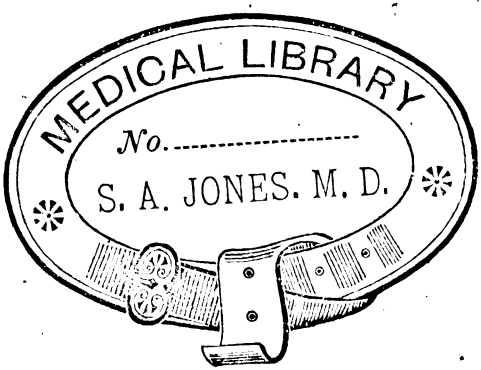


ON DIGITALIS.

ON DIGITALIS:

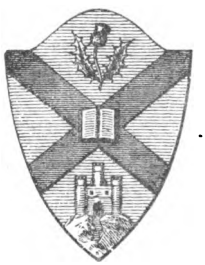
WITH SOME

OBSERVATIONS ON THE URINE.

BY

T. L. BRUNTON, B.Sc., M.B.,

LATE SENIOR PRESIDENT OF THE ROYAL MEDICAL SOCIETY, AND
LATE RESIDENT PHYSICIAN TO THE CLINICAL WARDS,
ROYAL INFIRMARY, EDINBURGH.



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TO

DOUGLAS MACLAGAN, M.D., F.R.S.E.,

AT WHOSE SUGGESTION THIS INVESTIGATION WAS BEGUN, BY WHOSE

ASSISTANCE IT WAS CARRIED OUT, AND TO WHOSE CONSTANT KINDNESS

THE AUTHOR

WILL EVER BE DEEPLY INDEBTED,

This Work

IS RESPECTFULLY DEDICATED.

PREFACE.

ENCOURAGED by the distinction awarded to this Thesis by the Medical Faculty of the Edinburgh University, and believing that it contains some facts not altogether without interest or importance, I have been induced to publish it, though fully conscious of its very imperfect condition. Though my time was not only short, but much broken up, the omissions would probably not have been so numerous, and the amount of new material greater, were it not that, fearing lest I should see, not what was actually before me, but what others had seen, and I thought I ought to see, I left myself, during the greater part of the time, purposely ignorant of the literature of Digitalis, only reading it up after most of my experiments had been already performed, and then learning that many of my observations had been already made by various experimenters, whose results they only confirmed.

Here I gladly take the opportunity of acknowledging my great obligation to Dr Maclagan, who first suggested this

say how much is owing to the drug, and how much to the natural course of the malady.

Perhaps no better example of the imperfection of our knowledge can be given than the views entertained respecting digitalis, for although it is in daily and hourly use, and, for several years back, hardly a month has passed without an article upon it in one or other of the medical journals, it is regarded by some as weakening the heart's action, by others as strengthening it, some placing it at the head of the list of diuretics, others denying that it possesses this property at all; and even when two authorities agree as to the results produced by it, their views as to its *modus operandi* are of the most dissimilar nature. Such being the state of our knowledge of this valuable medicine, I have been induced to make the following investigations with the view of deciding some at least of the disputed points; and if I have not done so much as I would wish, I trust that my labour may not be entirely in vain, but prove, at least, a stepping-stone towards the desired end.

HISTORY.

So striking is the appearance of this elegant plant, with its tall stem rising from the midst of a thick bunch of downy leaves, and gracefully bending at the top under the weight of its beautiful purple bells, that it is impossible to believe the ancient herbalists would have passed it over in silence. As no notice of it is found in their works, we are led to believe that they were unacquainted with it. Its popular name of Foxglove[1] occurs in Saxon writings of the eleventh century; but it seems to have been unknown to

[1] Pereira's Mat. Med.

the learned till near the middle of the sixteenth, as it had no Latin name till 1535, when Fuchsius, professor of medicine at Tübingen, gave it that of Digitalis, which it still retains. It seems formerly to have enjoyed a great reputation as an external application[1] for the cure of wounds and scrofulous ulcers,[2] and for causing the absorption of scrofulous glandular enlargements.[3]

The internal administration of its juice has been noticed as a remedy for scrofula by Van Helmont,[4] Haller,[5] Fourcroy,[6] and Merz.[7]

According to Lobel, digitalis was employed on account of its emetic and cathartic properties by the peasantry of Somersetshire as a cure for fevers. Ferrein[8] alludes to these properties, and observes that it was reckoned a cure for inveterate apoplexy, but ought only to be administered to robust persons. It occurs in the list of simples of the London Pharmacopœias for 1650, 1678, 1682, and 1721, is excluded from that of 1746, but appears again in 1788, and in that of 1809 it is not mentioned merely, but the preparation of its tincture and infusion are described, and in all subsequent editions it has held a prominent place. At an early period it seems to have been less used on the continent than in England, as it is absent from the Pharmacopœia of Leyden for 1718. Drake affirms that its action as a diuretic was unknown till 1770, and in 1775,

[1] Ferrein, Matière Med., t. iii. 1770, p. 67. *Vide* Homolle & Quevenne, p. 139.

[2] Geoffrey, Trait. de Mat. Med. 1743, t. vi. p. 202 (H. & Q., p. 140.)

[3] Ferrein, *op. cit.*

[4] Apparatus Medicarium, 1776-1794 (H. & Q., p. 138).

[5] Hist. Stirpium Indig. Helvetiæ, 1768 (H. & Q.)

[6] Encyclopedie Methodique, t. v. p. 456 (H. & Q.)

[7] Dissert. Inaugural, Jena, 1790 (H. & Q.)

[8] Ferrein, *op cit.*

Withering wrote the first monograph on its action as such, noticing also its power of lowering the pulse. From this latter property it began to be used in hæmorrhages, and Ferriar,[1] giving it for hæmoptyses in the early stages of phthisis, thought that it also prevented the farther formation of tubercle—Beddoes,[2] Drake,[3] Fowler,[4] Mosman,[5] Barr,[6] Maclean,[7] and Darwin,[8] have all recommended its use in phthisis, and Brinton[9] says that it is the best remedy for hæmorrhage from cavities in its advanced stages. Ferriar[10] thought it useful in inflammatory fever, and Currie,[11] Thomas,[12] Rasori,[13] Hirtz,[14] Millet,[15] Oppolzer,[16] Schneider,[17] and Traube,[18] all hold the same opinion. In continued fever, it has been recommended

[1] Ferriar on Digitalis.

[2] Beddoes on Consumption, Digitalis, and Scrofula, 1801 (H. & Q.)

[3] Drake, Letter to Beddoes (H. & Q.)

[4] Fowler, Letter (H. & Q.)

[5] Mosman Essay on Scrofula, Glandular Consumption, and Observations on Digitalis (H. & Q.)

[6] Barr, Letter to Beddoes (H. & Q.)

[7] Maclean, Med. & Phys. Journ. lxv. p. 180-201 (H. & Q.)

[8] Darwin, *vide* H. & Q., p. 323.

[9] Brinton, quoted by Handfield Jones in Clinical Remarks on Functional Nervous Disorders.

[10] Ferriar, *op. cit.*

[11] Currie, Medical Reports.

[12] Thomas, Practice of Physic.

[13] Rasori, Annales de Therapeutique de Rognetta, 1845 (H. & Q.)

[14] Bulletin de Therapeutique, Feb. 28 and March 15 (*vide* Yr. Bk. of Sydm. Soc. 1862, p. 110.)

[15] Millet, Bullet. de Therap. Ann. par Jamain, 1860, p. 55 (Syd. Soc. Yr. Bk. 1860, p. 221.)

[16] Oppolzer, Canst. Jahrb. vol. 3, p. 273, *vide* Syd. Soc. Yr. Bk. 1860, p. 219.

[17] Schneider, Annuaire de Thérapeutique, 1859, pp. 82-88 (Syd. Soc. Yr. Bk. 1859.)

[18] Traube, Deutsche Klinik, No. 47, 1859, Canst. Jahrb. v. 3, p. 273, *vide* Syd. Soc. Yr. Bk. 1860, p. 219.

by Clutterbuck,[1] and in bad cases of typhoid fever by Wunderlich.[2] It has been proposed as an antiperiodic in ague by Davy,[3] Graffeneuer,[4] and Gerard,[5] and Bouillaud[6] has treated between forty and fifty cases successfully by it. It has been recommended in hemicrania by Debout[7] and Serre,[8] and it was found to be highly efficacious in neuralgia by Boison[9] and Hardwicke.[10] According to Thomas,[11] it effects a permanent cure in epilepsy, and Parkinson,[12] Moll,[13] Corrigan,[14] Crampton,[14] Sharkey,[14] Neligan,[14] and Duclos[15] have employed it with success. Dr C. L. Robertson[16] finds it extremely useful in the second stage of general paresis of the insane. Mr G. M. Jones,[17] of Jersey, employed it in large doses in delirium tremens; and Peacock,[18] Carey,[19] and Reid[20] record success-

[1] Clutterbuck, Inquiry on the Nature and Seat of Fever, 1807, (H. & Q.)

[2] Wunderlich, Med. Times and Gaz., 1862, p. 2040.

[3] Davy, *vide* H. & Q., p. 324.

[4] Graffeneuer, Merat & Delen's Dict. de Mat. Med., t. 2, p. 645-47 (H. & Q., p. 324.)

[5] Gerard, Thesis Montpellier (H. & Q.)

[6] Bouillaud, Traité de Nosographie Médicale, 1846, t. 3, p. 471, and Clinique Medicale de la Charité, t. 3, p. 236 (H. & Q.)

[7] Debout, *vide* Yr. Bk. Syd. Soc., 1861, p. 161.

[8] Serre, Bullet. de Ther., April 15, 1861, and Canst. Jahrb. v. 3, p. 29, (*vide* Yr. Bk. Syd. Soc., 1861, p. 164.)

[9] Boison, Bul. de la Soc. Med. de Gent, May and June 1861 (*vide* Yr. Bk. Syd. Soc., 1861, p. 164.)

[10] Hardwicke, quoted by Handfield Jones, *op. cit.*

[11] Thomas, *op cit.*

[12] Parkinson, Theatre of Plants, p. 654 (H. & Q.)

[13] Moll, Epilepsia Digitali Sanata, dissert. Bonn, 1823 (H. & Q.)

[14] H. & Q., p. 144.

[15] Duclos, Bul. de Ther. lix., 1860, Yr. Bk. Syd. Soc. 1861, p. 161.

[16] Robertson, Brit. Med. Journ., Oct. 3, 1863.

[17] Jones, Med. Times and Gaz., Sept. 29, 1860.

[18] Peacock, Med. Times and Gaz., Aug. 3, 1861.

[19] Carey, Med. Times and Gaz., Aug. 24, 1861.

[20] Reid, Edin. Med. Journ., 1864-65, p. 112.

ful cases. It has long been recognised as an excellent diuretic in dropsy depending on disease of the heart, but its administration was sometimes thought dangerous when there was much weakness of that organ. Drs Handfield Jones,[1] Fuller, Germaine, and Wilks[1] believe, however, that it strengthens rather than enfeebles the heart, and is, therefore, most useful when that organ is weak, and dangerous only in hypertrophy. Mr W. H. Dickinson has found it an excellent remedy in menorrhagia, and a powerful oxytoxic. The general poisonous action of digitalis has been examined by Orfila, Bouley and Reynal, Dupuy and Delafond, Bouchardat and Sandras, Stannius, and others. Its action on the arterial tension and the heart has been studied by Blake, Traube, Winogradoff, Briquet, Kölliker, Dybkowsky and Pelikan, Eulenberg and Ehrenhaus, Handfield Jones, Fagge and Stevenson. Its influence on the temperature has been examined by Traube, Dumeril, Demarquay, and Leconte, &c.; on the metamorphosis of tissue by Winogradoff and Stadion.

CHEMICAL HISTORY.

Up to the year 1841, when Messrs Homolle and Quevenne succeeded in obtaining from digitalis a neutral principle in the form of a yellowish powder, presenting the bitterness and possessing the physiological action of the plant, the active principle had been sought for in vain, though several chemists believed they had obtained it in the shape of brownish or yellowish extracts, to which they had accordingly given the name of digitaline, a name afterwards applied to the substance obtained by Homolle and Quevenne.

[1] H. Jones, Assoc. Med. Journ., 1862, 2, p. 188.

The results of the analyses given by these gentlemen of digitalis, and their description of the characters of its constituents, are as follows:—

Digitaline.—In scales or masses—pale yellow—easily powdered, and the powder of a yellowish colour, intensely bitter, with a peculiar faint odour, and causing sneezing if it be carelessly moved, heavier than water, and doubtfully crystallizable. It is unalterable in air, fuses at 100°, and above this becomes coloured and loses its bitterness, which is replaced by an astringent taste. It is neutral to test-paper, but gives off acid fumes when burnt. It contains no nitrogen. It is soluble in nearly 2000 parts of cold and 1000 of hot water. It is easily soluble in alcohol and wood spirit, in about 100 parts of pure ether, in a considerably larger proportion if the ether contain water, and more especially alcohol, completely soluble in chloroform, partly in almond oil and oleic acid, and insoluble in sulphide of carbon. It forms no compounds with acids. Concentrated sulphuric acid forms a brownish solution, becoming somewhat purple, and depositing olive-coloured flakes on the addition of water. With hydrochloric acid it forms a light green liquid, becoming darker as it stands, and lessened but not changed by the addition of water. Its aqueous solution is not precipitated by bichloride of mercury, acetate or subacetate of lead, nitrate of silver, perchloride of iron, chloride of gold or platinum, or acetate of copper.

Digitalose.—This has a white crystalline—almost micaceous—aspect. Its point of fusion is 200°, and it is soluble in concentrated sulphuric acid, giving it a pale yellow colour, but forming with dilute acid a rose-coloured solution. It is neutral, tasteless, soluble in alcohol and ether, insoluble in water.

