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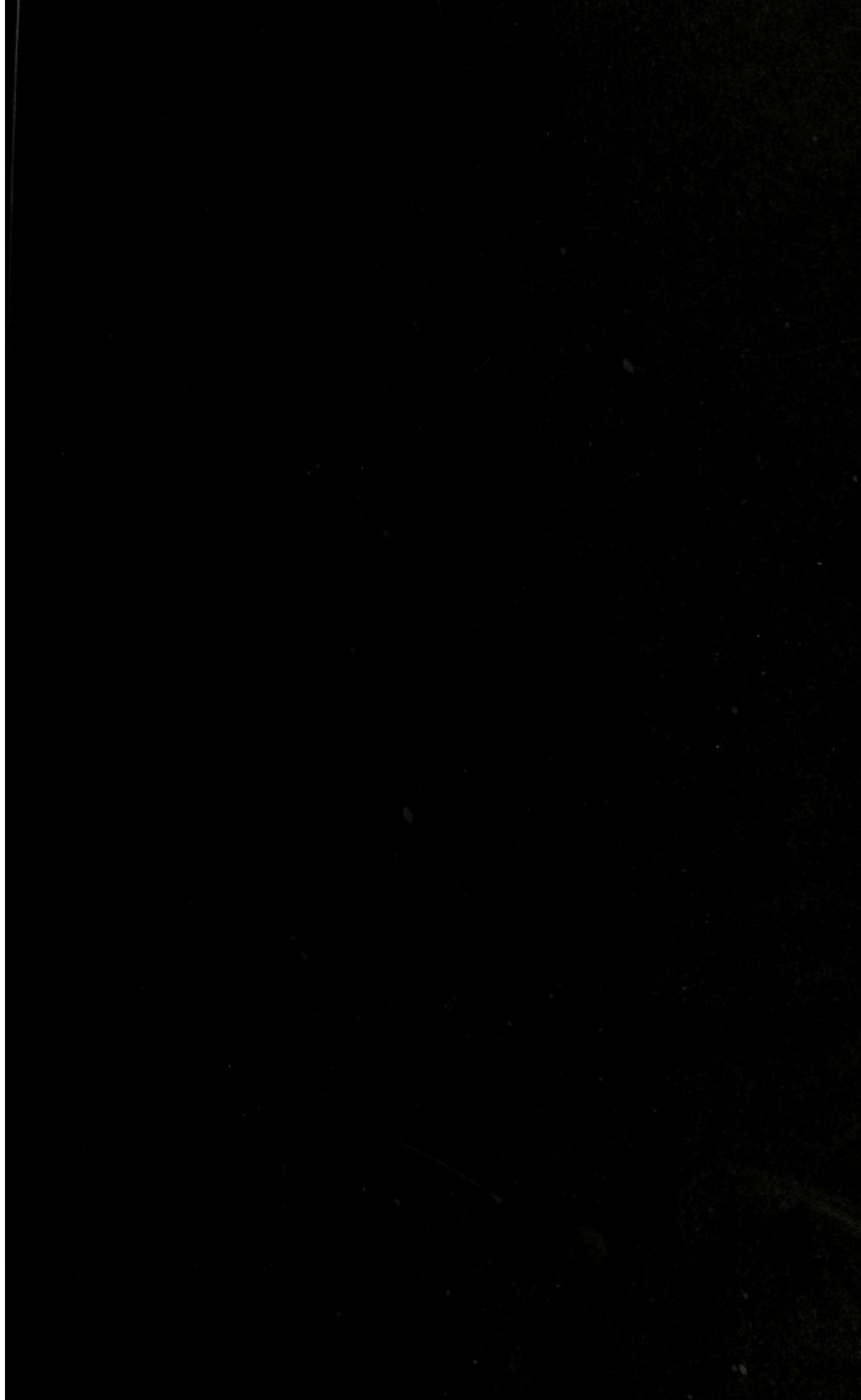
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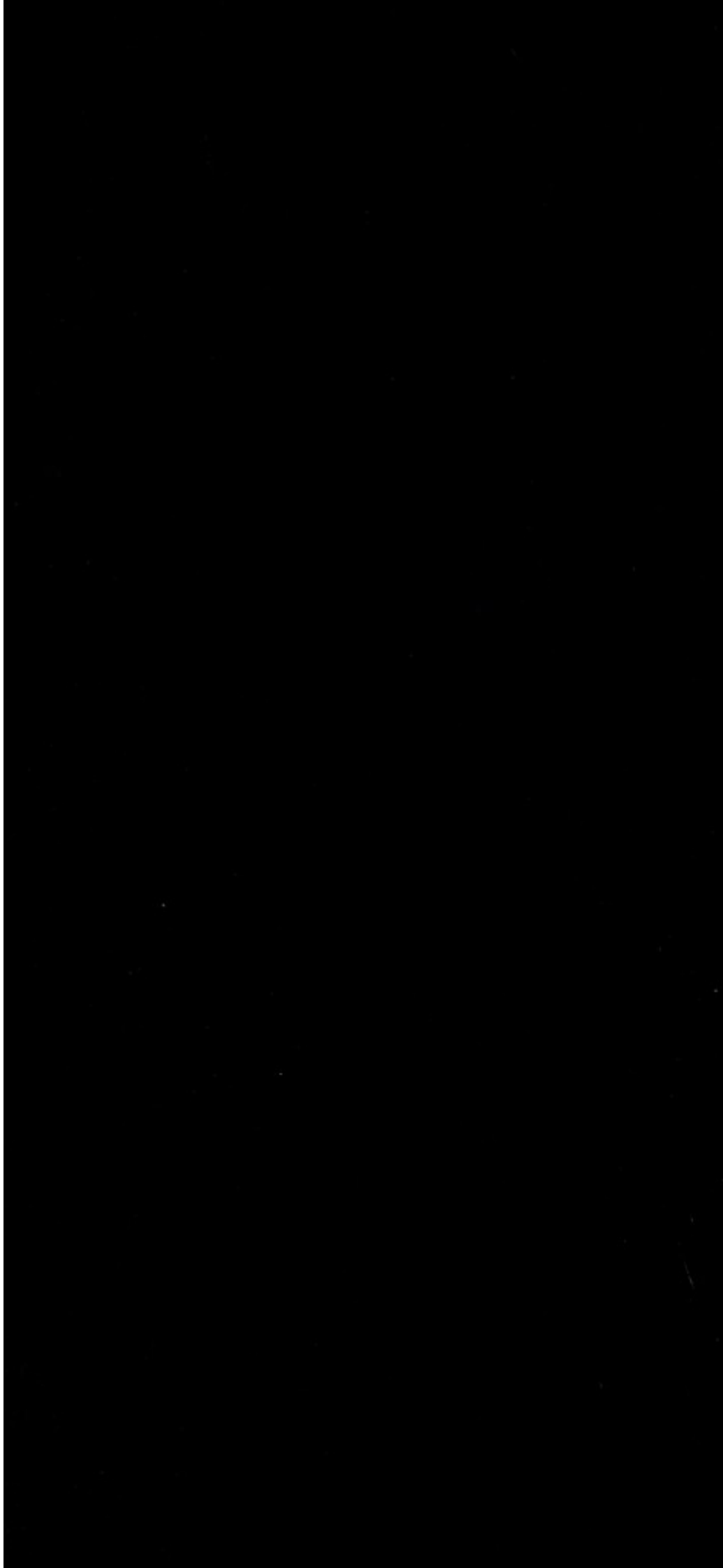
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11 The Author

ON THE
PHYSIOLOGICAL AND THERAPEUTICAL
EFFECTS

OF
COLCHICUM AUTUMNALE.

By ROBERT LEWINS, Junior, M. D.,
Member of the Royal Medical Society of Edinburgh, and of the Medical Society of
Paris, &c. &c.

[This communication is an abridgement of the Essay which the Harveian Society
honoured by presenting to the Author their Annual Prize.]

(From the *Edin. Med. and Surg. Journal*, No. 148.)

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CHAP. I.

PHYSIOLOGY AND PATHOLOGY

OF THE

COLLIGATED TISSUES

BY JAMES M. M.D.

London: Printed by J. B. Nichols, 1825.

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ON COLCHICUM AUTUMNALE.

THERE is no subject in the whole range of medical science of greater importance to the practical physician than an accurate knowledge of the precise action of potent medicines on the animal economy, and of their adaptation to the cure of disease.

The patient and laborious experimental trials that are essentially necessary to develop the therapeutical properties of medicinal agents, have retarded the progress of this department of science; and induced those who have directed modern medical opinion to cultivate more fascinating, but, to the practical physician, less profitable fields of investigation. The accuracy of this sentiment is palpably manifested by the works which have issued from the British medical press during the last twenty-five years, and by the condition of medical science on the continent of Europe, and especially in France, where we see the most consummate skill in diagnosis, but no corresponding activity in the employment of means to accomplish that which ought to be the grand object of the physician's solicitude—the prolongation of life, and alleviation of the pangs of disease.

In order that the physiological and therapeutical properties of any active medicine be rightly understood, it is indispensable to have an accurate knowledge of the effects it produces, when administered in large and small doses. Above all, it is necessary to ascertain the quantity which can be prescribed with safety.

That we were lamentably deficient on this essential point, with reference to *Colchicum autumnale*, is abundantly evinced by the remarks and prescriptions of medical writers. Indeed, it may be asserted that many highly respectable members of our profession are ignorant of the proper manner, and even of the dose in which this active medicine ought to be administered.

