Received May 18th, 1865.

Since the above note was sent in to the Society, I have completed the demonstration for the 7th degree, and in the course of the inquiry have had occasion to consider the conditions to be satisfied in order that a rational function of x, with r equal roots a, may undergo no loss of real roots for any assigned variation imparted to the function: for the theory of the 7th degree the case of three equal roots has to be considered, and the conditions in question are that the variation itself may contain the equal root a, and that its first differential coefficient may have the contrary sign to that of the third differential coefficient of the function which it varies when a is substituted for x—a theorem which is, of course, capable of extension to the case of an equation passing through a phase of any number of equal roots*.

II. "On the Application of Physiological Tests for certain Organic Poisons, and especially Digitaline." By C. Hilton Fagge, M.D., and Thomas Stevenson, M.D. Communicated by J. Hilton, F.R.S. Received May 4, 1865.

(Abstract.)

As the chemical processes for the detection of certain organic poisons are very inconclusive in their nature, and as many of these agents produce effects of a most remarkable kind on the lower animals, it is not surprising that their physiological action should have been employed as a test for their presence. Thus Dr. Marshall Hall suggested as a means of discovering strychnia, the tetanic symptoms which that alkaloid causes in frogs; and quite recently MM. Tardieu and Roussin produced a large mass of physiological evidence, in a French "cause célèbre", in which digitaline was believed to be the poison used.

Those who have recommended the employment of evidence of this nature have always relied on the similarity between the symptoms observed in the case of supposed poisoning during life, and the effects obtained on the lower animals by the extract believed to contain the toxic agent; and as the action of poisons on man and on the lower vertebrata is certainly not always the same, the value of these physiological tests has been much disputed, and is not now admitted by most authorities in this country. It appears to us, however, that physiological evidence may be made independent of any relation of this kind. It is sufficient that the action of the

* The above is on the supposition that one of the three equal roots remains unaffected in magnitude by the variation, whilst the other two change. If all three are to change simultaneously, infinitesimals beyond the first order and with fractional indices have to be brought into consideration; in that case, on making $x=a$, the variation need not become absolutely zero, but must contain no infinitesimal of the first order. And a further limitation becomes necessary in addition to the conditions stated in the text, in order that no loss of real roots may be incurred in consequence of the variation.

substance believed to contain the poison on the animal experimented on be identical with the known effects of that poison *upon the same animal*, and that these effects be capable of being produced by no other agent or, at any rate, only by a limited number of other agents.

In this spirit we have conducted a series of investigations, with reference to the detection of digitaline and of certain allied substances. We selected that poison, not only because of the interest which attaches to it at the present time, but also because the chemical tests for it are peculiarly inadequate. The animals which we employed in all our experiments were frogs. Their sensibility to small quantities of poison, the fact that they are but little liable to be affected by fear or other accidental circumstances, and the independence of their organs, which makes it possible to determine with accuracy the nature of the effects produced, have rendered them better adapted for this purpose than any other animals; and the objection ordinarily urged against their use, that the action of poisons on them is often different from that of the same substances on the higher animals, has no validity when the question of physiological evidence is looked at from our point of view.

It has been expressly denied, by those who have advocated the use of physiological tests, that animal extracts, such as those obtained from the contents of the human stomach, or from vomited fluids, could in themselves be poisonous to the lower animals. We thought it desirable, however, to make some direct experiments upon this point; and, to our surprise, we found that in almost every instance the toxic action of such extracts was most decided and unmistakeable. The effects produced were indeed very different from those caused by digitaline; and we think that we have been able to distinguish quite clearly between them. Still, the recognition of the fact that these extracts exert a poisonous action, independently of the presence of any of the ordinary toxic agents, must have an important bearing upon the application of physiological evidence. Unless some points of difference should hereafter be discovered, it will render impossible the detection of many vegetable substances (among which we may mention lobelia, emetina, veratrum viride, and delphinium staphisagria) by their physiological effects. And it makes invalid (at least so far as frogs are concerned) all evidence of this kind, in which the state of the heart is not more particularly described than has hitherto been the case, so far as the frog-test for strychnia is concerned; on the other hand, though this was not the primary object of our inquiries, we may remark that tetanic spasms were produced by none of the numerous substances with which we experimented, except veratrine and theine. It is of course well known that other agents, and notably some of the constituents of opium, produce tetanus in frogs; but on the whole our experiments lead us to hope that this test will hereafter be found of more value than is now generally supposed to be the case.