Digitalin.—This is a white neutral powder, soluble in alcohol, insoluble in water, insipid or faintly bitter; furnish-

ing to water a transparent material in which this bitterness resides. Its alcoholic solution is precipitated by caustic potash.

Digitalide.—This occurs in pale gummy-looking scales, is neutral, soluble in water and feeble alcohol, slightly in strong alcohol, insoluble in ether. Its taste is sweetish, with a bitter after-taste. Is perhaps the bitter part of digitalis, which is soluble in water, along with colouring matter. It is also precipitated by caustic potash, and distinguished from digitalin by its form.

Digitalic Acid.—White, crystallizable, and of an acid taste and peculiar odour, becoming suffocating under heat, soluble in water and alcohol, slightly in ether, decomposes in air, and becomes brown with extreme facility; the decomposition being favoured by light and alkalis.

Antirrhinic Acid.—This is volatile and oily in appearance. Besides these, there are *Digitaloic Acid*, *Tannic Acid*, *Sugar*, *Pectin*, an albuminoid azotized matter, a crystallizable orange-red colouring matter, chlorophyll, a volatile oil, and ligneous fibre.

The process they employed for the extraction of digitaline, was to precipitate a watery infusion of digitalis by sub-acetate of lead, to remove the excess of lead by a mixture of carbonate and phosphate of soda, and the lime by oxalate of ammonia. To the filtrate they added tannin, and the product of this was mixed with litharge, dried, powdered, and treated by alcohol. This was then evaporated, and the residue was treated with concentrated ether, which dissolved the other principles and left the digitaline. This process, as modified by O. Henry, and adopted in the British Pharmacopœia, consists in treating the syrupy alcoholic extract with acetic acid, decolorizing by animal charcoal, precipitating by tannin, decomposing by litharge, and thus freeing the

digitaline which is decolorized by animal charcoal and purified by ether.

The composition of digitalis has been examined by many other chemists, especially Radig, Morin, Buchner, Kossman, and Walz.

Walz[1] has obtained as volatile principles digitalosmin and digitalissic acid (valeric acid), and as non-volatile principles digitalin, digitasolin, digitalacrin, digitaloin, and digitaloic acid. Digitalosmin is the odoriferous principle of digitalis, and is a camphoroïdal substance obtained as a fatty film by distilling with water. When the crude digitaline, obtained after decomposing the tannin precipitate with litharge, is treated with ether to purify it, an acrid matter is dissolved, to which Walz at first gave the name of digitalacrin, thinking it a simple substance; but has since found that from it may be separated digitaline fat or digitaloin in white crystalline scales, which melt to an oil at a gentle heat, and digitaloic acid in white nacreous laminæ. The residue left by the ether, and which constitutes commercial digitaline, consists of two substances; one of which is much more readily soluble in water than the other. This soluble part is yellowish and amorphous, soluble in 120 parts of cold and 40 of boiling water; is said by Walz to be the active principle, and is called by him digitaline; others call it digitasolin. The insoluble residue is called by him digitaletin, but others called it digitaline. It is still doubtful if all these bodies are really distinct or have been obtained quite pure, but Walz's analyses and formulas agree well. Kossman has given the name digitalic acid to an acid in digitalis, and also to a product of boiling digitaline with soda, lye, or lime.

The name of the active principle has been spelt by

[1] Watt's Dict. Chem., Art. Digitalis.

Homolle as digitaline with a final e, and by English writers indifferently as digitalin[1] and digitaline.[2] It is to be regretted that Homolle gave such similar names to different bodies, and also that other chemists have given different names to the same body, as for example, Walz, who calls the pure active principle digitaletin. I have retained Homolle's orthography.

That digitaline is the active principle, or at least contains it, has been shown by the physiological experiments and clinical experience of various observers, among whom may be mentioned Messrs Hervieux, Shohl, Sandras, Bouillaud, Andral, and Lemaishe, Corvisart, Laroche, Duroziez, and Mandl, who have found that it produced the same effects as the plant itself, both as a poison and a medicine.

Digitaline is estimated by Homolle and Quevenne as being 100 times as strong as the leaves of the plant; but Stadion reckons it as only 30 times as strong, and from the trials I made on myself, I am inclined rather to agree with the latter estimate. In order to determine whether there was no other diuretic principle in digitalis, on account of which it might be preferable to administer the plant itself, or one of its pharmaceutical preparations,[3] M. Homolle made experiments on the products obtained from the plant by various solvents. The first substance was the residue, after exhausting the leaves with weak alcohol; the second, the substance taken up from the alcoholic solution by ether, consisting chiefly of a nauseous fœtid and acid principle, resembling the digitalic acid of Kosman; the third was the alcoholic solution after treatment with ether; the fourth is

[1] Brit. Pharm. [2] Garrod, Mat. Med.

[3] Arch. Gen. 5 ser., vol. 18, p. 5, July 1861. *Vide* Syd. Soc. Yr. Bk., 1861, p. 434.

obtained by treating the result of evaporation of No. 3 with chloroform.

No. 1 he found to be comparatively inert, the result of taking 3 grammes, or 46 grains, being only equal to 1 milligramme of digitaline, which is, therefore, 3000 times stronger. After taking 45 centigrammes, or about 7½ grains of No. 2, he had no symptoms for eight hours, but was then seized with great nausea, faintness, and vomiting, which continued at intervals of fifteen minutes for thirty hours. Next day his pulse had fallen, and, on the fourth day, was as low as 48. Vision was impaired, and he could not look steadily at a bright object. Urine was abundant, but the bladder's contractility was impaired, and external pressure was required to expel the urine. He had pulsation of the abdominal aorta, anxiety, epigastric constriction, and cough, with pneumonic expectoration, lasting for a week; but these, he thought, were caused by the continuous vomiting. About a year after this, he took 2 centigrammes, or about ⅓rd of a grain of No. 3. He repeated the dose in forty hours, and again after eight hours more. The symptoms were exactly those of digitaline. No. 4 had exactly the same action, but was much more powerful. M. Homolle concludes that digitaline is the only principle in digitalis which has any therapeutical value, that the greater toleration of the stomach of preparations made by water, is from the absence in them of the nauseating acrid principle (digitalic acid) contained in No. 2, that digitalis owes its sedative and diuretic effects entirely to digitaline, but that its nauseating effect, and probably the impairment of vision it produces, are due to digitalic acid. M. Homolle seems to prove that digitaline is by far the most important and active of the principles contained in digitalis, as the fall of the pulse, noticed after taking No. 2, may have been produced by digitaline contained in it; but

as I experienced impairment of vision and nausea after taking digitaline, which I had got from Mr Morson himself, who said it had been carefully prepared, and might be relied on, I believe these effects may be produced by digitaline, and are not, as M. Homolle seems to think, entirely owing to digitalic acid.

PHYSIOLOGICAL ACTION.

On Plants.—Marcet[1] found infusion of digitalis in a few seconds caused a slight crisping of the leaves of a haricot plant introduced into it by the root, and next day the plant was dead. On treating a haricot in the same way with solution of digitaline, (3-20ths of a grain in ʒii. of water), I did not notice the sudden crisping of the leaves, which, however, in the course of a day, became dry and rough, in two days were rolled in at the edges, and finally became quite dry and shrivelled, but retained their natural colour.

On Animals.—As the general action of digitalis, in varying doses, has been carefully examined, and the sequence of symptoms accurately noted by Messrs Bouley and Reynal[2] in their experiments on horses, I subjoin their account of them.

Six or eight hours after giving a large dose of digitalis to horses, they stand at the stretch of their halter, sad, dejected, and without appetite, and their coat lustreless and rough. Then signs of general excitement appear. The conjunctivæ are injected and of a bright red, the eyes brilliant and fixed,

[1] Annals de Chem. et de Physique, v. xxix.

[2] Receuil de Med. Veterin. Pratique, 3 ser. t. vi. p. 297, 1849, (H. & Q.)

the face pinched, the nostrils dilated and quivering, respiration hurried, the number being 15 to 20 or 25 in a minute, circulation more rapid, the beats of the heart being abrupt, their energy much increased, and accompanied, after a certain time, by a vibratory thrill, with a decided metallic tinkling, and as poisoning goes on, a distinct bellows murmur becomes audible, and is rendered louder by any exertion; the beats then show a decided intermittence, and the pulse is small, thready, and intermittent. The heat of the body is increased, and hot sweats appear on the ears, nose, shoulders, and flanks. The mouth is hot, and filled with saliva, which is sticky and scanty. The tongue is of a purplish red at its tip and edges, and is covered on the dorsum by a thick coat, which gives it a leaden hue, the fæces are of their normal form or colour. During the first twelve hours the animals often show signs of transitory intestinal pain.

At the end of twenty-four or thirty-six hours the stage of excitement has passed, and the animals become comatose, their heavy heads hanging down towards the litter, or kept at the bottom of the manger completely insensible to external noises or stimuli, their eyes fixed, without movement or expression, sometimes half-covered by the falling lids, and at other times haggard and ready to start from their orbits, the pupils greatly dilated, and the conjunctivæ, previously of a bright red, are now of a violet brown, and their secretion dried up. The previous acceleration of the respirations is now succeeded by great slowness, their number descending to 8, 7, or even 6 per minute, and being deep, broken, and trembling. The heat of the body is diminished, the sweats stop, and the skin becomes cold. The fæces are now of a browner character, and covered with a layer of mucus more or less thick. The urine is at first suppressed, but at the end of thirty-six or forty-eight hours is passed in abundance, pale,

clear, and inodorous, voided very frequently, and in small quantity at a time. There is great muscular weakness, staggering gait, oscillation of the posterior extremities, and a kind of paralysis, which slows their movements. In some there are slight vertigoes, in others spasmodic fibrillary contractions of muscles of the face and of the alaenasi. The severity of the symptoms rapidly increases. The muscular weakness becomes extreme, the legs are no longer able to support the weight of the body, and the animal falls *en masse*. The respiration becomes more disturbed, sometimes jerking, difficult, and plaintive, most frequently very slow, but in some instances slightly accelerated. In some it presents a remarkable intermittency, and its time of stoppage coincides with that of the heart when the latter also intermits.[1] In some cases, twenty-four to thirty-six hours before death, there has been noticed a paralysis of the lips, chiefly the upper, and a thick and stringy saliva flows from the mouth. Diarrhœa appears, and quantities of a very fœtid, soft, blackish paste are discharged, and when the intestinal canal is completely emptied, the diarrhœa becomes serous, the expelled matters being liquid, blackish, and of a repulsive odour. The skin becomes icy cold, the thermometer introduced into the mouth, rectum, or subcutaneous cellular tissue standing in some cases at 31°.5C., or even before death at 25°C. Death generally comes on quietly, but is sometimes accompanied by unconnected movements.

When given in doses less rapidly fatal, so that each dose would only produce slight symptoms, which would soon pass away if the dose were not carefully repeated, the influence which it exerts on the circulation is by far the most prominent phenomenon. At first there is slight excitement of the heart, and its pulsations are a little quickened, then,

[1] This also occurs in dogs.—Exp., Appendix.

later on, they undergo a remarkable diminution, falling to 25 or even 20 per minute. If the dose be still repeated, the beats become quicker and more energetic, rising to 55, 60, 65, and 70. The cardiac sounds are more clearly heard, more distinct from each other than normally, and following a different rhythm, there being occasionally intermittences, usually after the same number of beats, but this number varying in different subjects, and in the same subject according to the date of the poisoning. There may be 5 or 6 pulsations between the intervals in some, 15 or 16 in others, and in yet others the intermissions are completely irregular. As the poisoning goes on, metallic ringing appears, and becomes more and more distinct and sonorous. Still later, a vibratory thrill appears, and is followed by a bellows murmur. As death approaches the beats of the heart become more and more rapid, being 92, 100, or even 114. The beats of the pulse correspond in time to those of the heart; but as the latter increase in energy, in the same ratio the former become more and more feeble, and less and less perceptible, till at last, when poisoning is complete, it becomes completely imperceptible.

In doses so small as to have no poisonous effect, its action is shown first on the urine, and secondly on the circulation. To show this, Messrs Bouley and Reynal give the following typical case:—

A Hungarian horse of an excellent constitution, employed in the service of the veterinary school of Alfort, aged ten years.

Normal state at time of experiment:—Respirations 16, pulse 37, full, mucous membranes rosy, digestive functions intact,—all the signs of health.

Jan. 1, 1849, 10 A.M.—6 grammes (93 grains) of digitalis powder were given in an electuary, when the animal was completely fasting. 2 P.M.—Respirations 14, passed water,

which was clear and plentiful. 6 P.M.—Respirations 13, pulse 35. The water is always passed in abundance, and with the same limpidity. The next day the effects had disappeared.

Jan. 4, 10 A.M.—6 grammes given as before. At the time of giving, respiration 16, pulse 37. 3 P.M.—Respirations 14; urine clear, abundant, and odourless. 6 P.M.—Respiration, circulation, and urinary secretion the same. 8 P.M.—Respirations 13; cardiac beats a little diminished in intensity—otherwise quite healthy.

Jan. 5, 7 A.M.—Conjunctivæ pale, pulse 22, small and not well felt, the beats of the heart have diminished in intensity, remain quite distinct, marked intermittence after each beat, respirations 6 to 7. Noon.—Same state. 2 P.M.—Pulse 25, intermittence less sensible, respirations 11, urine always clear—less abundant. 7 P.M.—Lying down quietly, the litter much soaked with urine, pulse 30, intermittence has disappeared, respiration 15.

Jan. 6.—All the symptoms of the medicine disappear, and the functions return to their normal state.

Jan. 8.—6 grammes of digitalis. At the moment of administration, pulse 30, respirations 10 to 11, thermometer in rectum 38°.75C., and 31°.25C. in the nasal cavities—all the signs of health. 1 P.M.—Nothing particular. 4 P.M.—Pulse 28, no change in the rhythm of the heart, respirations 10, urine clear, and in considerable quantity, 36°.25C. in rectum, a little tenderness of abdomen. 8 P.M.—Appetite good, pulse 26, cardiac pulsations ringing, respirations 14, urine always abundant.