Dr J. Johnson, editor of the Medico-Chirurgical Review, at a public discussion a few years ago, expressed his disbelief that one drachm

of the tincture of the seeds given every three hours would produce a fatal effect.* The late Dr Duncan, in his Dispensatory, has stated that half an ounce of the tincture of the seeds is the proper dose,† and in Dr Spillan's work lately published, entitled a collection of Medical Formulæ, a draught, containing amongst other ingredients, half an ounce of the tincture of the seeds, is ordered to be given every sixth hour, Dr Elliotson prescribed half a drachm of the wine of the seeds of colchicum, to be taken three times a day for a period of three weeks,‡ and, in another case, he gave the same dose every eighth hour for several days together.§ Dr Armstrong recommends one, and even two drachms of the wine of the colchicum to be taken in the course of twenty-four hours, and continued for some time.|| Dr Barlow of Bath, certainly very high authority on this or any other medical subject, gives the following hazardous directions with regard to its employment. "It may be given either in full doses, so as to purge actively, or in divided doses, frequently repeated. One drachm, one drachm and a half, or two drachms of the tincture of the seeds should be administered at night, and repeated, if necessary, next morning. This quantity will generally purge briskly, but if it fail, another dose the following night will be pretty sure to succeed, at least, as far as my experience goes, I have seldom found it necessary to exceed these doses."¶ Other distinguished members of our profession have given equally dangerous directions as to the mode of administering colchicum. I may here also remark, that death resulted from a dose of two drachms of the wine of the seeds, given to a patient in a public hospital a few years ago. A fatal case is also recorded by Mr Haden in his translation of M. Magendie's Formulaire, where two drachms and a half of a tincture, made by infusing four ounces of the root in eight ounces of proof-spirit for three days, had been administered; and I may also allude to a case which fell under my own observation only a short time ago. On Sabbath, November 22, 1840, I had an opportunity of seeing W. D. aged 23, who had consulted a distinguished practitioner of Edinburgh, in consequence of pains in his extremities, and cough, from whom he received a prescription, of which the following is a copy:

Rx. *Vin. Sem. Colchici Vin. Antimon. a ʒi. ; Tinct. Hyoscyami, ʒss.*
M. S. A tea-spoonful to be taken three times a day, which is equivalent to one drachm of the *Vinum Colchici* daily. This quantity had been persisted in for a week regularly, with the most prejudicial effects. The patient laboured under violent diarrhœa since the second day after taking the medicine, and had he persevered in its use for twenty-four hours longer, it is probable he would have perished. His pulse was 170 in the minute; his strength most alarmingly reduced; he could only speak in a whisper; he

* See Lancet, Vol. xv. p. 698.

† See last edition of Edinburgh New Dispensatory, p. 953.

‡ See Lancet, Vol. xii. p. 540.

§ See Lancet, Vol. ix. p. 395.

|| See Lancet, Vol. vii. viii. p. 97.

¶ Cyclopædia of Pract. Medicine. Article Gout.

complained of great pain in the abdomen ; and the bowels had been moved upwards of twenty times in the course of the day. Astrin-gents, in various forms, were had recourse to in vain, until a combination of opium and acetate of lead was prescribed, which speedily checked the exhausting diarrhœa, and obviated the other mischievous effects which had resulted from the improper administration of the colchicum wine.

The effects of colchicum, when administered in larger and poisonous doses, are well exemplified in the following cases related in the twenty-sixth volume of the *Medico-Chirurgical Review* ; which coincide, in most respects, with those which I witnessed in dogs, where a sufficient dose was administered to produce death, as will be related in a subsequent part of this paper.

Madame de B. 25 years of age, swallowed a large quantity (a wine glassful) of the tincture of the bulbs of colchicum, with the view of destroying herself. She was immediately seized with most severe pain in the epigastrium. Two pints of milk were administered in about half-an-hour after the act had been committed, and subsequently two grains of tartar emetic were given. Copious vomiting of a brownish fluid ensued. M. Caffè did not see the patient till nearly six hours after the accident. He found her cold and very pale, complaining of tenderness in the epigastric region, a sense of constriction around the chest, and of great dyspnœa. There was no stiffness nor any convulsive movements of the limbs ; the lips were of a purple hue ; the pupils were not dilated, nor was the vision affected ; the tongue was pale and cold to the touch ; there was an almost constant vomiting, but no purging ; the pulse was very slow and thread-like ; and the patient, who was quite sensible, was tortured with a burning thirst ; and every now and then she uttered the most distressing groans. M. Caffè administered iced aerated water, and ordered sinapisms to be applied to the feet, and embrocations to the limbs and abdomen.

On the following morning there was complete prostration of all the vital powers, the retching continued, and the cramps in the feet, although not so severe, were still present. Sinapisms were applied to the thighs, and a few leeches to the epigastrium. The patient became gradually weaker, and death took place in the afternoon—twenty-two hours after the poison had been swallowed.

The body was examined seventy hours after death. Putrefaction had already commenced. Most of the parenchymatous viscera were congested with dark-coloured fluid blood. The stomach and intestines were removed, and set apart for the purpose of analysing their contents. On the following day they were examined, but unfortunately putrefaction had already advanced so far as to have altered considerably the appearance of every part. The mucous membrane of the intestinal canal, in different places, was of a wine-red colour ; but no dependence could be placed on the result of such an examination. Equally unsatisfactory was the chemical analysis of the contents of the bowels.

Strange to record, the sister of this patient, a girl of about 20

years of age, made a similar attempt on her life some months afterwards, by drinking between four and five ounces of a weak vinous tincture of colchicum. The symptoms were nearly the same as in the preceding case; violent pains in the epigastrium; constant vomiting, without, however, any diarrhœa; a sense of constriction around the chest; extreme dyspnœa, gradually increasing coldness of the whole surface of the body, and absence of convulsions, excepting in both feet. The pulse was small and very feeble; the pupils were not affected; and the mental powers remained to the last undisturbed. Milk, iced-drinks, emollient enemata, and blisters to the extremities, were the means employed, but without avail. The patient died on the following day, twenty-eight hours after swallowing the poison.

The body was examined forty-three hours after death. The stomach was much distended with gas, and contained several spoonfuls of a turbid inodorous fluid. Its mucous membrane was quite exempt from any appearance of inflammation or unusual vascular congestion; but its texture was much softer than usual, so that it could be easily detached from the submucous tissue in the form of a *detritus pul-tacé*. Throughout the whole tract of the intestines, the muciparous glands were observed to be very prominent and distinct, and in the lower third of the ileum, the area of the conglomerate glands were of a livid colour.

The other organs did not exhibit any obviously abnormal appearances.

In the fourteenth volume of the Edinburgh Medical and Surgical Journal, page 262, another case of poisoning is related, in which one ounce and a-half of the vinous tincture of colchicum was by mistake given to a feeble man, aged 56, labouring under chronic rheumatism. No complaint was uttered for at least one hour after the accident, but then he became sick, next retching came on, with acute pains, referred to the stomach, to which vomiting and purging presently supervened. This state continued the whole of the succeeding night and day, when the alvine evacuations ceased, but the most distressing nausea continued with retching frequently. The stools were in the course of the night often involuntary, but not bloody. Excessive thirst came on the day after the accident, and continued till death, with severe pains of the stomach and bowels, which occasioned fomentations to be employed. In the evening the patient seemed nearly exhausted; delirium appeared; the pulse could scarcely be perceived; he lived, however, through the second night, but died the following morning. On dissection there was no appearance of inflammation of the bowels, but redness of the stomach.

Professor Berndt has noticed (vide Christison on Poisons) the case of two children who were poisoned by a handful of colchicum seeds, and who died in the course of a day, affected with violent vomiting and purging. In the bodies of these children there was considerable redness of the stomach and small intestines.

The symptoms which I witnessed on dogs differ in some material

points from those related above, as having taken place in the human subject, as will be seen from the perusal of the following cases. On the 15th December 1840, at half-past three P. M., I administered to a middle sized dog 70 minims of the *Vinum Seminum Colchici* without any immediate sensible effect. A short time afterwards it devoured a large quantity of meat very greedily, and continued gnawing bones for some time with great avidity. At 7 P. M., nearly four hours after he had swallowed the colchicum, he eat another large quantity of beef and lapped barley broth with great eagerness. He was visited for the last time that night, at about 9 P. M., when he appeared in his usual state of health. Next morning, 16th December, at half-past eight, sixteen hours after the colchicum had been given, he seemed weak, low, and very sick. He remained prostrate on some straw in a corner of the room, and could not be induced to move. During the night he had been most severely purged, and in every part of the room were egesta from the stomach, in some places mixed with a fluid of a dark-brown colour, in other places mixed with food, and near where he was lying, there were large watery evacuations intimately mixed with a fluid resembling blood. No attempts were made to vomit during the visits on this day, nor did he express by outward symptoms any indication of suffering acute pain. The eyes were hollow, and had a dull glazed appearance. On presenting food of the same kind that he devoured greedily the previous afternoon, he would not touch it. The prostration of strength, and insensibility to external impressions became greater and greater throughout the day. On visiting him next morning, 17th December, at a little after eight o'clock, he was quite dead, cold, and stiff. The food which had been placed before him yesterday morning had never been touched.

The body, examined at half-past eleven, presented the following appearances; the intestines were found very much contracted and vascular. The internal surface of the stomach presented rather more rugae than natural, and was lined with mucus; its cavity was nearly full of dark-brown coloured bile, and the pyloric orifice was contracted; the duodenum was much injected and coated with mucus; the whole course of the jejunum and upper part of the ileum were of the most intense red colour. On the lower part of the ileon were observed a number of dark streaks slightly raised, running in a longitudinal manner. The large intestines were likewise very vascular, although not so vivid as in the small intestines. In the ileon a large tapeworm, measuring considerably upwards of a foot, was found dead. There was not the slightest appearance of food or faecal matter in any part of the intestinal canal; a large quantity of bloody serosity mixed with thin mucus lined the parietes in almost their whole extent. The gall-bladder was full of dark brown bile, and the urinary bladder was distended with natural coloured urine. All the other organs were perfectly normal.