We have devoted a considerable number of experiments to the solution

of the practical question, whether it be possible to obtain the characteristic effects of digitaline, not only from the extracts of liquids to which it had been artificially added, but also from extracts of the stomach-contents and vomited matters of dogs poisoned by that substance. The results of these experiments were perfectly satisfactory; and we think that our observations show conclusively that there is no difficulty in obtaining from these complex mixtures physiological effects identical with those of a pure solution of digitaline.

Far more difficult to decide than the question of practical applicability, is the question as to the theoretical accuracy and conclusiveness of the physiological test for digitaline and the allied poisons. To this question we do not venture to give a positive answer. Our experiments justify, as we think, the hope that this test will be hereafter found of very considerable value in aiding in the detection of these substances; but it can be only by the combined labours of many observers, and not merely by one series of experiments, that this point can be finally settled.

The following are the conclusions at which we have arrived, and which are deduced from our own experiments in every instance, except where the contrary is expressly stated, under heading 2.

1. Digitaline is one of a small class of substances of which the action on frogs appears to be identical. As the heart is the organ primarily affected by them, they may be called cardiac poisons, so far as frogs are concerned.

2. These substances are, besides digitaline, the *Upas Antiar*, the *Helleborus viridis*, and perhaps other species of *Helleborus*, the *Tanghinia venenifera*, the *Dajaksch* or arrow-poison of Borneo, the *Carroval* and *Vao*, South American arrow-poisons, and the *Scilla maritima*. Of these we have ourselves experimented only with digitaline, antiar, the *Helleborus viridis* and the *H. niger*, and the *Scilla*; and we believe that we are the first observers who have recognized the identity of the action on frogs of the last of these plants with that of the other substances placed in this group. Besides digitaline, only two of them, namely, the *Helleborus* and the *Scilla*, are likely to be the subject of medico-legal investigation in this country, and that but rarely.

3. The characteristic effect of each of these agents on frogs is the production of irregularity of the heart's action, followed by complete stoppage of its pulsations; the ventricle remaining rigidly contracted, and perfectly pale, after it has ceased to beat; the muscular power of the animal being at this time unimpaired, and persisting as long as in frogs in which the circulation has been stopped by other means, such as ligature of the heart.

The irregularity in the heart's action, which precedes its stoppage, under the influence of these poisons is peculiar. The rhythm is but little altered; and the beats are not necessarily diminished in number, as has been supposed. Sometimes, however, the ventricle makes only one pulsation for two of the auricles, the number of its contractions being therefore lessened

by one half. More frequently the irregularity consists in one or more portions of the ventricle (especially the apex) becoming rigidly white and contracted, while the remainder of the organ continues to dilate regularly. When these yielding pulsations are small, a peculiar appearance, as if the wall of the ventricle formed crimson pouches or protrusions, is produced.

4. No other substance, except those mentioned above, has been found to produce this chain of effects, even in a single experiment. We have ourselves tried nineteen different substances, consisting of vegetable extracts and alkaloids. Of these, *emetina*, and the extract of the *Delphinium staphisagria* caused somewhat similar irregularity of the cardiac beats; but in frogs, poisoned by these agents, the muscular power was always lost before the heart had ceased to beat, and the ventricle stopped in the dilated, and not in the contracted, state.

5. When digitaline is applied endermically to frogs, the characteristic effect is invariably produced, if a sufficient quantity be used. This quantity no doubt varies with the size of the animal, but may be stated generally at $\frac{1}{100}$th of a grain. Quantities less than $\frac{1}{150}$th grain usually produce no effect, or at most only temporary irregularity of the heart's action, of a more or less characteristic kind. The result of the injection of doses larger than $\frac{1}{100}$th grain is to diminish the interval between the administration of the poison and the stoppage of the ventricular beats. This interval appears to be seldom less than six or seven minutes, however large the quantity of digitaline.