Jan. 9.—Conjunctivæ pale, pulse 24, small, hardly sensible, beats of the heart enfeebled, respirations 6, temperature 36.°25C. 2 P.M.—Mucous membranes more coloured, pulse 30, beats of the heart more intense, respirations 12, urine less abundant and less limpid. The functions now began to return little

by little to their normal state. In almost every case which they experimented on, the history was exactly the same. In these experiments we note a steady diminution of the respirations, temperature, pulse, and intensity of cardiac beats, with increase of the amount of urine, these effects reaching their maximum in twenty-four to thirty-six hours, and then gradually disappearing. The effects of digitalis upon other mammals and man seem, *cæteris paribus*, to correspond closely to those on horses, except that in the latter, and in herbivora generally, there is no vomiting.

Having given this description of its general action, I will now consider its action on various organs more in detail.

On the Blood.—Magendie[1] states that decoction of digitalis, when mixed with blood, prevents its coagulation, and Thackrah,[2] that it suspended coagulation, and the clot at length resulting was black. Davy says that ʒss of extract of digitalis in ʒj. of water, added to ʒii. of blood as it flowed from the arm, gave it the consistence of paste; after thirty-six hours it appeared much the same; on the following day, the lower part was more viscid, as if from subsidence of fibrin—it was coagulated on dilution with water. It is impossible to draw any definite conclusion from these statements, as to whether it has any specific action on the blood or not, as the prevention or suspension of coagulation in the first two cases may have been merely from dilution, and the black colour of the clot may be due to the colouring matter of the decoction. In the third case, the prevention of coagulation seems due to the viscosity induced by mixing the sticky extract with the blood, and as soon as this mechanical effect was removed by dilution, the blood coagulated. Orfila[2] found, that after poisoning dogs with watery extract of digi-

[1] Quoted by *Lancet*, 1837.

[2] Orfila's Toxicology by Waller, 1817, vol. ii. p. 231.

talis, the blood was fluid in all the five cases in which he mentions its condition. He concludes that "alcoholic (resinous) extract appears to act especially on the heart or blood, since this fluid is *constantly* found coagulated immediately after death, whenever this extract has been applied to the cellular tissue, or introduced into the stomach." This conclusion appears to be rather more general than facts, at least those which he details, warrant, as in five cases he found the blood coagulated in both ventricles only in one case, in the right ventricle completely in one, and partially in another, while it was fluid in the left ventricle in both these cases, and in both ventricles in two others. In four cases in which dogs were poisoned with digitaline, I found the blood coagulated in the right ventricle, the other being empty in one case, partly fluid and as if curdled in both ventricles in another case, and quite fluid in two others.

What is wanted in this subject, however, is not so much loose observations of this sort, but definite experiments on the changes of the chemical relations of the blood in regard to the interchange of gases, such as Bernard made in reference to woorari, and Harley has lately been doing with several of the organic alkaloids.

On the Circulation.—Before considering the effect of digitalis on the circulation, it may be advisable to glance at the cause of the pulse, and the arterial tension and the modifications they undergo.[1] The pulse is the feeling of a sudden rise experienced by the finger when it presses on an artery, and is caused by the wall of the vessel, which had lost its cylindrical form under the pressure, becoming tense and hard each time that the arterial tension is raised by a systole of the heart, and tending to regain its original form

[1] Marey, Physiologie Medicale de la Circulation de Sang.

in which all the points in its wall offer an equal resistance to the intense pressure of the blood within.

The arterial tension on which the pulse depends, is the force expended by the heart, put in reserve by the aorta and large arteries, and regulated by the elasticity of these vessels. If the arterial system were empty, and the heart began to beat, the blood which it sent into the arteries would remain there, very little escaping by the capillaries,[1] as the arteries would have no tendency to contract and press it on between each systole. As they became fuller, however, their elastic force or the arterial tension would increase, sending more and more blood through the capillaries, till the quantity escaping through between each systole exactly equalled the amount driven in each time. The arterial tension would then remain nearly fixed, or at least steadily oscillating round one point, becoming somewhat increased as each wave of blood was sent in from the heart, (each wave being equal, not only to the blood escaping by the capillaries during its continuance, but to that escaping during the interval, in addition; this additional amount of blood distends the arteries, and increases their tension), and becoming somewhat diminished as it escaped from the capillaries. The arterial tension may be altered in two ways: (1.) If, *while the cardiac pulsations remain the same* (*a*) the capillaries be somewhat dilated, the blood will escape more quickly, and the tension will be diminished. (*b*) If the capillaries be contracted, less blood will escape, and the tension will be increased.

(2.) The *capillaries remaining the same*, (*a*) if the beats of the heart be reduced in number, less blood is sent in, and the tension falls; if they be increased, the tension rises. (*b*) If

[1] Wherever I use the word capillaries, I do so in a general sense, and without entering into the question as to the difference between capillaries properly so called, and small arteries, so that if contractile power be denied to capillaries proper, the word may be read "small arteries."

the wave of blood sent in at each pulsation be increased in size, the tension rises; if it be reduced, it falls. The arterial tension or force with which they tend to drive the blood through the capillaries, is easily measured by the hæmadynamometer, and its amount expressed in inches of mercury. It is obvious, then, that the arterial tension is the product of *two* factors, viz.—1. The amount of blood pumped into the arteries by the heart in a given time. 2. The amount of blood escaping through the capillaries in the *same* time. This was clearly enunciated by Blake,[1] and more fully worked out by Marey. The first factor depends on the amount of blood in each wave, multiplied by the number of waves in the given time. The second, only on the size of the capillaries, and the rapidity of the flow of blood through them, and this latter, again, depends on the arterial tension.

Influence of Respiration on Arterial Tension.—If inspiration and expiration be made with difficulty, as, for instance, by closing one nostril, and thus obstructing the passage of air, the arterial tension *rises* with *ex*piration, and *falls* with inspiration. But if respiration be freely performed as with open mouth, the tension *rises* with *in*spiration, and falls with expiration. This difference is due to the pressure upon the aorta and large vessels of thorax and abdomen.

The enlargement of the thoracic cavity during inspiration causes a vacuum which is at once filled by the external air, if there be no obstacle to its entrance, and thus no great suction is exerted. If the air enter with difficulty, the enlargement of the thoracic cavity by the respiratory muscles, acting like the withdrawal of the piston of an exhausting syringe, greatly lessens the internal pressure, and causes much suction, the blood is drawn to the aorta and large vessels of the thorax from the periphery, and the tension is much diminished. During expiration, the contractility of

[1] Edin. Med. Journ., 1839.

the lung, and the expiratory muscles combine to expel the air; but this being done with difficulty, the aorta and large vessels are much compressed, the blood driven towards the periphery, and the tension raised. While this is going on in the thorax, the diaphragm descends into the abdomen during inspiration, lessening its cavity and pressing on the abdominal aorta and increasing the tension, while, during expiration, it ascends, lessening the pressure, and, consequently, the tension. In a normal state, the thoracic and abdominal pressures counteract each other; but when there is any obstacle to the passage of air, the thoracic influence predominates, and the abdominal, when there is any hindrance to the expansion of the abdominal parietes. In the normal state of the animal economy, the number of the pulse and the arterial tension are in inverse ratio to each other, the law given by Marey on this point being, "The heart beats so much the more frequently the less the difficulty it has in emptying itself."[1]

I have entered at length on this question of arterial tension, as a knowledge of the facts I have stated is necessary in order to understand fully the way in which the circulation is modified by digitalis.

On the Pulse.—When given in small doses, digitalis first reduces the number of beats without rendering them irregular. If its influence be pushed farther, the pulse remains slow, but now and then a quick beat is interpolated.[2] These quick beats, as the influence increases, become more numerous, so that the slow beats which now occur only occasionally become intermissions; and in a still further stage, the slow beats entirely disappear, and the pulse becomes regular and extremely rapid.

This slowing, intermission, and final rapidity have been frequently examined in animals, and though I am not aware

[1] Marey, *op. cit.*

[2] Case of Daniel G.

that the gradual succession of the quick beats to the slow, which occasions the intermittence, has been shown, probably from the readiness with which it would escape the observation of the finger, though at once detected by the eye, yet we see it with great clearness in the case of Daniel G., and though this was not during the increase but the decrease of the symptoms, I think we may infer that these came on very much in the same order in which they went off.

Some have held that there is an acceleration of the pulse before the retardation appears. Bouley and Reynal[1] noticed this in horses poisoned with large or moderate doses, but never observed it after therapeutical doses had been given. The doctrine of primitive acceleration from medicinal doses was advanced by Sanders,[2] and supported by Joerg[3] and Hutchinson.[4] This acceleration is of two kinds,—1st, Following immediately on the administration of digitalis, and disappearing, or at least diminishing, much within half-an-hour or three quarters; and 2nd, A more permanent acceleration lasting for 24 to 48 hours or longer; the effect of the temporary acceleration not passing quite away during the interval between the doses, so that each succeeding one raises the pulse a little higher than before, till at last the acceleration gives place to retardation, and the number gradually falls, passing even below the normal standard. Though Sanders adduced 2000 observations in support of his view, yet most succeeding authors have denied it. I have occasionally found my pulse increased after taking digitaline, but sometimes not; and even had the acceleration been frequent, I would not have been able to conclude very much from it, as the pulse varies not only with position but with

[1] *Op. cit.* [2] Sanders on Foxglove.
[3] Joerg, Arch. de Med., prem. ser. t. xxvii., p. 107, (H. & Q.)
[4] Hutchinson, (H. & Q.)

mental states, and that to a considerable extent in a person of nervous temperament. As to the secondary acceleration, it is perfectly true that you often find, on looking over a table of the pulse, a seeming acceleration of the pulse on the second or third day after beginning to take digitalis, yet it is to no great extent and not greater than we find in health.

Though the primitive acceleration be denied by almost all authorities, few doubt that digitalis causes retardation of the pulse either immediately or in the course of a few days. I have found that my pulse was sometimes quicker, sometimes slower, while I took small doses of digitaline, but that under larger doses there was marked lowering of the pulsations.

This lessening of the number of beats may have two causes: 1st, It may be central, from the heart being primarily affected by the drug, and contracting more slowly. 2nd, It may be from contraction of the capillaries opposing a greater resistance to the passage of blood, and by thus requiring greater propulsive force, slowing the heart's action according to the physical law, that what is gained in power is lost in speed. If the latter were the case, the blood flowing slowly through the capillaries would cause the arteries to become full and tense, the heart would be able only slowly to distend their resisting parietes, and that only to a small extent; so that if we applied a sphygmograph to the artery, we should find the line of ascent very oblique, the height of the curve small, and the line of descent also very oblique. But this is not the case, for if we examine the tracing taken on March 15, we observe that while the pulse is slow and the duration of each beat long, it presents the very opposite characters of those we have mentioned, the line of ascent being sudden and abrupt, the lever rising so rapidly that its *vis viva* carries it too far, so that in its descent it makes a point; the height of the curve is great, and the line of descent is sudden and dichrotic.

We see that the pulse in Daniel G. presents the same characters. From these facts I believe we cannot avoid the conclusion that it exerts a slowing action *directly* on the heart.

In poisoning by digitalis the force of the pulse bears no relation to that of the heart's impulse; for while the latter is strong and hammering, the former is small, thready, and nearly imperceptible. Marey[1] gives this law, "The force of the pulse is not in correspondence with the energy of the ventricular contraction, but is regulated by the state of the circulation in the ultimate ramifications of the vascular system." The force of the pulse increasing with the arterial tension and diminishing along with it, the weak pulse that occurs in digitalis poisoning is due to the low tension; and this, again, as we shall see hereafter, probably depends on the relaxation of the capillary system, and the rapid transit of blood through it.

On the Heart.—Having seen that digitalis exerts a primary influence on the heart, the question now arises, What is this action? And, first, as to its force. Does digitalis weaken the muscular power of the heart? Does it increase it? or does it do neither, but simply lessen the number of pulsations, either by diminishing its irritability, and so rendering it less sensitive to the stimulus of the blood, or by increasing the power of the regulating part of the nervous system?

Very different opinions have been held on these points by different authors. Stannius[2] says, that after the injection of a strong dose of digitalis, there is at once a surprising feebleness of the cardiac pulsations, which soon changes into paralysis of this organ, at first partial and then complete; and this he attributes to paralysis of its muscular contractility, rather than to any affection of its nervous arrangements.

[1] Marey, Physiol. Med. de la Circ. de Sang, p. 235.

[2] Stannius quoted by Homolle and Quevenne, p. 234.

Kolliker,[1] Dybkowsky, and Pelikan hold a similar view. On the other hand, many observers have been inclined, by clinical observation and physiological experiment, to think that digitalis acts rather by increasing the power of the heart; and that it causes death not so much by paralysis as by spasmodic contraction. Among others who have held this doctrine of stimulation may be mentioned Kinglake, Briquet, Handfield Jones, Fuller, Winogradoff, and Traube. This opinion has been founded on the observation that digitalis strengthens the weak and dilated heart, and is injurious in hypertrophy, on the increase of the arterial pressure often observed after its injection into the veins, and on the contracted state of the ventricles found after death constantly in frogs, but only occasionally in the mammalia. Mosman thinks that it acts by diminishing the muscular irritability of the heart, and thus lessening the number of pulsations without diminishing their force. Others believe that the slowing of its action is produced through the nervous system, and probably by an increased action of that part of it which exercises a regulating influence.

The settlement of these questions is of extreme importance, in reference to the medicinal administration of digitalis, in cases of weak heart. In order to their solution, let us consider what would be the effect of increasing the muscular power of the heart. Supposing that the size of the capillaries and the number and size of the waves of blood remained the same, but the muscular power of the heart were increased, how would the arterial tension be influenced?