In the Philosophical Transactions of the Royal Society of London for 1816, there are several experiments detailed by Sir Everard Home, for the purpose of ascertaining the effects produced on dogs by injecting the vinous infusion of colchicum into the veins. In his

first experiment he injected into the jugular vein thirty drops of colchicum wine (made by infusing two pounds of the fresh roots in twenty-four ounces of sherry-wine, in a gentle heat for six days, the spirit being previously carried off by heat,) diluted with a drachm of water. It produced a tremulous motion of the muscles and fluttering of the pulse, with some nausea. In fourteen minutes the pulse increased in frequency from 140 to 180 in the minute, but became intermittent. In four hours it still intermitted, but had fallen in frequency to 120, and was of natural strength. In seven hours the pulse was in every respect natural; the dog had a natural stool and appeared in perfect health. In another case, where 160 drops were injected into the jugular vein of a dog, the dose proved fatal at the end of five hours, after having produced, first, loss of voluntary motion, then tremors and great debility, with nausea, vomiting and purging, the pulse being rendered irregular and weak; the inspirations varying in like manner, being in ten minutes, 40 in the minute, which is the natural number; in twenty minutes 30; and in one hour and a-half 54.

On opening the body, the stomach contained mucus tinged with blood, and its internal surface universally inflamed. The same appearance in a less degree, was met with in the jejunum and ileum, and more strongly marked in the colon than in the ileum.

For the purpose of testing the accuracy of these investigations, I performed the experiment to which Sir Everard Home alludes, with nearly similar results. The only discrepancy which exists between us is, that the dog upon which I operated retained the power of voluntary motion entire until death; and the difference in the length of time between the operation and the fatal termination, Sir E. Home's case having proved fatal in five hours, and mine not until after the lapse of twenty-seven hours.

Saturday, 19th December 1840, at a quarter past three P. M. with the assistance of Dr Mercer, I injected 180 minims of the *Vinum Seminum Colchici* into the external jugular vein of a middle-sized dog. During the introduction of the fluid, its breathing was momentarily very much oppressed, owing, I presume, to the congestion produced by the entrance of the fluid into the right side of the heart. On being let loose, the animal endeavoured to make its escape from the room; the gait was perceptibly unsteady, and in the course of a minute it lay down on some straw in a corner, from which it could not be tempted to move. On being roused, however, it remained standing for a short time, but very soon again resumed the recumbent posture. The muscles were affected with a universal shivering; and on endeavouring to count the pulsations of the heart, these tremors simulated the contractions of this organ so completely that there was difficulty in distinguishing the one from the other. Pulse 112; inspirations 44 in the minute; the action of the heart fluttering and intermitting. During nearly an hour, no decided alteration took place; and at no time was any perceptible change observed on the pupil. At half-past six, about three hours after the operation, the dog had passed a large quantity of fecal matter, some

watery stools, and likewise a large quantity of a fluid resembling dark venous blood. A very considerable quantity of inky-coloured serous fluid had also been vomited. The poor animal was seated upon the hinder extremities, but, upon being roused, stood on its legs. Pulse 102, irregular and weaker; inspirations 42 in the minute. At half-past nine P. M. there was no very decided change since last report. On being roused, he had a very unsteady gait. The eyes were dull and glazed, and he had vomited large patches of a frothy fluid.

20th December, at half-past eight A. M., had passed throughout the night more stools resembling dark blood, and a quantity of the same fluid seems to have been ejected from the stomach. He had not touched food since the operation. Some frothy sputa were found in a plate which had been placed beside him, containing soup and meat. Could not be roused so as to stand up. Pulse weaker; 120 in the minute. At half-past four P. M. appeared more prostrated than at last report. The pulse was 150 in the minute, weak, thready, but not intermitting. Inspirations 32 in the minute. Remained much in the same state until seven o'clock, when he expired.

The body was examined at seven A. M. on the following day, twelve hours after death. The intestines were very much contracted. The inner surface of the stomach presented many more rugæ than natural, and was highly vascular. The whole course of the intestinal canal was of a deep-red colour, most intensely injected, and these appearances were better marked in the lower portion of the tube. In the colon were the same longitudinal striæ mentioned in the other case; and the whole tract of the canal was lined with mucus, intimately mixed with bloody serosity, similar to the fluid which had been evacuated. The gall-bladder and urinary bladder, as in the former case, contained a large quantity of their respective fluids. The kidneys were in a state of congestion, and the heart was in a state of hypertrophy, which, however, had evidently no connection with the administration of the medicine.

The whole intestinal tube, with the appearances which I have described, is deposited in the museum of the Royal College of Surgeons of Edinburgh.

My father published in 1837, in the forty-seventh volume of the Edinburgh Medical and Surgical Journal, (p. 345) a series of experiments instituted for the purpose of elucidating the action of this drug, and for regulating his practice as to the extent to which it might be prescribed with safety. From the results of these experimental trials he discovered that more than 170 minims of the *Vinum Seminum Colchici* cannot, in general, be safely administered, in the course of twenty-four hours, to an adult; and that even this quantity, administered in doses of from fifty to sixty drops, at considerable intervals, is often more than advisable, as its cathartic and irritating effects on the mucous membrane of the stomach and alimentary canal were very violent. These results coincide exactly with my own experience, and satisfactorily prove that the directions given by many other writers are highly dangerous, and calculated to do much mischief.

Its principal effects, when administered in this manner, are im-

paired appetite, nausea, increased secretion of bile, depression of strength, increase of the cuticular exhalation, griping pain in the abdomen, copious watery alvine evacuations of a yellow colour, increased secretion and turbidity of urine, of which I shall speak more fully at a subsequent part of this paper. *Colchicum* also produces a direct influence on the action of the heart and arteries, and relieves pain in almost every part of the body ; but more particularly in the joints. Before concluding the remarks which I have to make on the physiological part of our subject, I would observe, that *colchicum* is a medicine of such activity that it should never be given, except in minims. Indeed, Paulus Ægineta seems to have been aware of its violent action, as also of its great influence over some kinds of disease, as seen by the advice he gives with regard to the administration of hermodactyl, which, as will be shown afterwards, is a *colchicum*. “Sunt qui in omnibus articulariorum vitiorum accessionibus purgatione ex hermodactylis ipsis alvis sollicitaverint ; sed attendendum est quoniam hermodactylus stomacho facessit negotium, anxietatem et cibi fastidium movet.” A drachm dose, even to a patient who has been in the habit of taking this medicine, and who may have previously swallowed that quantity with impunity, or even advantage, ought not to be rashly prescribed, since *colchicum* produces very different effects, even on the same individual at different times, according to the state of the digestive organs, and probably of other circumstances with which we are not yet properly acquainted. In speaking of the administration of this drug, my father remarks, “From what I have observed I should conclude that there is most risk of danger from the violent action of any plant containing veratrine (and this is still more applicable to *colchicia*) in debilitated constitutions, particularly in individuals whose digestive organs are weakened by intemperance.” This opinion I have repeatedly seen verified, and I am convinced that great caution is requisite in administering *colchicum*, when disease exists in any abdominal organ, as, from a comparatively small quantity being given in that condition of the system, intractable vomiting and purging are produced, accompanied by alarming depression of the vital powers. The following assertion of Dr Stokes, in his work on the Diagnosis and Treatment of Diseases of the Chest, in speaking of the tartrate of antimony, applies with even greater propriety to the exhibition of *colchicum*. “The more sthenic the disease, and the greater the exemptions from complications, especially with abdominal disease, the more safe and efficacious will be the remedy ;” and the necessity of attending to these directions cannot be too strongly impressed on the minds of those who administer *colchicum*, as they involve a point of the utmost practical importance, the neglect of which cannot fail to be followed by the most disastrous consequences.

Notwithstanding the powerful effects which *colchicum* produces upon man and dogs, we find that it acts with very different degrees of energy upon other classes of animals. For the purpose of ascer-

taining precisely in what respects this action differs, I instituted the following experiments, which were performed with the utmost care, and are, therefore, I trust, exempt from any source of fallacy.

On the 7th December 1840, I gave a small rabbit half a drachm of the *Vinum Seminum Colchici*. It commenced eating immediately afterwards, and on the following day nothing unusual was observed, except that it appeared to have passed a larger quantity of urine than natural.

On the 8th, at six P. M., twenty-four hours after the last dose, one drachm was administered, and, with the exception of a diuretic effect, no particular change was observed.

On the 9th, no perceptible effect having resulted from yesterday's dose, at nine P. M., twenty-seven hours after the last experiment, two drachms more were swallowed, and no evident change was observed in the animal.

On the 10th, at six P. M., twenty-one hours after the last dose, three drachms more were given. After one drachm had been introduced, the rabbit began to squeak and to struggle violently; and upon being let loose, ran about as if in pain. The same effect followed after the exhibition of the second drachm, but after the third, it began to eat, and appeared quite as lively as usual.

Thus, to a very small animal, in the course of four days, six drachms and a half were given; more than six times the quantity which proved fatal, with the most violent symptoms, to a dog, with little effect except acting upon the kidneys.

To a larger rabbit, on the 7th, at six P. M., one drachm of the *Vinum Seminum Colchici* was given; and at the end of twenty-four hours no effect was perceptible. Twenty-four hours afterwards, at six P. M. two drachms more were administered without any marked change taking place. It did not begin to eat immediately afterwards, but on being put into its box, it soon did so, greedily.

At nine P. M. on the 9th, three drachms were administered without any decided effect.

On the 10th, at six P. M., the rabbit appeared to have been well purged, and to have voided a very large quantity of urine. It had, however, eaten the usual quantity of cabbage, and on giving it more, fed most heartily. Half an ounce of the wine of the seeds of colchicum was then given. Almost immediately afterwards, it passed a very unusually large quantity of urine, and an almost constant flow of this secretion continued for nearly half an hour afterwards. In every other respect he was as lively as ever.

On the 12th, no other effect having been produced from the last dose, seven drachms more were given. The same increased secretion of urine was observed, but in no other respect did this differ from the former experiment.

Thus, in this case, seventeen drachms were given in the course of six days, without any material change being produced on the animal, and when we consider the comparatively small quantity which in man and dogs produces the most deleterious consequences, we

seem justified in arriving at the conclusion, that this medicine acts but feebly on the system of these herbivorous animals.