6. Very poisonous effects are produced in frogs by the endermic application of alcoholic or acetic extracts of matters vomited by patients, or taken from the human stomach after death. The extracts are less poisonous, if at all, to the higher animals.

7. The symptoms produced by these extracts in frogs are in marked contrast to those caused by the cardiac poisons. Like these agents, the animal extracts impair the action of the heart; but their tendency is to cause paralysis of its muscle, and stoppage in the dilated condition. At the same time, they generally destroy the muscular power of the animal.

8. The cause of the toxic action of these animal extracts has not been ascertained; it is probably not always the same, as the effects produced by different extracts are not perfectly similar. These effects are perhaps the result of the combined action of different substances. They are certainly not caused by bile or pepsine, and probably not by any substance in a state of decay.

9. The vegetable acids, when injected in sufficient quantity, stop the action of the heart more rapidly than any poison with which we are acquainted, the organ remaining distended with blood when it has ceased to beat. The toxic action of the animal extracts is not, however, caused by these acids; for the quantity of them contained in the extracts is too small, and the effect is not diminished by neutralization with an alkali.

10. When digitaline, in quantities of $\frac{3}{4}$–$1\frac{1}{4}$ grain, is added to vomited

matters, or to fluids taken from the human stomach *post mortem*, the extracts obtained from such fluids almost invariably produce on frogs the effects of digitaline.

11. This is due partly to the fact that the action of digitaline is generally more rapid than that of the poisonous constituents of the extracts themselves, but principally to the circumstance that it was necessary to give only small doses of the extracts containing digitaline, in order to get the characteristic action.

12. The method of dialysis fails in many cases to separate digitaline from complex organic mixtures which contain it; and this method is rarely of service in aiding the detection of this poison by the physiological test.

13. When digitaline was administered to dogs in quantities little more than sufficient to destroy life, the extracts derived from the matters vomited by these animals, or from the fluids contained in their stomachs after death (when vomiting was artificially prevented), were found in each of those experiments to produce on frogs unmistakeably the effects characteristic of the presence of one of the cardiac poisons.

NOTE.—Received 18th May, 1865.

We have now to add to the list of "cardiac poisons" the Manganja, an arrow-poison, brought from the Zambesi Expedition by Dr. Kirk. Our attention was directed to this substance, which is the fruit of an Apocynaceous plant, by Dr. Sharpey, who informed us of the results of experiments he had made on its action; and we owe to his kindness the opportunity of confirming his observations by our own experiments.

III. "On the Corrections for Latitude and Temperature in Barometric Hypsometry, with an improved form of Laplace's formula." By ALEXANDER J. ELLIS, F.R.S. Received May 11, 1865.

Adopting the notation in Table I. (p. 284), and the data of M. Mathieu (*Annuaire du Bureau des Longitudes*, 1865, p. 321), Laplace's hypsometrical formula, after some easy transformations, becomes

$$\begin{aligned} h_1 - H_1 &= [\log B - \log b - \cdot 00007 \,.\, (M' - m') \,.\,] \times [500 + A' + a'] \\ &\quad \times \left[\frac{18336}{500 \,.\, (1 - z \cos 2L)} \cdot \left(1 + \frac{15926}{6366198}\right)\right] \times \left[1 + \frac{h_1 + H_1}{6366198}\right] \\ &= [\log B - \log b - \cdot 00007 \,.\, (M' - m')] \times [500 + A' + a'] \\ &\quad \times \frac{36 \cdot 764}{1 - z \cos 2L} + \frac{h_1^2 - H_1^2}{R_1} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (a) \\ &= W \,.\, T' \,.\, G_2 + v_1 - V_1 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (b) \end{aligned}$$

In the last term in (*a*), $h_1 - H_1$ represents the product of the three preceding factors, $W \,.\, T' \,.\, G_2$; and z is left for the present undetermined.

If γ be the total increase of gravity in proceeding from the equator to the