The power of the heart being greater in proportion to the resistance it has to overcome, it would act with greater abruptness, and force the wave of blood more quickly into the arterial system; and as thus less blood would escape from

[1] Carpenter's Physiology, p. 229.

the capillaries during the time of its systole, the arteries would be more distended and the tension higher. This greater amount of arterial tension, in its turn, would force the blood more quickly through the capillaries at first, and the tension would rapidly diminish; but as the rapidity of the flow of blood would proportionally decrease, the amount passing through the capillaries in a *given* time would be much the same, and the mean arterial tension much the same, but the oscillation much greater. If now the capillaries be contracted, we will have the same phenomena with a higher mean arterial tension, and if relaxed, a lower tension. We would also say, that when the capillaries are contracted, less blood escaping by them during the systole, there would be more surplus, and the height of the oscillation still farther increased; but the reverse when the capillaries were relaxed. But what would be the effect of increasing the size of the wave of blood, the muscular power remaining the same? The increased quantity of blood would take longer to be driven in, the oscillation would not be abrupt, and, in fact, it would merely cause a higher mean tension. The increase of the wave, along with the increase of force, would cause a similar effect.

Intermittence or slowness of the pulse would cause greater oscillation, the long interval allowing the escape of more blood from the capillaries; the tension would fall much. From the length of the interval, the heart would have received more blood than usual, and the succeeding wave would be larger; but there being more room for it in the arterial system, it would not raise the maximum height of oscillation much, if at all, above the normal. If the force of the heart were lessened, the opposite results would take place, and the oscillations be less abrupt and of smaller amplitude.

Let us now see with which of all these conditions the effects observed from digitalis agree.

In experiment 6, a strong well-fed dog was operated on. At 3′ 48″ the respiration was 20, the pulse 84, the mean tension 5.65 inches of mercury, and the oscillation 5–6.5. A grain of digitaline was then injected into the jugular vein. At 59′ 45″ the mean tension is 5·7, or only 1-20th of an inch higher, but the oscillation is now 4-8· or 4 inches instead of $1\frac{1}{2}$. This increase in oscillation we have seen can be due only to slowness or intermittence of the pulse or increase of the force of the cardiac contractions, as far at least as the circulatory apparatus is concerned, and that in the former case the maximum would not be much above the normal, which in this case it is; and therefore we would consider as proved that the force of the heart is increased, were it not that we observe the remarkable decrease in the number of respirations, and are led to inquire whether it is not to the greater influence of these, rather than to any increase of the heart's force, that the oscillations are due; and this indeed seems highly probable, as the amount of oscillation is so great that we cannot easily imagine it caused only by a difference in the rapidity with which the blood is impelled into the arteries; and the fact that we notice, that while the average oscillation at the cardiac beats in one case is 3-10ths of an inch, that at inspiration is one inch. Though my own observations are as yet too incomplete to enable me to eliminate the disturbing effect of respiration, and the observations of Winogradoff,[1] in the short abstract that I have seen of them, are liable to the same fallacy, they yet seem to render the increase of force somewhat probable. It is obvious, however, that by examining a tracing by an instrument such as the registering hæmadynamometer of Sctschenow, which

[1] Yr. Bk. Syd. Soc. 1862, p. 452.

was employed by Winogradoff, and which registers at once both the cardiac pulsations and the respirations, and comparing its indications with those which we have seen would occur from increase or diminution of the heart's force, the problem might be solved with mathematical accuracy, not only for digitalis but for any other poison.

Though unable at present thus to afford complete proof of the increase of force, there is another line of argument open, —viz., the effect of increase or diminution of the contractile power of the heart upon its impulse. If the contractile power be increased relatively to the resistance to be overcome, or arterial tension, the contraction will be rapid, and the heart's impulse abrupt and strong. If the power be lessened, the contraction will be slow, and the impulse consequently weak.

Though this necessarily follows from physical laws, some might yet be inclined to urge as an objection—'But you find this strong and abrupt impulse in nervous palpitations and weakly persons, and is it to be supposed that the power of the heart is increased in these?' But in these cases, though the power of the heart be not absolutely increased, it is relatively to the resistance, for the arterial tension in these cases is low. After the administration of digitalis, we find not only that the impulse is abrupt and strong, showing increased power relative to the tension, but that the tension itself is increased (Exp. V. 3. 25′ 50″), and the absolute increase of contractile power is completely proved.

From the nature of the impulse generally remaining much the same till the last, or nearly so, the power of the heart appears to be relatively increased all along; but as the arterial tension, though it may be increased at first, greatly diminishes afterwards, the absolute force of the heart may be, and probably is, very greatly diminished before death.

From his observations on the effect of small doses, such as slow the heart's action, Winogradoff found that no change was produced; and as I found (Exp. X. 12. 35′ 20″) that not only was there no change in the mean pressure, but none in the oscillation, and the breathing quiet, though the pulse had fallen from 140 to 78, though not certain, I am strongly inclined to believe that the force of the heart is neither increased nor decreased. Later on, and after a farther dose, as at 1.20′, I am inclined to think that it may be feebler, though possibly it is only because the pulsations are more frequent.

The observation of Stannius, that after a strong dose of digitalis a surprising weakness of the cardiac pulsations becoming finally complete paralysis is observed, may be true in regard to overwhelmingly large doses; and in the sheep, which I killed by 2 grains, the condition of the heart was not noted, but in general the impulse is increased, so generally in fact, that often I have not noted it, looking on it as to be always expected.

(2) **On the Heart's Rhythm.**—Dybkowsky and Pelikan[1] found in frogs which were poisoned by digitaline (or other cardiac poisons, producing an identical effect), the rhythm of the heart was at first unchanged, but soon after three, five, or ten minutes (according to the poison), irregularity was noticeable. This was of two kinds—(1.) The ventricular contractions became peristaltic, so that after the contraction of the auricles, the ventricle did not contract as a whole, but first its upper third, whence the contractions gradually passed down to the apex; but before this had contracted, the upper third was again dilated. Two or three minutes before complete paralysis, the contractions became still more irregular, so that the upper or right half was dilated, while the lower or left half was contracted, and sometimes the auricles

[1] Mem. de la Soc. de Biologie, t. 3, ser. 3, p. 97.

did not contract simultaneously. Finally, when the ventricle completely stopped, one or more palpitating points could still be observed in it.

(2.) The second form, which was especially notable in poisoning by digitaline and green hellebore, consisted in a notable diminution of the number of beats, the heart contracting regularly, but very slowly, just as under galvanization of the vagi. This sometimes happened before peristaltic movements occurred, or even after their appearance. Fagge and Stevenson[1] found that the beats are not necessarily diminished, and sometimes the ventricle contracted only once for two pulsations of the auricles, and often one part, generally the apex, continued white, and contracted while the rest dilated regularly. They also observed palpitating points, such as Dybkowsky and Pelikan had described, and liken them to little crimson pouches on the white contracted ventricle. All these observers found that the ventricle stopped always in a state of firm contraction.

(3) **Impulse.**—The cardiac impulse seems almost invariably to be increased both in the lower animals and man, and becomes abrupt and hammering.

(4) **Sounds.**—When digitalis is given in poisonous doses, after the pulse becomes intermittent, a change is noticed in the cardiac sounds, there being first a vibratory thrill, and then a blowing murmur with the first sound. The first I have not observed; but Dr Gamgee felt it in a dog on which I was experimenting. The blowing murmur with the first sound I have noticed several times. It occurs in horses, dogs, and the human subject, and probably in all mammalia. It is probably due to mitral or tricuspid regurgitation from irregular contraction of the musculi papillares. I noticed it in one dog after section of the vagi and before digitaline was

[1] Proceed. Roy. Soc., vol. xiv., 270.

injected; but unfortunately, not having listened before dividing them, I cannot say whether or not it was due to their section.

On the Arterial Tension.—In small doses, digitalis, injected into the veins, causes no change, either in the mean tension or amount of oscillation. In larger doses it almost invariably increases the tension, sometimes very slightly, at other times considerably; and in one case of Mr Blake's, where he injected it into the arteries, the rise was enormous, the maximum being 14 inches instead of 5. The tension attains its maximum in three or four to nine or ten minutes, and then gradually diminishes. The oscillation is generally greater at first, and also gradually diminishing. Sometimes there is a rise just before death, and the tension diminishes very slowly after the heart has ceased to beat.

On the Capillaries.—In small doses, digitalis, while it slows the heart's action, seems at the same time to contract the capillaries. If we look at the results of Exp. X., we see that, although the cardiac pulsations were reduced from 140 to 78, yet the mean tension remained the same. This can only be explained by supposing that the capillaries are contracted, or that the heart is sending in at each stroke nearly double the amount it did before. This latter hypothesis seems extremely improbable, for though the blood has longer time to collect in the heart, yet we find when the same time is given by slowing the cardiac pulsations directly, without any action on the systemic capillaries, as we can easily do by galvanizing the vagus, the arterial tension at once falls to a very considerable extent. At other times we find that the tension not only does not fall, but rises to a considerable extent, as in Exp. VI., where, at 3. 41.′ the number of pulsations was 85, and the mean tension 5.65, and at 4. 4′ the pulse was 80, with a mean tension of 7 inches—a fall of four beats with a rise of nearly an inch and a-half. Few

observers, if any, have noted a higher rise of the arterial pressure than $8\frac{1}{2}$ inches, which was the maximum of oscillation in this case, when they injected preparations of digitalis into the veins, so that they passed through the heart first before getting into the systemic circulation; but on one occasion in which Mr Blake injected infusion of digitalis into the carotid, pushing it with some force, so that it entered into the systemic circulation, and had thus an opportunity of acting on the capillaries before reaching the heart, the pressure rose to 12 or 14 inches. From all these facts, I think, we must conclude that it really possesses the power of contracting the capillaries which Mr Blake assigned to it.

As the poisonous action of digitalis becomes more fully developed, the capillaries become dilated (and probably paralyzed), the arterial tension falls, and, there being less resistance, the heart's action becomes *pari passu* (Bouley and Reynal) more violent, while the arterial pulse becomes more weak and small, and often seems rather a kind of indistinct wavering, than decided strokes. The objection may be raised that this is due to the rapidity of the pulse, and the small size of the waves of blood; but we find that the heart is acting powerfully, and if the capillaries were either of the same size or contracted, the impulse being brisk, the waves of blood, however small, would each give a distinct stroke to the finger, as is shown by Marey.[1] Owing to this dilatation of the capillaries, and the easy transit of blood through them, we find that almost immediately after death the arterial system is empty, and the venous full and turgid. From the patency of the capillaries less of the force of the heart will be expended in forcing the blood through them, and we would expect to find a higher pressure in the veins, at least, if the heart be not much weakened. This I have not yet been able

[1] Marey, *op. cit.* p. 243.

to determine. It would be well also to see, in the web of a frog's foot, the changes caused by digitalis when applied locally or generally.

Occasionally, however, at or immediately before death, this relaxed state of the capillaries seems to give place to one of spasm, so that the arterial tension rises and continues at the same height for a considerable time after the heart has ceased to beat, diminishing very slowly as in Exp. IV. and VI. This could not possibly be owing to clots forming in the apparatus, at any rate in VI.; for if the tube had been stopped by one, the two columns of mercury would have found their level by the higher column decreasing, while the lower rose, and not by the upper one remaining stationary, while the lower one rose up to its own level.

Of the changes in the cranial circulation, caused by digitalis, I can say nothing, several trials which I made on animals to trephine and lute in a glass plate having proved total failures.

On the Respiration.—Bouley and Reynal[1] found that digitalis given to horses in large doses at first caused acceleration of the respirations as well as of the pulse; and after this exciting action had passed away the number became remarkably diminished, falling to 8, 7, or even 6 per minute, being deep, broken, and trembling, and, in some instances, remarkably intermittent, the intermittence coinciding with that of the heart.

Messrs Delafond and Dupuy[2] also noticed primary acceleration with subsequent retardation. My own observations on the respiration are extremely imperfect; and though I have no note of previous acceleration in large doses, such may have existed. In most cases, the respiration has become slower and deeper, and, in one case, in a dog, I noted that it was

[1] *Op. cit.* [2] Bull. de l'Acad. de Med., t. 16, p. 428 (H. & Q.)

not only slow (8 in 65 seconds), but distinctly intermittent, the intermissions being of 4 seconds duration, and coinciding exactly as to time and duration with those of the pulse. At the time I noted this, and for a good while after, I was perfectly unaware of Messrs Bouley and Reynal's observations.

In smaller doses, the primitive acceleration has not been noticed, and the decrease has gone on gradually from the first. In one case,[1] after injection of a small dose of digitaline, I observed acceleration of the respiration, which might have been accidental; but there was no apparent cause for it, and I had not noted it in the dog before, nor have I since, though he has been under constant observation.

In several sick persons, in whom M. Joret[2] noted the respirations before and after taking digitalis there was sometimes acceleration, and sometimes slowing of the respiration; but the results show nothing, and he himself only mentions them in passing. M. Duroziey[3] has not found any slowing of the respiration.

On Digestion.—In small doses, digitalis is said to cause increased appetite.[4] While taking digitaline I have had a good appetite, but I had this as well while I was not taking it; nor do I think my appetite was better after recovering from the sickness caused by the digitaline, than it was before beginning to take the drug, as Withering[5] found, but his observations had been made on invalids.