On the 16th, at six o'clock P. M., forty minims of the *Vinum Seminum Colchici* were administered to a large cock, which did not appear to have produced any effect on the following day.

On the 17th, at a quarter to ten P. M. increased the dose to eighty minims.

On the following day, it seemed to be languid, and a large quantity of watery evacuations had been passed throughout the night. The appetite was less than for some days past ; the same quantity of oats not having been swallowed, and its crop was almost empty. At a quarter to six P. M. gave it 120 minims ; offered considerable resistance to the introduction of the medicine ; it threw up a considerable quantity of thin mucus, and soon afterwards passed a large quantity of a white watery evacuation *per anum*.

At half-past eight on the following morning, the bird appeared very weak and languid, had been purged throughout the night, the dejections being of the same kind as mentioned at last report. At nine P. M. had taken no food throughout the day ; seemed very weak and lethargic. One hundred and eighty minims more were given ; it offered less resistance than yesterday, and threw up some more mucus. On being placed upon the ground, seemed very feeble and almost unable to stand ; being laid on its side or back, it remained quite motionless, making no attempt to regain the erect posture.

At nine A. M., on the 20th, was very feeble and weak ; has taken no food throughout the night, and there is nothing in its crop ; died at ten A. M. ; slight spasms came on before death.

On laying open the abdomen immediately afterwards, the intestines were found very much contracted and vascular. In the stomach was found a small quantity of oats quite unchanged, along with a large mass of greenish half-digested matter. Close to the pyloric extremity of the duodenum, was a small dark red coloured patch ; several others of which were observed along the whole course of this gut. In the upper part of the small intestines was a very vascular spot, extending around the whole circumference of the canal, from which a vascular line extended downwards in a longitudinal manner for a considerable distance, from which striæ of vessels shot out on each side. In the lower part of the bowel these appearances were still more distinct, and in some parts intestines were studded with livid spots of extravasated blood, resembling petechial eruptions, which in other places coalesced so as to form one continuous purple-coloured patch. The vascularity was much increased towards the extremity of the intestinal tube, so that the whole parietes of its canal were of one uniform red colour, intersected by longitudinal striæ of a deep red-hue ; the separate streaks being united by a plexiform arrangement of vessels highly injected. In the whole extent of the intestines there was a large quantity of mucus mixed with half-digested food tinged of a green colour. The gall-bladder was very much distended with green bile ; all other organs were healthy. In this case, 480 minims were administered to the animal

in the course of four days, and the fatal termination did not supervene until the fifth day, presenting thus very different results from those obtained in the experiments on dogs, sufficiently proving, that the system of these animals is less susceptible of being acted on by colchicum than that of man and dogs, though much more so than that of rabbits.

The next animal which I subjected to experiment was a large frog. On Friday morning at ten A. M., 15 drops of *Vin. Sem. Colchici*, mixed with a little water, were injected into its stomach. Immediately afterwards it seemed inclined to vomit, the breathing appeared to be a good deal oppressed, and the inspirations amounted to 80 in the minute. At night it seemed completely recovered, and was as active and lively as ever.

On Saturday morning at nine A. M., when the animal was apparently in a natural state, forty drops of colchicum were injected into its stomach; immediately afterwards convulsive gulps were made, as if attempting to vomit. The respiration was disturbed and feeble, there being only thirty inspirations in the minute. The animal was very weak, and, instead of its usual sitting posture, squatted down on its belly. The inspirations gradually increased in frequency, and at one o'clock were 90 in the minute.

Sunday ten A. M. Seems more languid to day, although still abundantly active. Inspirations only 70 in the minute. Twenty-five minims of colchicum wine were given, immediately after which it made several convulsive gulps, and cleaned its tongue and mouth with its foot. It seemed much weaker, the inspirations being very irregular, and only 28 in the minute. At two P. M. the inspirations were weak and 100 in the minute.

At half-past three P. M. 30 minims more were administered; it appeared very languid immediately afterwards, and ejected from its mouth a quantity of fluid like saliva. At twenty minutes past eleven P. M. the inspirations were 110 in the minute; 30 minims more of colchicum wine were injected into the stomach, which at first appeared to occasion a slight degree of excitement, five minutes after which it remained in a somewhat fixed and rigid state. Respiration slow and irregular. After the lapse of ten minutes still remained in the same rigid state, with the head erect and the eyeballs exceedingly protruded. Respiration for half-a minute together, not perceptible. After the lapse of fifteen minutes the inspirations were 46 in the minute. Twenty minutes after the colchicum had been given, a quantity of a fluid like saliva issued slowly from its mouth. The respiration was slow and irregular; a peculiar motion was observed in the hinder legs, as if arising from irritation in the internal and lower parts of the body, there appeared less rigidity of the muscles, and it seemed more inclined to squat.

Monday nine A. M. Gave it thirty minims more of the *Vinum Colchici*; the same effects were produced as described yesterday morning. At seven P. M. forty minims more were given. It seemed languid immediately afterwards, and the respiration was impeded for some time afterwards, being occasionally imperceptible for half-a minute at a time.

On Tuesday, twelve o'clock noon, forty minims more of the *Vinum Seminum Colchici*. Seemed more languid than upon any former occasion; lies quite prostrate upon its belly, and for upwards of a minute no sensible breathing was observed.

At eleven P. M. forty drops more were given, and the effects that followed corresponded exactly with those observed after this morning's dose.

On Wednesday at two o'clock P. M. sixty minims were injected into the stomach, and thirty were at the same time introduced into the rectum by the anus. The appearances observed after these experiments were exactly the same, though perhaps more marked, than on former occasions, and at the end of 48 hours the animal seemed to be in exactly the same condition as before the commencement of the experiments.

In this case, in the course of six days, 350 minims were administered with comparatively very slight effects being produced, and which might very well be attributed to the quantity of wine swallowed. At all events, I conceive this experiment amply demonstrates that the action of colchicum on frogs differs widely from the effects produced on man and dogs.

Desirous of ascertaining the effects of colchicum on fishes, I recently made the following experiment.

Thirty minims of the meadow saffron wine were injected into the stomach of a well-grown gold-fish, weighing about one ounce, without any sensible effects being produced, except causing a copious discharge from the bowels, consisting apparently of the natural excrementitious evacuations with a quantity of mucus.

Not being able to procure a carnivorous animal, owing to the season of the year, I subjected to experiment a sea-gull, which had been slightly wounded in the wing. Thirty minims of the *Vin. Sem. Colchici* were injected into its stomach at ten P. M. No very decided effects were observed during the following hour. On being visited next morning at seven o'clock, it was found quite dead, cold and stiff. On examination after death, the intestines were found much contracted and vascular, containing a large quantity of pulpy fluid. The alvine evacuations had not been profuse, but were very fluid.

From the result of the investigations detailed above, it appears that we are warranted in concluding, that the action of *Colchicum Autumnale* is most decided upon carnivorous and omnivorous animals, while its action on herbivorous, graminivorous, and cold-blooded animals is comparatively feeble.

Having concluded my observations on the physiological action which colchicum produces on man, and on some of the lower animals, I proceed to speak of its therapeutical effects when administered in disease. In the first place, I shall consider its effects and mode of action in gout, a malady over which, as is almost universally believed, it exerts a decided influence.

Colchicum owes its virtues to colchicia, an alkaloid, which in its general character resembles veratrine, the active ingredients in *Veratrum album*; indeed, so similar are those alkaloids in their properties, that,

until lately, they have been held to be identical. It was well known to the ancients, that several plants, which the researches of modern chemistry have ascertained to contain veratrine, or colchicia, possessed powerful anti-arthritic virtues. Aretæus appears to have placed his chief dependence on hellebore in gout ; and Pliny makes particular mention of this medicine, as being an antidote to that formidable disease. Veratria or colchicia were likewise the active ingredients in most of the empirical remedies, which in all ages have been lauded for the cure of this class of complaints. “ Conradus Gesnerius,” says Bergius, “ medicus quondam candidus pariter ac doctus Helleborum album antimonio longe antehabuit et passim in epistolis suis ampliter eum laudavit. Sumsit ipse aliisque propinavit Helleborum, et dicit se nunquam usus ejus pænituisset. Addit semel creberrime Helleborum usum esse non ad purgandum sed ad reserendos meatus et crassos humores attenuandum, eosque a centro et interioribus corporis ad superficiem et vias excretionum variarum educendum. Recreat et roborat et hilariorum facit et acuit ingenium quod in me et aliis saepissime expertus scribo. Sed tenendus est modus. Semper in forma liquida adhibuit Helleborum.” It was believed on very strong grounds that the celebrated *Eau Medicinale* d’Husson consisted of a vinous tincture of white hellebore or colchicum, and opium ;* but what is of still more importance to our present inquiry, it was discovered a few years after the *Eau Medicinale* had been used in this country, that a vinous tincture of *Colchicum Autumnale* had the same or superior virtues, and is unquestionably a more manageable, and less dangerous medicine, than one containing hellebore in its composition.

Alexander Trallian, in the fourth century, ascribed effects similar to those produced by colchicum, to a medicine called hermodactylus, which at one period was very extensively employed by the Arabian physicians, by Paracelsus, Crollius, Turner, and others. Paulus Ægineta mentions that hermodactylus proved very successful in the treatment of gout, although he disapproves of its administration, for the reason mentioned in a former part of this paper, “ quoniam stomacho facessit negotium, anxietatem et cibi fastidium movet.” In the twelfth edition of Quincy’s Dispensatory, published in 1749, we have a very interesting account of that medicine, under the more modern name of the *Colchicum radice siccata alba*, where it is much lauded for its efficacy in arthritic affections.

