, we must conclude that the choice of ether as a menstruum is improper, that the tincture formed by it is powerless, and that the active principle is excluded. Yet the French Codex of 1816, as well as that of 1835, directed the ethereal tincture of *digitalis* : so also the Pharmacopœia Belgica, the Pharmacopœia Hannoverana, the Pharmacopœia Regni Poloniæ, (1817,) the Pharmacopœia Borussica, and the Pharmacopœia Saxonica ; it is also sanctioned

* Journal de Pharmacie, XXI. p. 130.

in the Pharmacopœia of Brugnatelli, in that of Cadet de Gassicourt, and of Van Mons. But if we rely on the affirmation of Brault and Poggiale, that the active principle is soluble in sulphuric ether, the foregoing authorities have given adequate formulæ. Again, if the active principle is insoluble in water, as asserted by Brault and Poggiale, though contradicted by Du-long, the decoction and infusion of digitalis of the American and European Pharmacopœias are worthless ; and the tinctura digitalis aquoso-ætherea, added by Niemann to the Dutch Pharmacopœia, and also introduced into the Pharm. Man. Anvers, 1812, is doubly absurd, as it employs both water and ether.

In place, therefore, of relying on this or that authority, when they differ so widely, as to the principle on which the medicinal powers depend, the more prudent course will be to use such process of extraction only as will deprive the subject of the greatest number of its principles, care being taken that none of them shall be excluded unless such as are manifestly inert.

In the following observations I shall confine myself to the consideration of the tinctures of digitalis at present in use, reserving other preparations for some future communication.

The alcoholic tinctures of the pharmacopœial processes vary in the strength of the alcohol. In the British isles, however, that made use of is proof spirit. Let us therefore inquire, how far this menstruum is effectual, and whether the previous treatment of the plant occasions important changes in its powers.

The first step towards forming the tincture is to dry the leaves, and this process is differently directed by the colleges. We have no experiments on record of the results of various methods of drying, we are therefore left to draw our conclusions from analogy.

We know that in the case of *some* active medicines, drying, especially by heat, effects considerable changes. White briony, a highly acrid and poisonous substance when recent, becomes comparatively mild by drying : and I have found that its chemical constitution is so far altered, that although an infusion of

the fresh root affords a precipitate with tincture of galls, the infusion of the root dried, even without heat, does not.

The recent root of *arum maculatum*, if chewed, will blister the mouth ; and if rubbed on the hands will excoriate them : yet when dried, it is not only innoxious, but is used as an article of food.

The bitter Cassava root, “ when raw, is a most fatal poison to man and beast ; but prepared by fire (baking) it is very safe, and the natural bread of the Indians and several Europeans.”*

Garlic is highly acrimonious ; by drying it loses this quality ; the same observation applies nearly to the whole onion tribe. The acrid seeds of the *Palma Christi* become mild by drying. *Mezereon* bark, if applied to the skin while recent, raises a blister : but by drying, it loses this quality.

Many other instances might be adduced : it is true that they *prove* nothing in the case of *digitalis*, and they may be opposed by the known efficacy of *digitalis* powder when well preserved. But do they not render it highly probable, that were it not for the injurious effects of drying, this plant might be much more active, much less liable to disappoint the practitioner than it is well known to be ; and perhaps universal in its control over all constitutions.

Several more direct evidences may be adduced in support of the opinion, that the powers of the growing plant are different from those of the dried leaves. When first taken from the ground, the leaves are strong, erect, and vigorous ; in a short time, an hour is sufficient, they become collapsed and limber, lose their firmness, grow flaccid and droop.

This is the first symptom of change. If an adequate heat be now applied, the smell of the plant is extensively diffused throughout the apartment, which proves the dissipation and loss of some ingredient of the leaves, probably the volatile oil. The

* Stedman's Narrative, i. 382.

brilliant green colour on the surface is also changed for a dusky olive. It is not easy to conceive, that such striking changes in the physical constitution of the plant can take place without some modification of medicinal power.

But if to these sources of change we add, that arising from the very bad mode of drying which the pharmacopœias inculcate, it can scarcely be considered doubtful, that much injury is sustained. The Dublin Pharmacopœia directs the herb to be enclosed in paper bags, exposed to 90° or 100° for an hour, and then dried on a wire-gauze. The London Pharmacopœia orders leaves to be lightly strewed, and hastily dried by a gentle heat. The Edinburgh Pharmacopœia merely desires, that such small quantities as can be hastily dried, shall be exposed to the moderate heat of a fire hearth; and adds the following test, “*sic enim eorum vires optime servantur, cujus indicium est color nativus quam perfectissime constans.*”

This preservation of the green colour is universally admitted as the test of good drying; and when the green colour is destroyed, it is conceived that the medicinal efficacy of the subject is not to be relied on. It is a convenient test; for without it we should in every case have recourse for proof to the actual exhibition of the medicine.