Its emetic and cathartic effects, when given in large doses, have been long recognised, and seem to have been the first properties to attract attention. Before these effects appear, however, there are symptoms of digestive derangement of a

[1] Exp. XI. [2] Archives de Med., 2 ser., t. iv., p. 27 (H. & Q.)
[3] Thesis, Paris, 1853, p. 36 (H. & Q.)
[4] Germain Med. Tim. and Gaz., Sep. 7, p. 250, 1861.
[5] Withering on Foxglove.

slighter character, consisting of loss of appetite, bad taste in mouth, borborygmi, abdominal distension, pain in the stomach, occasional nausea, and a vague desire to vomit.[1] When vomiting occurs, it is violent and painful. Faure[2] describes its characters, as seen by him in dogs, as being peculiar in the expulsive effort of the stomach, far from being the principal circumstances, as in vomiting from other causes is only the result of a series of convulsive contractions, beginning in the limbs, and extending, first to the lower part of abdomen, and then to the upper part and thorax, and under violent contractions the stomach is exposed to pressure, and expels its contents. The vomited matters are mixed with bile, sanguinolent mucus, and fluids of the stomach. The vomitings are intermittent, and the animal rapidly recovers from the effects of one, and seems well till attacked by another fit, the amount vomited after the first fit or two having emptied the stomach, being very small. This description I think correct in regard to dogs, except the small share which Dr Faure seems inclined to give the stomach in the act of vomiting; for this must be considerable, if we may judge by analogy from the human subject, as well as by the extreme pressure necessary to make the stomach reject so little as a teaspoonful at a time, unless it were contracting violently itself. The sensation I experienced, while vomiting on the morning of the 16th March, was as if the stomach were contracting with extreme violence as in cramp, much more so than in vomiting in general, and a feeling of soreness continued for some time after. The stomach was entirely empty on that occasion, and nothing (except perhaps a little mucus) was ejected. After taking 30 milligrammes more, during the course of the next day, the vomiting recurred on the morning of the 17th; and on

[1] Appendix, March, 17. [2] Edin. Med. Journ., Nov. 1864, p. 461.

this occasion I vomited some bilious matter, liquid, and resembling somewhat yolk of egg, and the crampy contraction was less marked. Dr Faure says that sometimes the convulsions seem directed towards the intestines, and after contractions of the limbs, &c., such as he describes before vomiting, a glairy, greenish substance, often tinged with blood, is expelled per anum. In horses there is no vomiting,[1] and the stools are first natural, then covered by mucus, and gradually becoming softer, are first pasty and then liquid, blackish, and fœtid. This blackish colour may be owing, however, to the colouring matter of the digitalis.

On the morning of the 17th March, shortly after vomiting, I had a loose stool, but no persistent diarrhœa, and in small doses it seems to produce constipation, and this is occasionally the case even when there is a fatal result.[2]

The action of digitalis on the intestinal canal is not merely local, for it produces it quite as certainly when introduced into the subcutaneous tissue or injected into the veins. The pain in the epigastrium, which I felt after the vomiting passed off, remained for several days, and just as it was going away it was succeeded by severe pain in the left side, apparently in the descending colon. At first I was afraid it was inflammatory; but when taken in connection with the peculiar form of the stool passed on the 20th March, which was that of small round pellets, like those of rabbits, I am now disposed to attribute to spasmodic contraction of some part of the intestines similar to that which I think occurred in the stomach.

On Secretion.—On the Saliva.—When digitalis is taken in rather large doses, there is occasionally a feeling of dry-

[1] Bouley and Reynal, *op. cit.*

[2] Case related by Dr Magee, Gazette des Hopitaux, *vide* Edin. Med. Journ., 1864-5, p. 170.

ness in the mouth,[1] along with some salivation,[2] but it is not constantly observed.[3] I have occasionally noticed the salivation from poisonous doses.[4] Bouley and Reynal[5] observe that the saliva is rather thick, and flows slowly from the mouth.

On the Secretion of the Nasal Mucous Membrane.—Stadion[6] found that a peculiar affection of this membrane, resembling corriza, was a characteristic symptom of digitaline, and I found that for some days before vomiting came on, clear drops of water were always gathering at my nose;[7] but I had no reason to suppose that I had caught cold, and I believe this increase of the secretion in my case is confirmatory of Stadion's view.

The conjunctival secretion was found by Bouley and Reynal to be dried up in poisoning by large doses.

On the Sweat.—In cases where it has been taken in doses a little too large, for some time there is usually profuse sweating.[8] In poisoning, hot sweats appear at first, which, as death approaches, dry up and become cold.

On the Urine.—Since Withering first brought the diuretic properties of digitalis into notice, it has steadily kept its place as one of the best remedies under this class. But though most members of the medical profession believe that it possesses this power, M. Duroziez,[9] though not entirely denying it, maintains that it is much less frequent than has been alleged, and says that he has not met with a single case clearly proving it. Dr Germaine[10] goes still farther, and

[1] Case of Daniel G.

[2] Christison on Poisons, p. 887, and Henry, quoted by Holland, Med. Notes and Reflect., p. 555.

[3] Holland, *op. cit.*, p. 555. [4] Exp. vi. 4. 42. [5] *Op. cit.*

[6] Yr. Bk. Syd. Soc., 1862, p. 451.

[7] I was then ignorant of Stadion's observations.

[8] Christison, *op. cit.*, p. 888.

[9] Thesis, Paris, 1853 (H. & Q., p. 296).

[10] Med. Times and Gaz., Sept. 7, p. 250, 1861.

boldly declares that "there is no proof that digitalis possesses diuretic properties, the reputation conferred upon it to this effect by Withering having been accepted without discussion; and that the diuresis, which often follows when an amelioration of the condition of the circulation has been produced by it in organic disease of the heart, is only a mediate effect resulting from the return of the circulation to its normal condition." The observations on its diuretic effect, especially in anasarca, and to a less degree in effusion into serous cavities, are so numerous that we can hardly doubt its existence. Among others who have remarked it, may be mentioned Christison, Andral and Lemaitre, and Hervieux. Several, who admit its diuretic action in disease, entirely deny its possessing this power in health,—as, for instance, Krahmer, Kluyskens, Vassal, and Shohl. Others again, as Pereira, say that it sometimes acts as a diuretic even in health. Joerg,[1] who experimented on several healthy persons, men, women, and children, found the urine increased, with only one exception. Hutchinson, in experimenting on himself, found it increased in three experiments. Hammond, from a three days' observation, says that the amount in health was 1474 cub. cent., and, after taking 60 drops daily of the American tincture, found it was 1822. The amount of water in the ingesta was not determined. Bouley and Reynal, and Dupuy and Delafond noted the diuretic action in health markedly on horses. In my own case, I found that, with small doses, the urine varied just as my pulse had done, being generally increased to a slight extent while I took the digitaline, but sometimes not, while, with large doses, the diuretic effect was marked, as will appear from the following table:—

[1] Joerg, Archives de Medicine, prem. ser. t. xxvi, p. 107 (H. & Q.)

Feb. 2—14.....1304	cub. cent. or 45.9 oz.		Dose.		
„ 15—24.....1326	„	46.6 „	Grains. $\frac{3}{20}$	10 milligrammes of extractiform digitaline.	
„ 25—Mar. 2....1303	„	45.9 „			
Mar. 3— 6.....1216	„	42.8 „	$\frac{3}{60}$	4 „ powdery digitaline obtained from Morson.	
„ 7—14.....1421	„	50. „	$\frac{9}{60}$	12 „	
„ 15 & 16.....1137	„	40. „	$\frac{9}{20}$	30 „ intoxication.	
„ 17—22.....1517	„	53.4 „			

From this we notice, that with the larger doses, especially of the digitaline in powder, there is a marked increase in the amount of urine before intoxication appears, then a sudden fall during its continuance, and another rise of still greater extent after it has passed off, and after the medicine had been discontinued. The actual increase in the amount of urine may to some appear small; but when it is considered that the amount of fluid ingested is the same, and that, in a normal condition, very rarely has a large amount of urine been passed on more than two consecutive days, the distinct and persistent diuresis from the digitaline is remarkable. Winogradoff, from his experiments on moderately large doses of digitaline, concluded that it cannot strictly be called a diuretic, as it was given for five days without marked increase in the quantity of urine. The doses given were from 3-10ths to 2-7ths of a grain. Stadion, subjecting himself to a weighed diet of milk, eggs, bread, and butter, found that during a period of 18 days, during which he took digitaline, beginning with 2 milligrammes the first day, and increasing it by one each day, the urine was somewhat diminished. The amount of urine in my own case was markedly diminished during the period of intoxication, when the gastro-intestinal canal was most affected; and in the case of Daniel G., when the pulse was most

affected, it fell from an average of between 40 and 50 oz. to 30 oz. on Dec. 2, 25 and 26 oz. on the 3rd and 4th, and 18 oz. on the 5th and 6th, again slowly rising, till on the 10th it rose from 25 to 44 oz., and then remained at its normal standard. In very large doses it occasionally causes not only diminution, but total suppression of urine—lasting for three days in a case quoted by Christison,[1] and one narrated by Mazel.[2] Bouley and Reynal noticed suppression in horses for about 36 or 48 hours, and then followed by abundant diuresis. In Mazel's case it is not noted whether or not there was diuresis, only that urination was performed freely; but as it was after rising to make water that death occurred, it seems not improbable that it was present. Christison thinks that the sedative and diuretic actions are mutually incompatible; but in horses Bouley and Reynal found them distinctly co-existing; and though my pulse was somewhat lowered at March 13, there was yet diuresis. It is probable, however, that when the action on the pulse is so great as to cause intermittence, the diuresis is diminished. It increases the frequency of micturition.[3]

From all these observations, then, we may conclude—(1), That in anasarca, especially from heart disease, digitalis acts as a diuretic. (2), That it sometimes, but not always, acts as such even in health. (3), That when it acts upon the intestinal canal so as to cause vomiting and purging, or when it affects the pulse so much as to cause intermittence, and possibly before this takes place, diuresis is much lessened, though a moderate degree of retardation may coexist with diuresis. (4), That in large doses it causes suppression of urine, lasting in the human subject for three days.

[1] Edin. Med. Journ. vii. 149, Christison on Poisons, p. 889.

[2] Mazel, Gaz. des Hopetaux in Edin. Med. Journal, 1864, p. 169. Med. Times, 1855, p. 381.

On the composition of the urine, Stadion,[1] having put himself on a weighed diet of bread, butter, milk, and eggs, and determined the normal amount of his urine and of its constituents, took digitaline for 18 days, beginning with 2 milligrammes, and daily increasing the dose by 1 milligramme, found that the urine was not only diminished in quantity, but its specific gravity and chief solids were also diminished. The acid reaction was unaltered, but the urea, chloride of sodium, phosphates, and sulphates were lessened, and the uric acid increased. Urea was determined by Liebig's method, after the elimination of phosphoric and sulphuric acid and chlorine, and the uric acid by Neubauer's method. He draws the conclusion that it causes rapid wasting of the body, and depression of the exchange of material.

Winogradoff,[2] from observations made for five days on several healthy persons of all ages, while taking from 3-10ths to 2-7ths of a grain in the twenty-four hours, found that there was no marked increase in the total quantity of urine, and in one case a diminution. In every case there was a falling off in the quantity of urea and chlorides and salts which resist calcination, but there was invariably an increase of the phosphoric and sulphuric acids. The results which I obtained will be seen from the table on the following page, and the tables in the Appendix:—

In determining the amount of urea, chlorine, and phosphoric acid, I used nitrate of mercury for the two first, and nitrate of uranium for the last, according to the processes described by Neubaur and Vogel in their work on urine.

[1] Yr. Bk. Syd. Soc., 1862, p. 451. [2] Yr. Bk. Syd. Soc., 1862, p. 452.

Date.	Urine.	Urea.	Proportion of Urea.	Phosph. Ac.	Proportion of P_2O_5	Chlorine.	Temp.	Pulse.	Sleep.	Work. Hours in Laboratory.	Work. Minutes Walking.	Dose. Grain.	Dose. Milligram.
Nov. Dec. 19—12	1048	31.88	30.4	2.67	2.54	6	43.6	68	8	..	..	..	
13—22	1189	30.90	26.	2.75	2.31	7.2	41.2	64.3	7½	5	73	1-200th	
Jan. 4—16	1190	34.46	28.8	3.14	2.74	6.	34.3	78	7¾	5	72	..	
Feb. 17—1	1196	31.63	27.4	3.09	2.734	7.4	41.3	76	8	4½	74	1-16th	
Feb. 2—14	1304	31.90	25.4	3.14	2.577	..	38.5	71	8	3½	65	..	
15—24	1326	35.77	28.56	3.36	2.69	7	37.6	75.6	7½	3¾	..	3-20th	10 extractiform
Mar. 25—2	1323	33.95	26.1	3.26	2.5	7.6	38.2	71.4	7	4¾	.	..	
3—14	1352	35.46	28.5	3.09	2.64	6.6	36.8	68	7⅓	4	..	6-50th	9.6 Morson's
15 & 16	1137	35.18	30.4	3.11	2.75	5.7	38	65	8	2½	85	9-20th	30
17—22	1517	37.49	24.7	2.88	1.9	8.4	37.7	66	8	3	..	..	

From this table it will be seen, that, like the pulse and the amount of urine, the urinary constituents vary considerably when small doses of digitaline were taken; but that, when the dose was large, the pulse fell, the urine increased, its sp. gr. was diminished, the urea was increased, and the P_2O_5 and Cl. were diminished. For comparison of these results with those of Winogradoff and Stadion, I tabulate them—Feb. 15–24. I do not reckon, as I am not sure of the quality of the digitaline.

CONSTITUENT.	STADION.	WINOGRADOFF.	BRUNTON.
Water.	Diminished.	No marked increase.	Decided increase.
Urea.	Less.	Less.	More.
Phosphoric acid.	Less.	More.	Less.
Chlorine.	Less.	Less.	Less.
Sp. Gr.	Less.	...	Less.

With the exception that I experienced diuresis, and had the urea increased instead of diminished, my experience agrees with that of Stadion. From the large increase of urea with less work, I believe that when it acts as a diuretic, it increases tissue change; and the diminution of phosphates, I think, is in a great measure due to the dislike to and inability for any kind of mental work.