Prosper Alpinus maintained the identity of hermodactyl and colchicum ; and Sir Gilbert Blane, in his work on Medical Logic, shows that this is highly probable ; and justly remarks, that, in establishing the identity of these plants, we have an example of a most valuable piece of knowledge, lost to the world for many ages, from a want of a description of the article, which on that account could not be recognized from one age and country to another. And we see what incalculable advantage must result to medicine in general, from the cultivation of natural knowledge, from this consideration ; an advantage peculiar to the present age ; for never till now have the

* See Moore on the composition of the *Eau Medicinale* d’Husson. London, 1811 ; and in the *Edinburgh Medical and Surgical Journal*, Vol. vii. p. 449.

various objects of natural history, particularly of botany, been so described, that in all ages to come, however remote, no ambiguity can arise, regarding the identity of the remedies recommended among the medical practitioners of this or any other future age.

That hellebore and colchicum possess similar medical virtues, there can be little doubt; but the active principle of the latter certainly differs from veratria, upon which alkaloid the medicinal virtues of hellebore depend. From not attending to this distinction, my father has fallen into error in the comments which he has made upon the aphorisms of Hippocrates, who enumerates convulsions as one of the worst symptoms induced by hellebore. Under the impression that colchicum owes its activity to veratrine, he concluded that when hellebore did mischief, it was not by occasioning convulsions, but by giving rise to inflammation of the bowels, producing diarrhœa, or, in fact, cholera; but that hellebore produces effects peculiar to itself, and differing from those of the meadow-saffron, is manifested by the following experiments on rabbits, animals, as we have seen above, which are very slightly affected by the administration of very large doses of colchicum wine.

On the 14th December 1840, at six P. M. half-a-drachm of the tincture of white hellebore was administered to a small rabbit. It appeared to make greater resistance to the introduction of the fluid than in the former experiments with colchicum, which might partly be owing to the greater bitterness of the hellebore. After being placed in a box, it passed a considerable quantity of urine; no other effect was perceptible.

On the 15th, at nine A. M., no decided effect having been produced from yesterday's dose, one drachm more was administered. During the administration of the tincture, it began to squeak. Immediately after the whole drachm was given, it panted, gasped, and fell to the ground, dying almost instantaneously in the most violent convulsions.

To a larger rabbit, on the 14th December, at six P. M., one drachm of the tincture of white hellebore was given without any very evident result.

On the 15th, at nine A. M., two drachms more were given, which made it very sick, much less food being eaten during the following twenty-four hours than on any former day.

On the 16th, at six P. M. thirty-three hours after the last dose, three drachms were administered; several convulsive gulps were made, the immediate consequence. The animal was very inactive during the remainder of the evening; but on the following morning, seemed considerably better, and had eaten some food during the night. No diuretic effect had been produced.

At half-past nine P. M. on the 17th, three drachms more were administered. After two drachms had been injected into the stomach, the rabbit began to squeak and to struggle violently. Upon being placed on the ground, it staggered, seemingly in great distress, gasping and making a sharp croaking noise. After the third drachm was taken, it discharged from the mouth about one drachm and a-half of clear fluid like saliva. The breathing became

spasmodic ; and in about a minute it fell down in severe convulsions, which continued with great violence for about half a-minute, when the animal expired.

In both these cases the chest and abdomen were laid open immediately after death ; the peristaltic movements of the bowels were remarkably feeble, and soon ceased. All the organs in these cavities perfectly healthy.

But to return to the therapeutical action of colchicum. The *Pulvis Diaturpethi* and Turner's powder, at one time so celebrated in the cure of gout, now little heard of, and scarcely known, were, I have no doubt, frequently used with advantage, and owed their medicinal virtues to the hermodactyls which each of these once famous medicines contained ; whilst the *Aqua Arthritica* of the Augustan Dispensatory, as well as the famous Portland powder, and the *Pulvis Arthriticus Amarus* of the Paris pharmacopœia, owe, I believe, the power which they assuredly possess of relieving arthritic pains and swellings to the ground-pine (*Chamæpityos*) which enter into their composition,—a plant which probably contains one or ~~two~~ of these al-^{other}kaloids. It is interesting to observe the language of early medical writers in regard to the effect of the medicine of which we have just been speaking ; and of others which contain these substances in their composition. Such were reported to be very efficacious in “rooting out and destroying the matter in the joints, which is supposed to cause those vehement pains, swellings, and sometimes chalky indurations”—language arising from their ignorance of physiology and imperfect pathology. The “scouring and preserving from the lodgement of gritty matters” was really a description of what actually occurred ; and which the light of modern physiology has shown to arise from the power, which some at least of the remedies mentioned possess of controlling arthritic inflammation, and consequently preventing calcareous depositions.

The power which colchicum possesses of alleviating the agonizing symptoms of gout is so unquestionable, that I conceive it unnecessary to occupy time in narrating particular cases of its efficacy.

The *modus operandi*, however, of this potent drug, demands upon the present occasion our special attention ; and it behoves us to consider the question as to the safety of its internal exhibition.

As surmised by physicians in all ages, it is, I apprehend, by acting on the fluids, and especially on the blood, that we can really reach the *materies morbi* in arthritic and rheumatic affections. It were vain to advert to the erroneous opinions of the ancients, as to the peculiar morbid humours from which they conceived gout to arise ; but the modern opinion of an excess of uric acid or of urea in the blood being, if not the proximate cause, at least mainly instrumental in constituting the disease, appears to be very probable, and to be confirmed by phenomena observed during its continuance, and by the effect of remedies which are efficacious in relieving it. In the present state of our knowledge, at least, we must, in considering the indications of cure, take into consideration all the elements obviously forming the constitutional and local affections present in

gout, namely, vascular plethora, topical or general; gastric, hepatic, and intestinal derangement, as well as impaired and exhausted nervous energy; but a careful consideration of all the phenomena as they occur in gout, would, I humbly conceive, lead to the conclusion, that in this disease the fluids of the body are primarily affected; that, in short, gout is a disease of the blood, and that a vitiated condition of this vital fluid is the first link in the chain; and that the deranged state of the organic system of nerves and its consequences are merely secondary, and dependent on the former.

If this view of the pathology of gout be correct, we need be at no loss to account for the astonishing efficacy which colchicum possesses of relieving this disease, as we find, by the experiments of my esteemed friend, Professor Chelius of Heidelberg, that the quantity of uric acid excreted by the kidneys is nearly doubled in the course of twelve days under the use of this remedy. The opinions of this learned Professor with reference to this subject are stated in the following letter, which I had lately the honour to receive from him.

“Monsieur, *Heidelberg, 10th Decembre 1840.*

C'est avec plaisir, que je reponds à votre lettre, et que je vous donne mon opinion sur l'action du colchicum. Des experiences repetées m'ont prouvé, que pendant l'usage de cette drogue la quantité de l'acide urique eté sensiblement augmentée dans l'urine, et j'ai publié le resultat de ces experiences dans le 3me vol. des Annales Cliniques de Heidelberg. Cette drogue produit lentement le même changement dans les affections gouteuses ou rhumatismales, que nous voyons s'effectuer plus subitement par les crises dans ces affections, c'est-a-dire, une evacuation plus copieuse de l'acide urique. Par cet effet on peut clairement demontrer l'action salulaire et quelquefois suprenante de ce remede dans la goutte, et c'est aussi pour cela que je me sers presque exclusivement de ce remede dans cette maladie, comme dans les affections rhumatismales. Jamais je n'en ai vu des effets nuisibles.

“Je suis bien curieux du resultat que vous obtiendrez par vos experiences sur ce remede et vous m'obligerez bien en voulant me le communiquer.

“Agreez l'assurance de ma consideration parfaite.

(Signed) Dr CHELIUS.”

The accuracy of these remarks with reference to the increased quantity of uric acid excreted by the kidneys during the administration of colchicum, have been confirmed in a great variety of cases which have fallen under my own observation, the following of which I subjoin as peculiarly calculated to exemplify the correctness of these views.

On Thursday, 12th November, Mr A. B., aged 48, of a gouty diathesis, after a debauch, in which he had indulged in champagne and different wines, felt very unwell during the next two days; he complained of slight headach, gastric derangement, and flying pains. His urine was also very turbid and of high specific gravity. At the end of three days felt rather better, but still remained uncomfortable on the 15th and 16th, although he was rather better on

the 17th. Urine on that day much less turbid, and its specific gravity 1020. On the 18th felt very ill. The urine voided in the forenoon of this day of a light yellow colour, its specific gravity being only 1014. At half-past five P. M. took 40 minims of the *Vinum Seminum Colchici*, and again, at half-past eleven, 40 minims more. Had not tasted animal food during the day, and nothing since two o'clock. Passed a restless night, suffering from griping pains in the abdomen. Vomited early on the following morning, 19th November, and frequently in the course of the forenoon. Urine turbid, and in appearance like lime suspended in water. Two ounces of this urine required three drachms of nitric acid to render it transparent. The patient remained feverish, ill, and unfit for exertion of any kind. Bowels moved twelve times in the course of the day, the evacuations being at first of a bright yellow colour, and of a peculiar cheesy odour. By degrees they became lighter, and by nine o'clock P. M. were almost colourless, and without odour. At bed-time, pediluvium was employed, and two glassfuls of mulled wine were taken. Slept well, and on the following morning felt greatly relieved.

On the 20th November, urine very turbid, and three drachms of nitric acid were still required to render two ounces of this fluid transparent. Specific gravity 1034.

November 21st. Feels still more relieved ; urine, when voided in the morning, quite clear ; at mid-day, however, it had become quite turbid, and its specific gravity was 1030. Dined early on roasted pheasant ; took no wine ; but drank a pint of porter. At six o'clock P. M. voided urine, which on cooling was less turbid, and in density 1021.

November 22, Felt in his usual state of health ; urine natural in appearance, and its specific gravity 1013.

Conceiving it to be of importance, in this case, to have an accurate analysis of the urine, specimens of it voided on the 17th, 19th, and 20th, were sent to Dr Christison, our highly distinguished Professor of Materia Medica, who had the goodness to analyse it, and report as follows.