Now by the process of the Dublin Pharmacopœia the colour is exceedingly impaired. There can be nothing more detrimental to it than the heating for an hour, in a bag at the temperature of 90° or 100°. I have over and over convinced myself, by processes much varied, that to allow the steam of the leaves to act on them for so long a time, or at all, is injurious to colour. I have dried these leaves sometimes in paper bags before the fire, sometimes stratified on large sheets of paper before the fire, or in the sun, or air, sometimes in a baker's oven, sometimes stratified on a wire-gauze over a sand-bath, or on a floor in the shade, and have sometimes hung them in bundles in a room, in which burned a fire; yet in no case did I ever, by these processes, preserve the brilliant green in the leaves, which

it is their nature to retain under a different management. Yet these are all the methods directed in the pharmacopœias, and practised by herb-dealers, druggists, and apothecaries. For proof of the injury done by these methods of drying, I refer to the powder of foxglove, procurable in commerce, the colour of which is far inferior to that which it is possible to obtain by adopting the process, which in some future communication I may describe.

It appears, therefore, that every step, from the collection to the drying, occasions deterioration. The softening of the substance of the plant when pulled, the expulsion of the volatile oil, or other odorous substance during the drying, and the change of colour owing to bad methods of exsiccation, are the sensible evidences of deterioration, and they are strengthened by the analogies which have been adduced. If to these injuries we add, that arising from the long delay, generally a week, nay often a fortnight, from the first collection to the final drying, there can be little doubt, that the plant sustains a great deal of injury.

The following observations of a competent judge correspond with the opinions here entertained :—"comme par le dessiccation, certaines plantes perdent une partie de leurs principes les plus volatils, ou subissent des modifications dans leur nature intime, il est certain que leur action médicale ne doit pas être la même qu'avant leur dessiccation. On doit en conclure qu'il est des teintures qui ne jouissent pas toujours des propriétés primitives des substances dont elles sont composées. Ce fait est d'autant plus à considérer, que depuis que la dessiccation des plantes a été en grande partie confiée à des personnes étrangères à la pharmacie, ces substances sont livrées au commerce dans un état de deterioration véritablement pénible à constater."*

If two tinctures be made, one with proof and the other with

* Bulletin des travaux de la Société de Pharmacie de Paris, Octobre, 1830.

rectified spirit, on equal quantities of the same coarse powder of foxglove ; the former will, after equal digestion, be brown, and the latter a brilliant green : the taste of both will be exceedingly bitter. If the residue of both be filtered off, and an equal quantity of rectified spirit be digested on each, the residuum of that on which proof spirit had been previously digested will afford a brilliant green tincture, and the other a tincture of pale hue. Thus the green matter of the leaf is but little soluble in proof spirit, although largely soluble in rectified spirit. We do not know whether this is merely chromulite, or whether it is this substance, combined with the active principles, if there be more than one ; and hence, in this state of uncertainty, it is prudent to retain the green matter. The resin, which is supposed by some to be the medicinal agent, the essential oil, the fixed oil, the fatty substance, and the bitter principle, are all soluble in rectified spirit ; but we are not so certain that they are equally soluble in proof.

This point settled, the plan which I propose is easily executed : it requires no skill, and can scarcely fail, if common care be taken. It consists in plucking the proper leaves off the living plant on the spot where it grows, instantly throwing them into the strongest alcohol, digesting for six weeks, pressing out the tincture, and filtering it. Here all the sources of deterioration are obviated, and we preserve the virtues of the recent plant unimpaired.

The ratio of the recent plant to the rectified spirit may be so contrived that the resulting tincture shall correspond with the ratio of the dried plant to the proof spirit as indicated in the Dublin Pharmacopœia.