On the Temperature of the Body.—Messrs Bouley and Reynal[1] found that poisonous doses of digitalis produced first increase and then decrease of the animal temperature, but that therapeutic doses caused a steady diminution, without previous increase; Messrs Aug. Dumeril, Demarquay, and Lecointe,[2] in experimenting on dogs with digitalis and digitaline, the latter in the dose of 10, 20, and 25 milligrammes, and the extract of digitalis 1 to 4 grammes. In a period of 11 or 12 hours, they found the temperature rise 8 times from 1° to 2°, and, in the only case in which it was lowered, they used 50 milligrammes of digitaline, and death ensued within the hour. Schwelgue says the fall of the pulse is accompanied by a fall in the animal temperature. In Exp. XIII.

[1] *Op. cit.* [2] Comptes Rendus, Mai 1851, p. 801 (H. & Q.)

I noticed a remarkable diminution, the animal feeling as cold as if dead for some hours before death actually occurred, and in several cases I have noticed the limbs grow cold a little while before death. Dr Mazel,[1] in his case of poisoning, noticed that the temperature of the skin, in those parts exposed to the air, was lower than usual. Hertz[2] says that there is first increase and then decrease of the temperature. Traube[3] found, that when infusion of digitalis was given in acute rheumatism, the temperature fell either with or a short time after the reduction of the pulse appeared. Schneider[3] says that the lowering of the temperature is independent of the slowing of the pulse, and begins from 36 to 60 hours after beginning to give the medicine; while the former begins within from 24 to 48 hours, and they both continue to fall after the remedy has been discontinued. Wunderlich[4] says that when digitalis is given in typhoid fever, in doses of 30 to 60 grains in 3 to 5 days, a remarkable diminution of the number of pulsations, simultaneously with marked decrease of temperature, takes place generally about the fourth day, and they fall after the medicine is discontinued; but the effect on the pulse is much more permanent than on the temperature, lasting in many cases for several weeks in succession. It should only be used when the pulse is 120, and the evening temperature is 108°, and with slight remissions; and less of the drug is required to produce its effects than in pneumonia and other acute diseases.

Notwithstanding the opinion of M. Schneider, it seems probable that the diminution of the temperature, from thera-

[1] Edin. Med. Journ., 1864, p. 168.

[2] Bull. de Therap., Feb. 28 and March 15, 1862. Yr. Bk. Syd. Soc., 1862, p. 110.

Annuaire de Therapeutique, 1859, p. 82-88.

Med. Times and Gaz., July 12, 1862.

peutic doses of digitalis, depends, at least in the first instance, on the slower circulation of the blood through the periphery; but though the weight of authority is in favour of this opinion, it is possible that the diminution is owing to alteration of tissue change, and that another alteration is the cause of the temperature rising, while the pulse remains slow. I think that it is not so much to the change in the circulation that the coldness in poisoning is owing so much as to absolute decrease of the animal heat, for on one occasion the breath felt cold to the hand, and the relaxed state of the capillaries, while it would aid in rapidly cooling the blood and thus the internal parts, would rather tend to keep the periphery warm.

Traube thinks that the lowering of the temperature is due to less rapid oxygenation of the blood from the slower current through the lungs.

On the Nervous System.—In large doses, in animals, digitalis affects both the sensory and motor system, causing a comatose or semi-comatose state, and insensibility to external impressions, muscular weakness which causes a stumbling, uncertain gait, and an appearance of a kind of paralysis of the hind quarters, so that the animal with difficulty drags them after him. In some cases there are twitchings of the muscles of the face and alæ nasi, or the muscles of the skin over the body, causing an appearance which is sometimes mistaken for convulsions;[1] and in other cases, and perhaps more frequently in dogs, at least there is staggering as if giddy, and convulsive movements of the extremities.

In smaller doses it produces giddiness, headache, tinnitus aurium, disturbed vision, dazzling weariness, languor, and general prostration, and in some cases a kind of intoxication, weakening of the intellectual faculties, and hallucinations and delirium, or even symptoms of acute mania. In some few

[1] Bernard. Leçons de la Physiologie.

cases digitalis acts as a soporific. I am not sure whether to attribute it to the digitaline, or look upon it merely as a coincidence; but on March 5, after taking 12 milligrammes of Morson's digitaline, I experienced a remarkable sleepiness at night, which continued till the 12th, when symptoms of abdominal irritation began to manifest themselves, and these increased till vomiting occurred. On the 14th I felt great languor and prostration, and either on this day, or at least while the languor continued, the mental faculties seemed enfeebled, as, while reading for an examination, the eye glanced over the words, but the mind refused to receive or retain their import. The derangement of sight which I noticed was of two kinds—1st, a general mistiness of objects, such as is seen before fainting; and 2nd, a large bright spot advancing before me, which sometimes resembled a ring showing prismatic colours faintly, and similar in character to, though less distinct than, that seen round a light when digitaline has been introduced into the eye. The headache occasioned by digitalis sometimes, as in the case of Daniel G., persists for some time after the medicine has been disused.

The motor nerves of muscles[1] have their power impaired by digitalis, as the muscles of the limb of a frog, which was prevented by a ligature from receiving the poisoned blood circulating through the rest of the body, preserved their excitability from eight to sixteen hours longer than the other limbs.

Action on the Eyes.—When digitaline is introduced into the eye, it causes smarting and profuse lachrymation, which passes off in a short time, and nothing more is felt, except perhaps an occasional rough feeling of the conjunctiva, till four or five hours after, when, on looking at a light, you see it surrounded by a halo, presenting the prismatic colours, and not

[1] Mem. de le Soc. de Biologie, t. 3, ser. 3, p. 97

quite close round the light, but with a dark space between. This halo increases in diameter the farther you move from the light, and becomes smaller and narrower as you approach. I have noticed an appearance exactly similar when light cirrhi were crossing the moon. Homolle and Quevenne say that a slight opalescence is noticeable in the lens (crystalline), and the pupil is somewhat dilated and less contractile. I did not notice any particular difference in the pupil, and the appearance is not due to its dilatation, for I found it quite distinct on looking through a pin-hole in a card. Though on looking, I could not detect any opalescence, Messrs Homolle and Quevenne are probably right as to there being opalescence somewhere, for this would produce the effect noticed.

On the Uterus.—Mr Dickenson[1] found that digitalis has a powerful influence in causing the uterus to contract and stop hæmorrhage. A few minutes after the draught of ʒiss. is swallowed, the patient complains of acute pain in the back and hypogastrium, like those of the first stage of labour, then blood, solid and fluid, is ejected, and the discharge is absent for some hours, when the pain subsides, and it returns, but less and less, after each dose, till it disappears.

On the Genital Organs.—Stadion[2] finds that digitalis and digitaline possess the power of temporarily annulling the activity of the sexual organs, and is thus a true anti-aphrodisiac; with this conclusion I am disposed to agree. M. Brughmans[3] has stated the same thing, and advises its use wherever turgidity of these organs is to be averted, whether as after treatment of surgical operations, or for other causes.

[1] Med. Chir. Trans., vol. 39, p. 1.

[2] Yr. Bk. Syd. Soc., 1862, p. 451.

[3] Revue Med. Chir., Paris, Dec. 1858. Half-yearly Abst., vol. 24, p. 168.

Mode of Action of Digitalis.—Having considered the general action of digitalis, and the manner in which it affects different parts of the animal economy, we now come to a question of great difficulty, and one on which there has been much dispute,—the mode in which it acts.

This question has generally been limited to the mode in which it affects the heart, and the two great theories on this point are,—(1). That of M. Traube,[1] who thinks that digitalis exerts its influence on the heart through the regulatory (vagus) and musculo-motor system of nerves; and (2), That of Dybkowsky, Pelikan, and Kölliker, that it exerts its action on the regulating and motor apparatus, contained in the heart itself, without the intervention of the vagi. Traube at first proposed the theory that digitalis, (1), first stimulated the regulatory nerves, (2), paralyzed them, and (3), paralyzed the musculo-motor nerves. The musculo-motor nerves are the cardiac ganglia, which can of themselves carry on the rhythmical movements of the heart; but these are aided by the sympathetic, as, according to the theory of Von Bezold, the cardiac ganglia originate continuous excitations, which, meeting with constant resistance in the cardiac nerves, are only able to overcome it periodically, and then to act on the muscular tissue. To these ganglia, two sets of fibres pass from the central nervous masses,—"One set reaches the heart partly through the cervical, and partly through the dorsal and lumbar portions of the sympathetic cord. The latter fibres originate in the medulla oblongata, and descending to the cervical, and to some extent through the dorsal and lumbar parts of the spinal cord, emerge at many different points to unite with the sympathetic nerve. The function of all these fibres consists in conveying an exciting influence from the medulla to the heart, so that the resistance in the

[1] Yr. Bk. Syd. Soc., 1862, p. 453.

cardiac nerves is more frequently overcome, and the heart beats more vigorously and with greater rapidity. The second set of fibres when acting, increase the resistance, and they run in the vagi, and probably also originate in the medulla. When strongly excited, they can increase the amount of resistance to so great an extent that it becomes superior to the combined influences of the exciting system of the medulla oblongata, and of the motor system in the heart itself. After a short interval it diminishes, and the successive discharges of the automatic centres can then reach the heart, though after somewhat longer pauses. By galvanizing the vagus, this resistance is much increased, and the heart stops in diastole.

The series of experiments on which Traube founded his views were as follows :—He injected infusion of digitalis, of such a strength that one syringe-full was equal to the extract of 8 grains of digitalis leaves, into the veins of dogs, and found that while salt and water produced no effect on the pulse, and one syringe-full of infusion raised it from 128 to 132, four syringe-fulls brought it down to 32; while after a 5th it suddenly rose to 160, and in 10 minutes more to 174. In another with a pulse of 108, it was reduced by $2\frac{1}{3}$ syringe-fulls to 33, but with $\frac{2}{3}$ of a syringe-full more it rose to 202. Several other experiments gave an exactly similar result. To find whether the action was through the vagus or not, he made seven more experiments. In one, for example, after reducing the pulse from 121 to 48, the right vagus was cut, and in two minutes, when again counted, the pulse was 66. On dividing the left vagus it then rose to 204. The same result was obtained by dividing both vagi at the same time. After dividing both vagi, the slowing of the pulse after the injection of digitalis was hardly observable. From these experiments, Traube concluded that digitalis operated through

the regulating system only. This theory was very generally adopted for some time, but Winogradoff, finding from experiments with the hæmadynamometer, that when the instrument was inserted into an artery, and the vagi stimulated so as to cause slowness of the pulsations, the arterial tension immediately fell; while, when the slowing was produced by the injection of digitalis, there was neither increase nor diminution of the tension, concluded that Traube's view was erroneous, and totally denied that the slowing of the pulse, produced by digitalis, was through stimulation of the vagi or medulla oblongata. Traube being thus induced to re-consider his theory, made some experiments by injecting a weak solution of woorari into the veins of a dog, and keeping up artificial respiration to obviate the disturbing influence which the rise in tension consequent on division of the vagi would have caused, and then injecting infusion of digitalis, he found that the tension rose in one instance from 159 to 260 millimetres, attaining its maximum in two or three minutes, and then gradually declining.

Traube was thus led to re-mould his theory, and to say that at first there was stimulation of the musculo-motory as well as the regulatory system, that the arterial tension was the product of these two factors, and that digitalis finally paralyzed both; and here the theory at present stands (as far as I can find out).

When we look at Traube's first experiments, they certainly seem perfectly conclusively to prove that digitalis acts through the vagus, and this I certainly believe to be the case. Winogradoff's denial of this is based on fallacious reasoning, assuming as he does that because irritation of the vagi does not possess the same action as injection of digitalis, therefore injection of digitalis does not produce the same effect as irritation of the vagi; whereas the action is the same so far

as the latter goes, but the former possesses the additional power of contracting tha capillaries, as Blake showed so long ago as 1839.

Traube's theory also is very imperfect, for he makes the arterial tension the product of what is really only one factor, leaving altogether out of account the other equally important one, the size of the capillaries, and, as I have stated before, if the capillaries remain the same, and the number of cardiac pulsations be diminished, no amount of force which each may exert from stimulation of the musculo-motory power will do anything whatever towards raising the arterial tension by the diminished quantity of waves and consequent amount of blood.

(2.) The second theory, that of Messrs Dybkowsky and Pelikan, and (Kölliker?) is that (*a*) digitalis exerts its action directly on the regulating and musculo-motory apparatus in the heart itself, and (*b*) not through the vagi, as their action is not delayed or altered by destruction of the medulla oblongata, or division of the vagi, or by the previous administration of woorari. The first part of this theory seems borne out by the experiments of Eulenburg and Ehrenhaus on the extirpated heart of the frog, which, when its lower third was immersed in a solution of digitaline, had its motion completely stopped, if the solution was strong, and if weaker, it became slow and intermittent. We see, too, that if we cut the vagus and irritate the distal cut end, the pulsations are slow, and the same result takes place if we apply galvanism to the uncut vagus, and it is only natural to suppose that the poison circulating over the heart's parietes might act either upon the terminal branches of the nerve, or on the apparatus in the heart on which these branches act, and through which they produce their effect, just as upon the central end of the vagus, though probably with less force.

The second part (*b*) of this theory I am not inclined to accept, because M. Traube's experiments, I think, prove that the action is altered in mammals by the division of the vagi; and although Messrs Dybkowsky and Pelikan state that they have found the same results in mammals as in frogs, they do not give definite details like M. Traube; and I am further hindered from accepting it, as in one of the two frogs which I have been able to obtain, and which was poisoned with woorari, its heart laid bare, and first a moderate, and then an enormous dose of digitaline introduced under the skin, the action was not so marked and distinct as Dybkowsky, Pelikan, Fagge, and Stevenson describe it to be.