" I examined the three specimens of urine. No date of the first I have now got, but I think it was November 17th ; but at any rate I understand that it was passed before the patient had taken any colchicum. There was no deposit of lithate of ammonia in it ; its density was 1020 ; it contained above forty-seven parts of solid matter in 1000, and of this quantity twenty parts were urea. The two specimens marked as passed on the 19th and 20th November were exactly alike. They were very turbid, and the turbidity disappeared with a gentle heat. The deposit was evidently lithate of ammonia. The density of the first was 1033.5, and that of the second 1034, which are both very unusually high for urine not diabetic. As they were obviously identical in their nature, I only analysed the second. It contained 79 parts of solid matter in 1000, and of this quantity 35 were urea. I suspect now that the proportion of urea was even greater ; for, having occasion the other day to refresh my

memory as to the process I usually followed for ascertaining the quantity of this principle in urine, I find that, in analysing that which you sent, I had not used so large a proportion of nitric acid as I ought to have done. Now, nitrate of urea is soluble in water, but is rendered insoluble by a large excess of nitric acid ; so that, if there was not a large excess, I could not have obtained all the nitrate of urea which was formed, because some of it would remain in solution. Even the proportion I did obtain is considerably above the standard of health."

I have only to direct attention to the quantity of urea contained in the urine on the 17th, before any colchicum had been prescribed, with that passed on the 20th, after its administration, to show that the quantity of urea was nearly doubled, which coincides precisely with the views entertained by Professor Chelius of Heidelberg.

Mr A. B. was again taken ill on Tuesday night, 29th December 1840, having been subjected to great anxiety and considerable mental irritation, and afterwards exposed for some time to severe cold. He was suddenly affected with confusion in the head ; an uneasy feeling in the region of the heart, with palpitation ; acute pain in the right side of the neck, from the angle of the jaw to the junction of the sternum and clavicle, with smart flying pains in the wrists and ankles. I did not see him till a considerable time had elapsed after the seizure. He was then in bed, and had somewhat recovered from the cerebral and cardiac symptoms ; but the pains in the back, throat, wrists, and ankles were still violent. Pulse 120 ; respiration natural ; tongue slightly furred. It was to us a matter of serious consideration, whether or not blood-letting should be had recourse to ; but, as the symptoms were less urgent than they had previously been, and as the patient himself was averse to that remedy being employed, it was not insisted on, we left him about midnight, with strict injunctions to his friends to call us in the event of his situation appearing to require assistance.

Wednesday morning. Has passed a very disturbed night, having suffered much from the pains in the limbs, neck, and integuments of the head. The pulse, it appears, had been rapid throughout the night, beating, by his own report, upwards of 100 in the minute ; now it is 90. The pained parts were ordered to be rubbed with an embrocation, consisting of the *Liq. Ammoniac fort.* and tincture of camphor, with spirit of rosemary. Has voided a great quantity of urine, which is very colourless, and of specific gravity 1009. Two colocynth pills were ordered to be taken, with a little extract of hyoscyamus.

Half-past one P. M., nearly as at last report. The bowels have not been moved. *Habeat Haust. Salin. cum Vin. Colchici. M. xl. Sig. Mox sumendus.*

7 P. M. Has experienced great relief since last visit. Bowels have not been moved, but the urine has been plentifully voided, which is excessively turbid, and was found to be of specific gravity 1033. Has no appetite for food, and has taken nothing to-day.

10 o'clock P. M. Continues better. Bowels have been moved ;

feels now a great craving for food for the first time since he was taken ill, and expresses a desire to take an egg and a little mulled wine, which he has found to agree with him under similar circumstances.

Thursday morning, is to-day almost quite well, but feels a little languid; pulse 72; tongue clean; bowels open; urine still very turbid, specific gravity 1034.

The gentleman who is the subject of the foregoing report is an individual of high intelligence and acute observation, and, from ample experience, fully competent to form an opinion of the comparative merits of different modes of treatment, as applicable to his own case. He has long been sensible that the state of his health is in some way connected with the condition of his urinary discharge, and is aware that derangement of health is the immediate consequence of any want in the due action of the kidneys, being fully satisfied that the state of his health is improved when deposits take place in his urine; and the practice adopted on the late occasion, to which I have referred, was in conformity with his own views. "Prescribe," says he, "for me a medicine that will occasion the excretion of the noxious matter in the blood by the kidneys, and I know that I shall experience relief." It was under these circumstances that colchicum was prescribed, and it was with very great interest that we watched its operation during the day. As was before stated, the medicine was taken at one P. M., and at four the urine was voided for the first time, which at first presented no unusual appearance, but upon cooling it became turbid, and when it had fallen to the temperature of 40°, it was as turbid, perhaps, as we had ever observed urine, and of specific gravity 1033. In the morning it had been of the specific gravity 1009. With the exception of some chicken-broth and tea, no other food had been taken throughout the day. As stated above, the relief which the patient obtained was coincident with the change in the urine. He improved every hour afterwards, and by two o'clock was able to leave his room, and enter upon the discharge of duties requiring exertions both of mind and body, with his usual alacrity. His own opinion, founded on much experience of his own case, is, that unless for the effect produced by the colchicum, he must have been confined for a week at least, and undergone severe medical discipline, as upon many former occasions, in the way of starvation, purgation, a *quantum sufficit* of sudorific medicines, and probably a bleeding from the arm.

Mr A. B. voided urine again at five o'clock, not in large quantity, which by mistake was removed, so that there was no opportunity of ascertaining its appearance or density; again at bed-time, and a third time this morning, (January 1st), which, on cooling, was excessively turbid, and in density 1037, a portion of which has been sent to the laboratory in the College of the Professor of Materia Medica for analysis.

With the exception of a small quantity of urine, which was passed when at the water-closet, this forenoon, none was voided until half-past eight o'clock, P. M., which, at nine, was found to be still turbid, but less so than the morning's. Specific gravity 1034.

I am indebted to my honoured friend, Dr Christison, for an analysis of Mr A. B.'s urine, referred to above, after the administration of colchicum. The learned Professor reported as follows: "The density is the highest I ever met with in urine not diabetic, namely, 1036. Suspecting there might be some sugar, I tried that point very carefully, and there is not a particle present. The turbidity is owing to lithate of ammonia, which is in excess, though not very much so. The specimen seems to me to be nothing else than urine loaded excessively with its ordinary soluble ingredients. The urea, in particular, is unusually abundant, for when one part of nitric acid and two parts of urine were mixed together, the whole liquid became a mass of pulpy crystals when cooled down to about 45° F. I am endeavouring to ascertain the actual proportion, but I fear I have committed a mistake. Not being satisfied with the common process, which I think cannot separate the whole urea, I tried another method, which seemed to me to promise better, but, on the contrary, it is worse; at least I have not obtained from concentrated urine with nitric acid, the firm, pulpy mass which I think I ought to have got, considering the very unusual amount of crystallization caused by nitric acid in unconcentrated urine."

In further illustration, I beg to subjoin the following remarks of Dr Prout in his excellent work *On the Nature and Treatment of Stomach and Urinary diseases*. "Whoever has attended much to urinary diseases must have remarked, that many individuals subject to derangements of the general health, seldom feel so well with respect to their health as when lithic acid deposits take place in the urine;" and at page 227, he makes the following remarks:—"We have said, that about the age of 40, the lithic acid may occasionally be considered as a sort of *materies morbi*, that is, the cause of irritation in the constitution, whatever it may be, is transferred to the kidneys, which are induced to secrete an extraordinary quantity of lithic acid, and thus to meliorate the system in general. On a similar principle, the good effects long ascribed to certain remedies of the active diuretic kind, may probably be explained: such remedies appearing to possess the power, when given in favourable conditions of the system, of exciting the kidneys to separate large quantities of lithic acid; and in this way, by bringing about an artificial crisis, to produce great and immediate benefit. Thus Dr Henry has mentioned cases in which *several ounces* of lithic acid were brought away in the course of a day or two by a remedy apparently composed of turpentine and laudanum chiefly."

Another circumstance tending to render this opinion probable is the fact now ascertained, that tofi or gouty chalk-stones do not consist, as was formerly supposed, of phosphate, but of urate of lime. Alkalis and other antacids have a most decided effect in diminishing the formation of urea; and, as is well known, are among the most useful medicines we can employ as prophylactics in arthritic habits of body; and before concluding, I may remark, that, if these views be correct, we must, in the systematic treatment of gout, principally direct our attention to the counteraction of its cause, an excess of urea in the

blood, which can be accomplished most readily, as above demonstrated, by the internal administration of *Colchicum Autumnale*.

Independent, however, of this effect, to which I am inclined to attribute much importance, we can easily understand, from a knowledge of its physiological action on the stomach, intestinal canal, liver, skin, and circulating system, the beneficial results it must produce in a disease characterized by the symptoms observed in gout.

Extraordinary and valuable as colchicum undoubtedly is as a remedy in paroxysms of acute gout, it is perhaps almost more so in the irregular forms of that dangerous and distressing disease, especially in affections of the heart and large blood-vessels, which are so apt to occur in persons of a gouty diathesis. As a student of medicine, I had frequently an opportunity of witnessing in the practice of my father, who has long made the medicinal properties of this drug a particular study, cases which, with others I have more recently seen, strongly corroborate the accuracy of this opinion; and I quote from his note-book the following case, which produced at the time on my mind a most favourable impression of the benefit to be derived from this medicine in these forms of disease.

April 7th 1836, Mr C. D., aged 67, of a gouty habit of body, has been subject to palpitation of the heart for eighteen months past, which have gradually been becoming worse, with severe cramps in the legs, of which he complains much, and during the last ten years has voided fusiform lithic concretions in large numbers, varying in size from a pin's head to a small cherry-stone. The feet had been tender lately, and the ball of the toe was slightly inflamed. The action of the heart was very irregular, as also the pulse at the wrist, which was in frequency 92 in the minute. For a considerable period past, he has been living comparatively in a very abstemious manner, and been taking a small dose of rhubarb and magnesia every morning, without much or any sensible effect. *Vini Sem. Colchici*, ʒss. Sig. twenty drops three times a-day in water.