I found from a mean of four trials that 100 grains of digitalis leaves, of a moderate size, gathered in dry weather, and immediately dried in a well-regulated fire-heat, lost seventy-nine grains of water. The same experiments made on small leaves

proved a loss of eighty-three grains for every hundred. Thus the mean loss of leaves of a moderate and small size is eighty-one grains on every hundred; and the numerical strength of the dried leaves is to that of the recent as five one-quarter to one. Hence ten ounces and a-half, Troy, of the recent leaves, would be equivalent to two ounces dried; and there would remain eight ounces and a-half by weight, that is 8.94 ounces, by measure, of water. If to this quantity of water contained in the recent plant we add 8.74 ounces of alcohol (0.814,) we shall have seventeen ounces and a half by measure of proof spirit, allowing for condensation, (instead of the sixteen ounces indicated in the pharmacopœia for two ounces of dried foxglove,) which is one ounce and a half too much. But if ninety grains of powder of foxglove be added, the whole will be of the pharmacopœial strength, so far as ratio of the ingredients is concerned. But the quantity of liquid being inadequate to cover the leaves, the bottle containing the ingredients should be digested for a month, one day standing on its bottom and the next inverted on its top.

The resulting tincture will be of an olive-brown colour, because the red colouring matter, observed by Welding, will only be dissolved, and the chromulite will not. This must happen while we adhere to the ratio of the colleges. But we can obtain a brilliant green tincture by regulating the ratio so that the menstruum will be reduced to the strength of rectified spirit (0.840).

In order to do this, let ten ounces and a half, Troy, of leaves be pulled from the growing plant, and plunged into a bottle containing two pints and three-quarters (wine-gallon measure) of alcohol 0.815. The strength of the alcohol will be reduced by the water to the strength of rectified spirit (0.840), and after the proper digestion, a brilliant green tincture will result, as perfect as it is possible to procure it. The strength of this tincture, compared with that produced by the

process of the Dublin Pharmacopœia, will be, so far as ratio is concerned, as one to three, and hence it might be given in three times the quantity for a dose. But as there is every reason to believe that its strength is incommensurate with this ratio, it might be prudent to begin with the same doses as have been always employed.

In this case the leaves will be covered by the alcohol ; but a month's digestion in a warm place will be required, with frequent agitation.

The defects of the tincture of digitalis, made according to the British Pharmacopœias, have been fully appreciated in other countries, and we find that efforts have been made to remedy them. The ethereal tincture of the Codex Français, (both 1816 and 1834,) as well as of some other continental pharmacopœias, is, perhaps, intended to obviate the inefficiency of the British formulæ, but the solvent power of ether on the active ingredient is rendered very doubtful by the contradictory statements which have been made on this subject.

The Dresden Pharmacopœia contains a formula, the object of which seems to be the attainment of the same advantages as are contemplated by mine. The recently expressed juice of foxglove is to be mixed with an equal weight of spirit of wine, and the mixture filtered. But the foregoing pages contain my reasons for believing it doubtful that the juice possesses all the qualities of the leaves, and that if it did, the feeble alcohol employed would not be competent to hold them dissolved. A formula for the preparation of tinctures of this kind has been given in the Bulletin des Travaux de la Société de Pharmacie for 1830.

In conclusion, I am compelled to believe, that our tincture of digitalis is far from being the best preparation of which the plant is susceptible: and I suggest to practitioners a trial of the process given in this communication. This trial should not be made by apothecaries in compounding prescriptions of physicians or surgeons: they are bound to the pharmacopœial pro-

cess, and it would be great impropriety in them to substitute any preparation of a more active nature than is there indicated, unless with the full knowledge and approbation of the prescriber.

11, CLARE-STREET, DUBLIN.

ART. VI.—*Observations on the Purulent Ophthalmia of New-born Infants ; on the Cause of the Disease ; its Progress in the Eye ; and Manner the Destruction of the Organ is sometimes effected by it ; as also of its Treatment.* By HUGH CARMICHAEL, A.M., Member of the Royal College of Surgeons in Ireland, one of the Surgeons of the Coombe Lying-in Hospital, and formerly of the Dublin Eye Infirmary.

THE eyes of children, a short time after birth, are liable to become the subject of an ophthalmia, which, if it do not subside of itself or yield to the intervention of art, terminates in the destruction of vision, attended generally with considerable deformity.

A profuse discharge of purulent matter being the most prominent feature of the disease, it has thence, coupled with the period of life at which it occurs, obtained the name of purulent ophthalmia of new-born infants. The correctness of this term has, however, been questioned by writers, the principal source of the danger (the inflammation) being thereby overlooked while the attention is directed to a symptom comparatively of but little importance, (the discharge,) and whose presence is productive of inconvenience rather than any thing very injurious to the eye.

The disease, however induced, is, after its formation, to be regarded as of an inflammatory description. The cause of its occasional unfortunate termination is also the result of inflammation and its consequences on the cornea, which, as I shall endeavour in the sequel to shew, is not only liable to be more easily in-