The hypothesis that I have myself formed in regard to the action of digitalis is as follows :—

Digitalis causes contraction of the small arteries, and at the same time acts on the regulating apparatus of the heart, both directly, and to a much greater extent through the vagus, thus causing slowing of the heart without loss of tension, it stimulates the musculo-motory apparatus, causing increased force of the cardiac contractions. This primary stimulus then gives place to paralysis,—first partial, and then complete. The regulating force gradually loses its power, so that the musculo-motory power causes a quick beat to be occasionally interpolated, as the regulating power gets enfeebled, it can only occasionally assert its influence, and the pulse, formerly slow with occasional quick beats, is now a quick one, with occasional slow beats or intermissions; as the regulating power becomes entirely lost, the intermissions disappear, and the pulse becomes regular but very quick, the capillaries have also become paralyzed and dilated, but occasionally, just before death, they become spasmodically contracted. The musculo-motor power gets weakened, the fibres connecting the different ganglia of the heart, and which by

keeping up a perfect correspondence between the different ganglia, enable the heart to contract rhythmically, now convey impressions slowly and imperfectly; the different parts of the heart no longer work in unison, and the contractions become irregular and peristaltic, by-and-by the fibres do not transmit impressions at all, and the ganglia working in independence of each other, we see some continuing to make the little area they supply pulsate when the rest has stopped, and finally the ganglia themselves become paralyzed, and the heart remains motionless and contracted. But it is probable this stimulating influence is not exerted on the heart and capillaries alone, but on involuntary muscular fibre throughout the body, or on the sympathetic nerves which supply it, since we find it causing contraction of the stomach, intestines, and uterus, and in those organs also, its stimulating effect would probably be followed by paralysis. Not only the nerves are affected, but the power of the muscular tissues themselves is impaired, as shown by Dybkowsky and Pelikan, who found that when two muscles were taken from a frog, one having been taken from a leg which the poison was prevented from reaching by a ligature applied previous to its administration, and the other being taken from the poisoned animal, the curve described by the former in the myographion was much higher than of the latter, showing its greater power.

The cause of death from digitalis seems to be stoppage of the heart's action, and defective supply of blood to the nerve centres. When death occurs from not very large doses, it seems often to be caused by some slight exertion at the time. As in the case of Daniel G., the pulse was of low tension and irregular, and when we know that any exertion still further lessens the tension, we can easily imagine how in such a case there might be syncope ending in death. This seems all the

more probable, as I noticed on the 17th of March, besides bright spots, a kind of haziness such as one sees before fainting, though not of so marked a character.

There are, several points which I have not yet made up my mind about, such as the remarkable intermissions observed in the pulse and respiration coincidently, the topical action of digitalis, the points of resemblance and difference between it and other cardiac poisons, and its action on the blood and capillaries, but I hope that I may yet be able to clear up these.

THERAPEUTIC ACTION.

Soon after Withering announced the property digitalis possesses of showing the heart's action, physicians began to employ it in hæmorrhages, and Ferriar especially used it in hæmoptysis, in the early stages of phthisis, and thought it might possibly heal ulcerated cavities in more advanced stages. Dr Brinton thinks it is the best remedy for hæmorrhage from pulmonary cavities, in the dose of 30 to 90 minims every four or six hours. It is also said to be useful in epistaxis, and Mr W. H. Dickenson found it of the utmost service in menorrhagia, curing in a few days a case thought to be almost at the point of death. He gives it in the dose of ℥ss. three times a-day. He thinks that as an oxytoxic it is quite as powerful as ergot. It is from the contraction of the uterus itself, and not from the contraction of its vessels, that the benefit is derived; and this idea he supports, not only by showing that it causes pains like labour pains, and expulsion of clots, but that, in a case of fungoid tumour of the os, it did no good whatever; while, if the benefit had been from the contraction of the vessels, it ought to have been as great in this case as it is when the cause of hæmorrhage is within the

uterus. Ferriar thought that in inflammatory fever it was useful instead of bleeding and purging, and Currie confirms his observations, saying he had found it useful, not only in acute inflammation of the brain, heart, and lungs, but in acute rheumatism. Several continental authors have borne favourable testimony to its use in acute inflammation. Hirtz gives a case of pneumonia, which he treated first by tartar emetic and venesection; but in two days these produced no amendment, the pulse remaining at 118, and the temperature at 104°.6. Digitalis was then given for two days, and the pulse fell to 82, and the temperature to 98°.6. Although the medicine was now discontinued, on the 3rd day the pulse was 53, and the temperature 97°.3. Returning crepitation was now heard on the eighth day of the attack, and the pulse and temperature began to rise, and three days later the patient was convalescent. He has found the same lowering of the pulse and temperature in acute bronchitis, pleurisy, acute phthisis, and acute rheumatism. He has rarely seen diuresis, and never met with any bad results. The amount taken has varied from 7 to 37 grains. He thinks that venesection may be used with the digitalis. In pneumonia, Millet abjures venesection nearly altogether, but combines the digitalis with kermes, giving to adults on the first day 1-7th of a grain of each every hour, and gradually increasing the dose by 1-28th of a grain daily, so that on the 9th day the dose is 3-4ths of a grain. The medicine is not stopped at once, when improvement takes place, but is continued some time longer. Improvement generally occurs about the sixth or eighth days, and the circulation is then affected. Among 87 cases of children, of which 53 were very bad, with much delirium and adynamia, there was but one death. Oppolzer gives it in small doses, along with ipecacuan and cold effusion externally, where the dyspnœa is more from the fever than from local

changes. In reference to a case of pneumonia, Traube remarks that the rapidity of action of digitalis varies much in different cases, taking much longer if the person be strong, and the disease at its height, than when it is near a close, or in a chronic case. Schneider says that in acute inflammation digitalis, in doses of 2½ to 3½ grains every two hours, reduces the pulse, and lowers the temperature of the skin. These effects, he says, are independent of each other. Clutterbuck advocated its employment in continued fever. Wunderlich recommends its employment in severe cases of typhoid fever, when the evening temperature rises above 108°, and the pulse one-half in the second week. It has been proposed as an antiperiodic in ague by Davy. Graffeneuer, Gerard, and Bouillaud have treated between 40 and 50 cases successfully by it.

Nervous Affections.—Serre, by the use of Debout's pill of quinine, 1½ grains, and digitalis, gr. 4-5ths, every night for three months, has cured several cases of long standing hemicrania, and, among others, his own, which had lasted fifteen years. Boison has used a pill of musk, 1 grain, ext. digital., 1½ grains, and ext. opii., gr. ½, in neuralgia, and its effects he describes as being magical. Mr Hardwicke gives ½ a grain of the powder in the same affection, and with similar results. According to Thomas, it effects a permanent cure in epilepsy; and Parkinson, Moll, Corrigan, Crampton, Sharkey, Nelegar, and Duclos, have all employed it with success. In the second stage of general paresis of the insane, that of mental alienation with maniacal excitement, Dr C. L. Robertson says, tinct. digit., in doses of ʒss., is a specific calming excitement, and enabling the patient to pass through this stage without wear or irritation. It steadies the pulse, and thus supplies the brain better with blood, and obviates the tendency to effusion of serum, consequent on inflammation going on in the arachnoid or pia mater.

In delirium tremens, Mr G. M. Jones recommended ʒss. of tinct. digit. at the first dose, to be repeated if necessary in four hours, and in some cases a third might be given, which did not exceed ʒii. It failed to produce sleep in only 3 cases out of 70, in 67 it was the only remedy used, and 66 recovered, the fatal case having a tumour of the brain. Peacock thinks this treatment especially useful in young and strong persons, and where the attack has been the immediate result of spirit drinking, and believes that in full doses it does not produce the depression which we would expect. Carey records 4 successful cases.

In anasarca, especially where this depends on cardiac disease, digitalis is one of our most potent remedies, especially when combined with squill, which is also a cardiac poison of the same class as digitalis. Withering[1] says it succeeds best when the pulse is feeble or intermitting, the countenance pale, the lips livid, the skin cold, and the swollen belly soft and fluctuating; but it seldom succeeds in men of great natural strength, tense fibre, warm skin, and florid complexion, or those with a tight and cordy pulse. In serous dropsy, its good effects are not so marked, and in encysted dropsy, it is totally useless. By some the infusion is preferred to the tincture as a diuretic, and it is best to give it in half-ounce doses, three times a-day. This action may sometimes be induced by cloths soaked in the infusion being laid upon the abdomen.[2]

As a sedative it requires great care, and, when the circulation falls, the remedy should be remitted; and though Sir H. Holland thinks that doctors are too much afraid of the intermittence caused by digitalis, I think it is a wholesome dread, and that when this sign appears they should at once

[1] Faggs and Stevenson, Proceed. Roy. Soc., May 1865.

[2] Christison, Dispensatory.

top the medicine, and have stimulants at hand in case of need. The tincture in doses of 30 minims is of great service in nervous palpitation, probably, I think, by inducing contraction in the capillaries, and, by thus raising the arterial tension, restoring the normal circulation.

With just one word of warning, I will close this brief summary of the therapeutical applications of digitalis, and that is to those who, thinking that there can be no danger in giving digitalis to those with very weak hearts, and that indeed it is the best thing for them to use it indiscriminately. I believe that I have proved that it increases the force of the cardiac pulsations; but if, while the motor nerves were stimulating it to contract, and the capillaries at the same time were opposing a resistance, the fibres of the heart itself were not composed of sound muscle, but were fatty and friable, some of them would be pretty sure to rupture, and the results would be disastrous. I therefore think that, in cases of fatty heart, great caution is necessary in administering it.

OBSERVATIONS ON THE URINE.

Within late years the attention of physicians has been turned much more than formerly to the observation of the urine for purposes of diagnosis, and physiologists have carefully noted the changes it undergoes in various circumstances, for the purpose of determining the way in which these circumstances affect the interchange of material in the living body.

Having lately made a very extensive series of observations on the urine and urinary constituents, with a view of determining, if possible, the changes effected in tissue changes under the use of digitalis, I have thought it not out of place to note down the chief facts which I have personally observed, and, in doing this, I will adhere strictly to the order adopted by Mr Parkes in his excellent work on the Urine.

AMOUNT OF CONSTITUENTS.

In the change of French into English weight, I have reckoned the gramme as equal to 15.43 grains, and the English fluid oz. as equal to 28.4 cubic centimetres.

On an average of 150 observations, chiefly taken during winter, but a few during summer, I find the amount of urine . . 1124 cub. cent. or 39½ ounces.
The maximum amount was 1855 c.c. or 63⅓ „
The minimum 610 „ or 21½ „

This difference is, however, much more than my normal, the one being in summer and the other in winter; and, moreover, the large number occurred after I had been taking digitalis.

My mean variation, from the lowest to the highest, is about 487 c.c. or 13 5-6 oz.

This variation amounts to more than a third of the total amount, and this is therefore considerably above the average, which is ¼.

Urea.—The mean amount of 105 analyses of urea is—
33.44 grammes, or 516 grains per day,
1.39 „ 21½ „ per hour.
The mean variation is 9.36 „ 144½ „ or rather more than ¼, while the average amount is 1-5th.

Phosphoric Acid.—From 108 analyses I find the average amount of $P O_5$, to be 3.1 grammes, or 47½ grains daily,
2 „ hourly.
The mean variation is .96 „ 14 4-5ths „
which is less than usual, the mean being 35 to 50 p. c.

Chlorine.—From 80 analyses I find the average amount to be 6.8 grammes, or 105 grains daily,
4½ „ hourly.
This seems much about the average amount.

The analyses of chlorine, however, were not so exact as the others, on account of there sometimes being a difficulty in settling when the point of saturation was reached.

Section II.

Relative Proportions of the Constituents.—The urea seems to be about 11 times greater than the phosphoric acid, and about 5 times greater than the chlorides. These, however, do not keep their proportions constant, nor is that of the urea to the water so much so as it generally is.

Section III.

On the amount of each constituent excreted in 24 hours by a definite amount of body weight.

Constituent.	In 24 hours. 1 kilogramme excretes in c.c. and grammes.	In 24 hours. 1 lb. avoir. excretes in drachms and grains.	
			Parkes' average.
Water.	23 c.c.	2.5 3 f. oz.	2.93
Urea.	5 gram.	4.12 grains	3.53
P O 5.	0.048	0.38	.336
Cl.	0.126	0.84	0.875

My weight is at present 134 lbs., and deducting 9 lbs. for clothes, and one or two lbs. which I feel sure I have gained since the end of the session, I have calculated this table for 125 lbs. weight. I have entered in red ink the average which Parkes gives, showing that the average in my water and chlorine is lower, but higher in the urea and P O_5.

Section IV.

On the acidity I have no observations.

Section V.

On the Specific Gravity.—The sp. gr. of my urine is notably high, though not more than that observed by Dr Christison, and a very great increase in it is always seen at night, probably from the solids of dinner passing off.

With this I must at present conclude, but I hope to be yet able to make farther use of the data I have collected; and I would notice that my observations entirely confirm Dr Bence Jones's opinion that the acidity of the urine is lessened or replaced by alkalinity during digestion, my urine being acid in the morning, neutral at mid-day (from breakfast), acid before dinner, and alkaline at night.

The close connection between brain work, and increase of phosphates in the urine, is also well marked, there being almost always an increase on the Saturday, from the effect of the discussions at the Royal Medical Society on the Friday nights, this increase extending over Sunday; and, when I have been attending examinations, or reading hard next day, the amount of phosphoric acid is increased.

APPENDIX.

DIETARY TABLE.

After some preliminary experiments, the following diet was adopted :—

BREAKFAST—

Coffee, 170 cc.

Bread, 7½ oz.

Butter not weighed, but much the same every morning, as the bread was the same.

1 salt herring—from Jan. 6 to March 22, 1866, 1 egg instead.

LUNCH—

4 oz. bread.