April 10th. Has been taking the medicine regularly as directed. Experienced a slight degree of nausea during the whole of yesterday afternoon, and in the evening felt considerable commotion in the bowels. Had two watery stools before going to bed, and five this morning. The heart's action was much less violent in the night than it has been for many nights previously; pulse fuller and more regular, in number 76. Omit *Vinum Colchici*.

12th April. As at last report. Bowels still open; pulse, 72. By Mrs C.'s report, the action of her husband's heart during the night was less violent than it was wont to be.

14th April. In every respect the same as on the 12th, except that the bowels are not so open. *Reptr. Vinum Colchici in dosibus viginti quinque vel triginti guttarum ter in die.*

18th April. Has been using the medicine as directed since last report, which acts upon the bowels, but not violently. The action of the heart and pulse greatly improved when compared with their condition on the 7th, but both still decidedly abnormal. *Continuetur Vinum Colchici.*

27th April. Has been taking of late from twenty to thirty drops of the *Vinum Colchici* daily. Bowels generally moved twice or three times in the course of twenty-four hours. No sickness produced by that quantity. Has taken in all half an ounce of the colchicum wine in twenty days. Action of the heart has become much more regular, with a corresponding improvement of the pulse. Has got completely rid of the cramp since he began to use the medicine. *Continuetur Vinum Sem. Colchici* in such quantities as to act sensibly but gently on the bowels.

May 5th. Has taken from twenty to thirty-five drops daily, which moved the bowels twice and sometimes three times a-day. The pulse is decidedly improved in character. The irregularity of the heart's action still perceptible, but much less so than formerly, and regular professional attendance was considered unnecessary. From that date he continued to use the colchicum, occasionally, in small doses for six months afterwards, so as to act gently on the bowels, with great relief to the cardiac affection. The number of urinary calculi passed was much less than formerly, and he was never again troubled with cramps.

This patient died of apoplexy eighteen months afterwards, and the following is a report of the *post mortem* appearances drawn up by my respected friend, Dr Handyside, one of our most accomplished anatomists.

"The viscera of the thorax, with the exception of the *heart*, were healthy. This organ was a little larger than natural, particularly its ventricular portion. Its surface was covered to a greater extent than natural with dense fat, and its lining membrane presented a uniform darkish mahogany hue. The right fold of the mitral valve was much thickened, and contained broad calcareous depositions, —appearances of which the arch of the aorta largely partook.

"The *gall-bladder* contained four or five small rough calculi mixed with viscid dark-coloured bile. The kidneys were each enclosed in about a pound and a-half of dense fat, into which texture the *papillæ renales* were converted. The pelvis of the kidneys were obliterated, and the ureters smaller in calibre, and thinner in texture than usual. The bladder was healthy, and in its texture quite healthy.

"On opening the head, much dark-coloured fluid blood was seen to escape, partly from the divided membranes, which were turgid with blood, and partly from a large cavity within the interior lobe of the left hemisphere of the brain.

"The substance of this last named organ was in every respect healthy, with the exceptions, first, of two cysts within the right *thalamus nervi optici*, one the size of a plumstone, the other, that of a split-pea, containing each of them a straw-coloured lymph, and the delicate membranous walls of which were lined by large turgid veins; and secondly, the presence of a cavity underneath and partly in the texture of the left *thalamus* and *corpus striatum*, which contained a clot of dark-coloured blood, the size of a nutmeg, part-

ly flocculent and free on its surface, partly adherent to the parietes of this cavity."

The above case certainly appears to afford a striking example of the excellent effects of colchicum when judiciously administered.

From the history of the disease,—from the gradual but steady increase of the symptoms previous to the use of this medicine,—from the rapid amelioration which took place during its administration,—and from the appearances observed on dissection, we may, I conceive, legitimately conclude, that, had this remedy not been employed, more confirmed disease of the heart must have been formed ; which would sooner or later have proved fatal ; whereas, under the controlling influence of colchicum we find the progress of the organic affection arrested, and the patient ultimately die of a disease totally unconnected with the one for which the remedy had been prescribed. We find colchicum, likewise, apparently preventing in this instance the tendency to the formation of lithic depositions.

The following statement of a case from Dr Abercrombie's *Pathological and Practical Researches on Diseases of the Stomach, and Intestinal Canal, the Liver and other Viscera of the Abdomen*, is applicable likewise to my present purpose, in as far as it tends most admirably to illustrate the efficacy of colchicum in that class of diseases to which our attention is at present directed. "A gentleman, aged 48, in November 1825, began to be affected with paroxysms of palpitation of the heart and intermission of the pulse. They attacked him daily, sometimes twice or three times a-day, and generally continued about an hour at each time, and they were occasionally accompanied with a considerable degree of dyspnoea. During the intervals, the pulse was calm and regular, and the action of the heart quite natural. The period of the attack was generally soon after meals ; but it likewise occurred at various other times ; sometimes on first getting up in the morning, and sometimes during the night. During the paroxysms he could take walking exercise without increasing the symptoms. His digestion was imperfect, and his stomach easily disordered ; his bowels were rather slow, and the motions were dark and unhealthy. A great variety of treatment and every possible variety of diet were employed with very little benefit. He went to London and then to Cheltenham, where much treatment was again had recourse to with little effect. He sometimes lost greatly in flesh and strength, and sometimes improved again ; his digestion was sometimes better and sometimes worse ; but, amid all these changes, the affection of the heart continued in the same form, namely, paroxysms of violent palpitation of about an hour's duration ; occurring once or twice every day, and at no stated hours. After the affection had continued in this manner for two years and a-half, it subsided at last under the use of the colchicum wine, in very moderate doses. I do not attempt to account for the action of the remedy in this singular case ; it acted at first strongly as a purgative, so that he was only able to take ten drops of the wine twice a-day. The patient's own account of the effect of it is in these words : "At the time of commencing the use of the colchicum, I had

once, at least, every day, a severe fit of palpitation of an hour's duration; often two, and sometimes three fits in a day. So immediate was the effect of the colchicum, that, with the exception of the first and third day after beginning its use, I have not had a single paroxysm of the palpitation." He adds, that he continued the use of it for a month, and then left it off entirely; and that the quantity did not in general exceed from fifteen to twenty drops in a day."

In other forms of metastatic gout, when it affects the head, stomach, or intestines, and in most internal affections occurring either in the gouty diathesis, or upon the sudden disappearance of the external disorder, as well as in other anomalous affections, which this protean disease often assumes, we may expect relief to result from the proper administration of colchicum, as we have seen to follow its employment in the acute and more evident forms of arthritic disease; and as I conceive its mode of action in these cases, as also in rheumatism, to be precisely similar to that of which we have just been speaking, I shall now examine its effects in other diseases in which it has been less frequently employed.

From the powerful physiological effects which we have seen colchicum capable of producing, we might reasonably expect that it will be a powerful therapeutical agent in most diseases, where excessive excitement of the vascular and nervous system prevails; an opinion which has been entertained and insisted on by Mr Want, Mr Haden, my father, and others. The latter published in 1837, cases of continued fever, in illustration of his views as to the efficacy of *Colchicum Autumnale*; and concludes that, by its judicious administration, we may break the force of fever more effectually than by any other known means.

From my own experience, I am inclined to think well of the efficacy of colchicum in fever, and, as an example of the manner in which it may be used advantageously in that disease, I may record the following case.

Mrs L. aged 26, at present pregnant, had attended her mother lately when in typhous fever; she shivered on the 18th December, was affected subsequently with headach, pain in the back and limbs; at present, (December 22d) labouring under all the symptoms of fever in an aggravated form, severe headach, great prostration of strength, heat of surface, tongue covered with a thick white fur, pulse 136; has taken several aperient pills with little effect.

R. Vini Sem. Colchici. ; Vin. Antimonii aa ʒii. ; Spirit. Etheris Nitrosi ʒii ; Aq. Fontis ʒiv. M. Sig. Two teaspoonfuls immediately, and one every three hours afterwards.

December 23d. The medicine was finished at seven o'clock this morning, she having taken it oftener than directed; has vomited frequently, and the bowels have been repeatedly moved; pulse 120; tongue much cleaner.

December 24th. Has been distressed with nausea and vomiting during the night, which continues until now (half-past ten A. M.); bowels had not been moved; pulse 122; headach very severe; specific gravity of the urine 1026. *Habeat Extracti Opii, Calomel.*

aa gr. i. *pil. ft.* Sig. to be taken immediately. 10 P. M. Took the above pill, and another grain of opium at five P. M.; feels now relieved.

R. *Liquoris Opii Sedantis* gtts. xxv.; *Aq. Menthae Pip.* ʒss.

M. Sig. To be taken at bed-time.

December 25th, *mane*. Slept pretty well, but the headach still continued severe; tongue cleaner; pulse 120; specific gravity of the urine 1025. P. M. Has been greatly distressed with retching and vomiting since last report.

R. *Creosoti* gtt. i.; *Syrup. Rosar.* ʒii.; *Aq. Menth. Pip.* ʒss.

M. Sig. To be taken immediately.

Vespere. Has vomited less frequently since she took the creozote draught; pulse 120; headach still very violent; tongue and other symptoms as at last report.

26th December, 12 noon. Vomiting returned violently since eight o'clock this morning. In other respects as at last visit.

R. *Kreosoti* gtts. ii.; *Liq. Opii. Sed.* gtts. xv.; *Syrup. Rosarum* ʒii. *Aq. Menthae Pip.* ʒv. M. *Hauslus ft.* Sig. To be taken immediately.

Vespere. Has vomited little since last report; pulse 120; in every other respect as in the morning.

27th December. Slept some hours last night; irritability of stomach entirely gone; tongue cleaner; pulse small, and more compressible; bowels not moved for two days past. To have a domestic enema.

Vespere. The injection operated satisfactorily; pulse still smaller, and more compressible. *Habeat statim Vini Rubri* ʒi.

28th December. Has had comparatively a good night's rest, but still a little headach; in other respects as yesterday; feels very anxious to enjoy sleep.

R. *Pulv. Doveri* gr. v.; *Carb. Magnes.* gr. vi.; *Pulv. Rhei*, gr. iii.; *Min. pulv.* iii. *divide.* Sig. One every three hours; *et continetur Vini.* ʒi. *quaque hora quarta.*

11 P. M. Has been tolerably easy all day, although she has had no sleep; pulse 120; tongue very clean.

R. *Extracti Opii* gr. i. *pil. ft.* Sig. To be taken at bed-time, and the wine to be continued.

December 29th. Has had a good night, but the irritability of stomach to a certain extent still continues; has occasionally retched slightly, and vomited once; headach entirely gone; pulse 104; no motion in the bowels; had taken a cupful of beef-tea prepared for her mother before she was visited to-day; tongue cleaner. *Continr. Vinum, et repr. enema.*

30th December. Has felt rather worse and more restless, with increase of headach and slight delirium since last visit, which she attributes to having taken the beef-tea; pulse 106; enema operated but very imperfectly; tongue as at last report. *Rept. Enema et habeat Pulv. Doveri* gr. v. *hora somni.*

31st. Enema operated well, and she feels better. *Habeat Pil. piat. h. s.*

1st January 1840. Slept well last night; headach quite reliev-

ed ; pulse 100 ; stomach slightly irritable, but she may be reported perfectly safe, if not quite convalescent ; and from this date she advanced rapidly to her accustomed state of robust health.

I venture not to decide whether the benefit which in this case, and in many similar which have come under my observation, was derived from colchicum, is to be attributed merely to its action as a purgative and emetic ; but I think it not unreasonable to suppose, that the effect which we have endeavoured to prove is produced by colchicum in the way of increasing the quantity of urea excreted by the kidneys, and of bile by the liver, may afford an explanation of the satisfactory terminations of such cases. Certain it is, that in a fatal case of pure uncomplicated typhus which I witnessed very lately, and where the patient died comatose, with symptoms similar to those caused by suppression of urine, although this fluid was secreted in considerable quantity, on accurate examination, it was found to be very deficient in urea.

In a paper published in the *Lancet*, Vol. i. for 1837-38, p. 198, by Mr Tait, the author mentions that he has derived equally good effects from this remedy in scarlet fever. His cases were all of the purely inflammatory type,—blood-letting, leeches, and blisters being occasionally employed. He commenced with from twelve to fifteen drops of colchicum every three or four hours to robust farm-servants, and in children of from four to six years, he administered three or four drops, and diminished the dose, watching its effects, stopping whenever these were manifested. The pulse was diminished in frequency and force ; the palpitation of the heart, which, in young subjects, was often perceptible to the eye, subsided ; the inflammation and pain of the throat were alleviated ; and the patient often expressed himself much better. Vomiting was excited in a few cases, but, as this seemed always to be followed by an improvement in the state of the tonsils, and generally abated after the rejection of a quantity of bile, it was never found necessary to interrupt the use of the medicine. The bowels were more or less purged, and the improvement was always so suddenly marked after a free discharge of dark bilious stools, that he always considered the patient out of danger when these appeared.

So early as April 1836, I had an opportunity of seeing colchicum extensively and very successfully used in the treatment of scarlatina by my father ; and more recently, when this disease prevailed epidemically, I had occasion in several cases to observe its powerful influence over the symptoms. In every instance, indeed, where colchicum was employed, the malady very speedily proceeded to a favourable termination ; while other cases, apparently similar in their character, in which this medicine was not administered, proved by no means so satisfactory ; several having terminated fatally, and the sequelæ of others being exceedingly troublesome.

The pathological tenets lately prevalent in France, and to a certain extent adopted by many in this country, first inculcated by Broussais, which prevented the treatment of Rasori from being fairly tried, will, I fear, act still more powerfully as an obstacle to the employment of colchicum in fever. That it may be used with perfect safety, if judiciously administered, especially during the first

days of the disease, may be considered a decided point ; and I would add, that the favourable opinion I entertain of its efficacy is not deduced from seeing its effects in a few detached cases of typhus ; but from the general results in a number, at different times ; but especially during the prevalence of the disease, epidemically amongst all classes of society ; and particularly among the poor of Leith—a town containing a population of 28,000 inhabitants, during the epidemic that prevailed there in 1836.

In addition to what I have said in regard to the probable manner in which colchicum acts beneficially in fever, I would suggest that, from what we have seen of its physiological action, the salutary influence may depend on its expelling from the circulating fluids, certain constituents by which they are contaminated or altered, in consequence of the impeded function of certain organs, in the early stage, and during its continuance, especially the kidneys and liver.

It is reasonable to infer, from the powerful influence which colchicum possesses in diminishing vascular and nervous excitement, and from its effects on the excretory organs of the body, and probably in the way of equalizing the circulation, that it may be useful in many local inflammations, both acute and chronic, so as to become a valuable auxiliary to the lancet ; and in some instances entirely to supersede its use. So long ago as 1820, Mr Haden published a work on this subject, in which he has related cases which prove, as we might have expected, the meadow-saffron to be a remedy possessed of great power in relieving such states of the system. He employed it principally in pulmonary and laryngeal inflammation with decided advantage ; and in such cases, he seems almost entirely to have trusted to its effects, to the entire exclusion of blood-letting. Although I am not so sanguine as to expect that, in acute forms of such diseases, we can depend upon colchicum alone, yet, from what I have seen, I speak with confidence when I state that, with the exception of depletion, there is no remedy capable of producing more beneficial results ; and, in many subacute inflammations, more particularly the evacuations of blood, need be very limited in extent, if promptly followed by the judicious administration of colchicum. In pleurisy, pneumonia, bronchitis, and croup, I have seen most decided benefit result from its employment.

In proof of its efficacy in the last named disease, I adduce the following case without comment.

November 24th 1840, at eight o'clock A. M. A. G. aged three and a-half years, labours under decided symptoms of croup, which have been coming on for the last forty-eight hours ; pulse 180. Directed four leeches to be applied over the region of trachea, and four grains of calomel, to be divided into three doses, one of which was ordered to be given every third hour, and each dose to be followed by four drops of colchicum wine.

5 o'clock P. M. Leeches bled well. All the calomel taken and sixteen drops of the colchicum wine. Has perspired freely ; bowels once moved ; symptoms of the disease somewhat mitigated ; had retched several times ; pulse 160. *Continuetur Vinum Sem. Colchici.*

11 P. M. Symptoms of the disease greatly alleviated ; skin moist,

but the perspiration less than at last visit; bowels have been freely moved; the evacuations resemble chopped spinage; pulse 116. *Intermit. medicamenta omnia.*

November 25, nine A. M. Has had a tolerable night, and is to-day greatly relieved. Pulse has fallen to 100; very slight croupy sound perceptible during respiration. Expresses a desire for food. *Continuetur Vinum Colchici ut antea.*

2 P. M. Continues to recover; several alvine evacuations have been passed since last report, which are less green in colour; pulse 96. *Intermit. medic. omnia.* Gave particular directions to avoid exposure to cold, and to be kept on farinaceous diet.

10 P. M. Is free from complaint.

26th November, noon. Continues convalescent.

In a very well marked case of icterus which lately came under my observation, the patient was cured in a very short time, (within the week,) by the administration of three draughts, composed of the following ingredients:

R. *Sulph. Magnes.* ζ iii.; *Carb. Magnes.* ζ ss. M. *Solve in infus. Sennae* ζ ii. *et adde Vini Sem. Colchici*, gtts. l. which were used every alternate day.

Each draught acted powerfully as a cathartic and emetic, besides producing most profuse diaphoresis.

In inflammatory affections of the head, as has been suggested by my father, it is probable that colchicum will be a valuable remedy, but of this I have had little experience. His expectation of its being an anthelmintic, is not, however, I fear, likely to be realized, as I have found it fail, though used to as great an extent as I could prudently do, in a case of tape-worm in the human subject; and in the dog which was the subject of my first experiments, strange to say, a large tape-worm alone remained in the bowels, all other contents from the stomach to the extremity of the intestinal canal having been evacuated by the operation of the colchicum.

I need now, I trust, say little in refutation of the opinion entertained by many, that colchicum is not only a medicine of doubtful efficacy, but that its internal administration is dangerous. That a medicine possessed of such active properties requires a degree of caution which has too often been disregarded, and consequently mischief done, I verily believe; but the same objections may be urged against every other active medicinal agent we are in the habit of employing. For my own part, I am perfectly convinced that, if judiciously administered, so as to secure the full effect of the medicine without the injurious consequences of an overdose, it may be fairly considered a safe and potent drug, and amongst the most valuable in the materia medica.

In prescribing this medicine, and in making my experiments, I have used the *Vinum Seminum Colchici* since the precise effect of a proper dose of that preparation has been accurately ascertained; but I have no objection to the substitution of the acetate recommended by Sir Charles Scudamore and others, as a preferable preparation, after proper pains have been taken to ascertain the dose requisite to secure the effect which colchicum in that form is capable of producing.

In conclusion, I have only to express my earnest hope that the foregoing pages will contribute towards the elucidation of the physiological and therapeutical properties of *Colchicum Autumnale*, and

that my investigations may tend in some measure to remove the prejudices that exist in the minds of many at home and abroad, against this potent medicine, the value of which, on the continent of Europe, is so little appreciated that, during a late residence of six months at Vienna, I never once heard of colchicum being prescribed, and during that time it certainly was not administered to a single individual in the Colossal General Hospital (containing upwards of 2000 patients) of that city. Nor did I once see it ordered in the practice of the physicians or surgeons at the Hotel-Dieu or La Charité in Paris, during a six months sojourn in that metropolis.

Leith, 1st June 1841.