2¼ oz. gingerbread.

190 cc. milk.

DINNER—

Mince collops, 8 oz. The water in which they were cooked was not measured.

Bread, 2 oz.; Nov. 16 to Dec. 2, 1865, 3 oz.

Potatoes, 10 oz.

Water, 320 cc.

TEA—

Tea, 375 cc.

Bread, 4½ oz.; Nov. 16 to Dec. 3, 1865, 4¾ oz.

Butter.

ABBREVIATIONS USED IN APPENDIX.

B.....Breakfast.	Reactn.....Reaction.
L.....Lunch.	ft.....Faint.
D.....Dinner.	c. c.....Cubic Centimetres.
T.....Tea.	clr.....Clear.
Amt.....Amount.	cld.....Cloud.

L. & H.....Hours spent in Laboratory and Hospital.

R. M. S....Hours spent at the Royal Medical Society, where debates were held every Friday.

prop.....Proportion of the ingredient to the amount of urine.

Under the head *dose* the first numbers are fractions of a grain—the second are millegrammes.

Date.	Urine.					Pulse.	
	Time when pass'd	Amt. c. c.	Sp.Gr.	Reactn.	Appearance.	Time.	Number.
1865. Mar. 17	8.45	413	1024	acid	Amber coloured, cld. at bottom.	9.25	67 mean, 59-71
	1.30	365	1020	acid	Straw, cloud. at bot.		
	7.15	320	1023.5	acid	Amber coloured, cld. at bottom.	P.M. 10.25	75 mean, 71-76
	12	160	1025	..	Not perfectly clear.		
	..	1258	1023	..	Turbid		
,, 18	..	..	..	..	..	..	..
	..	1200	1022	acid	Turbid		
,, 19	..	495	1021	fty. acid	Not quite clear.	8.30	61 mean, 60-62 Somewhat cold at the time.
	..	390	1019	alk.	Very pale coloured at top, clear.	9	..
	..	398	1022	fty. acid	Pale, clr. cld. at top.		
	1.30	572	1023	..	Pale straw not quite clear.		
	..	1855					

Meals.	Sleep.	Exercise.			Bowels.	Dose.		Remarks.
		L. & H.	R. M. S.	Walkg.		Time when taken.	Amt.	
		hrs.	hrs.	min				
B. 9.40 L. none D. 6.10 T. 7.30	1.45-4 4.30-8.30 6¼ ..	1½	1½	200	Open in morning. Stool copious Quite loose. In the evening, very scanty. A good deal of flatus.	..	..	At 4 A.M. I awoke, and vomited at intervals for about ½ an hour. Vomited matter yellow and liquid, somewhat like yolk of egg. Vomited again on rising at 9 A.M. Again, at 9.30. Frequent epigastric uneasiness and pain. In forenoon my sight was occasionally not quite clear (just as one sees when about to faint, but somewhat slighter), and a large bright spot occasionally seen, such as is seen after looking at the sun, and then looking away at a dark object. Languor and discomfort all day. Occasional nausea—no more vomiting. Pain in chest on drawing breath, from soreness of diaphragm from vomiting. No lunch, but took 200 cc. of water at 11.30 P.M.
B. 10.25 L. 1 D. 5 T. 7.30	12.30-10 9½	..	..	30	Open.	..	..	Appetite improved, though not very good. Sight somewhat dim, especially after rising up or walking, and bright spots occasionally seen, chiefly after rising or walking. Lunch, 6½ oz. of bread, some cheese, and about 225 cc. of water, and 25 cc. of water at bed-time more than usual.
..	10.45-7.45	3½	..	100	Open once. Stool copious, somewhat soft.	..	..	Appetite better to-day. Sight dim, and I see a large bright spot, especially after exertion. This not so bad in afternoon. Slight pain in epigastrium occasionally, lasting some time when it occurs. After dinner constant pain in left side, apparently in descending colon. Much flatus at night.
..	9							

Date.	URINE.					PULSE.	
	Time when pass'd	Amt. c. ct.	Sp.Gr.	Reactn.	Appearance.	Time.	Number.
1865. Mar. 20	9.5	348	1019	neut.	Amber, clr. clouded at bottom.	9.55	63 mean 60-67
	3	525	1020.5	neut.	Straw do.	P.M. 10.45	80 regular, sitting in dining-room.
	7	205	1019.5	acid	Pale straw do.	11.40	58-60 sitting in bedroom.
	11.40	215	1025	acid	Amber do.	..	..
	..	1293					
,, 21	8.40	450	1020	fty. acid	Pale amber colour, clouded at top.	9.10	66, 65-67
	1	390	1020	alk.	Straw clr., cld. at bot.	P.M. 10.30	67-68
	6	453	1021	acid	Pale straw do.	..	..
	11	230	1025	..	Straw do.	..	..
	..	1523					
,, 22	8.35	485	1023	neut.	.. ..	9.10	64 mean 63-66
	12.20	310	..	..	Straw clr., cld. at top.	Night. 1.25	72 regular.
	5.35	305	1019	acid	Not perfectly clear.	..	..
	12.20	555	1024	neut.	Straw coloured, cld. at bottom.	..	..
	..	1655	1020				

Meals.	Sleep.	Exercise. L. & H.	Exercise. R.M.S.	Exercise. Walkg.	Bowels.	Dose. Time when taken.	Dose. Amt.	Remarks.
		hrs.	hrs.	min				
B. 10	3.15-9	6	..	50	Open once, stool extremely scanty.*	..	.	Sight clear. After looking at a bright sky, and on looking away, I see a spot as if I had been looking at the sun. Appetite much better to-day. Pain in left side still there on rising, and continued for some hours. Had a slice of bun of about the same weight to lunch instead of the gingerbread I have formerly taken, and for which I at present feel a disgust. Pain in side again to-night. A slight threatening of headache before going to bed.
L. 12 45	5¾							
D. 7								
T. 7.45								
B. 9.15	12-8.30	3½	..	85	Open once, stool scanty, partly fromlarge, partly from small intestine.	..	..	Appetite good. Still occasionally see a bright spot like a large bright soap bubble, or like the halo that is seen round a light when digitaline is put into the eye without the central light, which is the cause of the halo in the latter case. It seems to come more after exertion, or after long writing, as in taking notes. I'm not sure whether it is the attention, or looking at the white paper, or the stooping that causes it. Took 1 orange and 100 cc. of water extra.
L. 12.45	8½							
D. 6.10								
T. 7.45								
B. 9.15	12.15-8.30	3½	..	90	Open once, stool copious, well formed.	..	..	Still see a bright spot occasionally. Attended the Royal Medical dinner. Liquids above some soup, 1 glass champagne, ¾ of a glass of claret, about 100 or 150 cc. of water, and 1 cup coffee.
L. 1.30	8¼							
D. 7								
T. 12								

*** Consisting of about a dozen pellets like those of rabbits, and one about the size of a walnut. The latter floated, the former sunk in water.**

RECAPITULATORY TABLES.

Date.	Temp.	Moist	Pulse.	Sleep.	Work.			Amount.		S. G.	Reactn.
1865.					hrs.	hrs.	min	c. ct.	oz.		
Nov. 14	..	..	..	..	..	..	..	1219			
" 15	..	..	..	..	..	..	..	1161			
" 16	..	..	..	..	..	..	..	1096			
" 17	..	..	.	..	..	..	..	1062			
" 18	..	..	..	..	..	..	..	1164	..	1031.5	acid
" 19	..	..	..	..	..	..	..	995	35.	1032	acid
" 20	44.2	dry	..	..	..	..	..	1240	43.6	1028.5	neut.
" 21	48.1	damp	71	..	..	..	..	1005	35.3	1028	..
" 22	45.	wet	67	..	..	..	..	960	33.8	1030	neut.
" 23	47.2	dry	65.5	..	..	..	..	1010	35.5	1031	acid
" 24	43.8	wet	71.5	..	..	..	..	1150	40.4	1031	..
" 25	40.3	damp	71	..	..	..	..	1010	35.5	1032.5	acid
" 26	..	...	..	..	..	..	..	1071	37.7	1031.5	acid
" 27	36.6	damp	69	..	..	..	..	1090	38.3	1030	acid
" 28	40.1	wet	71.5	..	..	..	..	1170	41.2	1027.5	acid
" 29	..	..	72.5	..	..	..	..	1055	37.1	1029.5	neut.
" 30	..	..	73.5	..	..	..	..	806	28.3	1033	neut.
Dec. 1	41.2	dry	68.5	..	..	..	..	1200	42.2	1030.5	alk.
" 2	38.9	dry	..	..	..	..	..	738	26.	1031	..
" 3	..	..	..	8¾	..	..	..	1008	35.5	1031.5	neut.
" 4	40.2	damp	62	8	..	..	..	1026	36.1	1028.5	acid
" 5	43.8	dry	65	8	..	..	..	1170	41.2	1026	ft. alk.
" 6	42.5	damp	66.5	8	..	..	..	1058	37.2	1029	neut.
" 7	46.5	dry	62.5	8	..	..	..	1110	39.	1030.5	alk.
" 8	48°.8	dry	70	7¾	..	..	..	1130	40.	1028.5	alk.
" 9	46.3	dry	62.3	7	..	..	..	1120	39.4	1028.5	neut.
" 10	..	..	..	8	.	..	..	1000	35.2	1031	ft. acid

RECAPITULATORY TABLES.

Date.	Appearance.	Urea.			Phosphoric Acid.			Chlorine.			Dose.
1865.		gram.	grains	amt. in 1000 c. c. of urine.	gram.	grains	prop.	grm.	gr.	p'n.	
Nov. 14											
" 15											
" 16											
" 17											
" 18											
" 19	Clear yellow	33.83	522	34.							
" 20	Clear yellow	35.96	555	29.							
" 21	..	34.17	527	34.	2.37	36.5	2.35	5.22	80	5.1	
" 22	..	29.76	459	31.	2.36	36.4	2.35	5.24	81	5.4	
" 23	Clear yellow	31.81	490	31.5	2.51	38.7	2.48	4.72	93	4.6	
" 24	..	35.65	550	31.	2.639	40.7	2.29	6.27	97	5.4	
" 25	..	32.82	506	32.5	3.41	52.6	3.37	5.77	89	5.7	
" 26	Clear yellow	37.48	578	35.	3.33	51.3	3.11	6.68	103	6.2	
" 27	Clear yellow	31.06	479	28.4	2.75	42.4	2.52	7.23	111	6.6	
" 28	Clear yellow	31.59	487	27.	2.35	36.2	2.	5.54	85	4.7	
" 29	Clear yellow	30.38	469	28.8	2.52	38.8	2.39	5.76	89	5.4	
" 30	Clear yellow	29.01	447	36.	2.18	33.6	2.70	4.86	75	5.	
Dec. 1	Great deposit of phosphates	..	..	..	1.95	30.	1.62	7.14	110	5.9	
" 2	Not quite clear	..	..	..	2.	30.9	2.71	4.79	74	6.4	
" 3	Clear yellow	..	..	..	2.98	35.9	2.95	5.24	80	5.1	
" 4	Large deposit of phosphates	31.39	484	30.5	2.48	38.2	2.41	5.46	84	5.32	
" 5	Not quite clear	29.62	457	..	2.42	37.3	2.06	5.93	91	5.06	
" 6	Not quite clear	29.62	477	28.	2.46	37.9	2.32	5.63	86	5.32	
" 7	Considerable deposit of phos.	30.63	492	27.6	2.84	45.8	2.55	7.07	109	6.36	
" 8	Large deposit of phosphates	31.86	491	28 2	2.94	45.3	2.63	7.34	115	6.5	
" 9	Turbid deposit of phosphates.	..	..	..	3.56	54.9	3.18	7.42	114	6.6	
" 10	Clear clouded at bottom	..	..	..	3.3	50.9	3.3	5.46	84	5.4	

Date.	Temp.	Moist.	Pulse.	Sleep.	Work.			Amount.		S. G.	Reactn.
					hrs.	hrs.	min	c. ct.	oz.		
1865. Dec. 11	38.6	damp	67	8½	..	..	..	1300	45.7	1024	acid
" 12	42.	dry	66.5	7½	..	..	..	1150	40.5	1028	neut.
Daily mean, not excluding Sundays,											
	43°.6	..	68	8							
Daily mean, excluding Sunday's urine,					..			1048	36.9	..	..
Mean on Sundays,					..	..	..	1018	35.8	..	..
Maximum,					..	..	..	1300	45.7	..	..
Minimum,					..	..	..	738	26.	..	..
Difference,					..	..	..	562	19.7	..	..
Dec. 13	40.5	dry	67.7	7	5	..	50	1075	37.8	1026.5	neut.
" 14	41.5	dry	67.5	7½	5	..	60	1054	37.1	1029	neut.
" 15	34.	dry	66.	..	4½	4¾	80	1464	51.5	1026.5	ft. alk.
" 16	37.3	dry	62.5	6	4½	..	75	1175	41.3	1025	acid
" 17	..	..	..	8	..	..	50	1120	39.4	1028	neut.
" 18	42.5	dry	62.	8¼	5	..	60	1128	39.7	1028	acid
" 19	39.4	dry	59.5	7½	5	..	65	1450	51.	1022	neut.
" 20	42.2	damp	60.5	7¼	7¼	..	75	1094	38.5	1029	neut.
" 21	45.8	dry	60.	7¾	6	..	60	985	34.6	1030.5	ft. acid
" 22	48.2	dry	66.5	7½	4	..	80	1278	45.	1029	ft. alk.
Daily mean,											
	41°.2	..	64.3	7½	5	4¾	73				
Mean,					..			1189	41.8	..	..
Amount of Sunday's,					..	..	..	1120	39.4	..	..
Maximum,					..	..	..	1464	51.5	..	..
Minimum,					..	..	..	985	34.6	..	..
Difference,					..	..	..	479	16.9	..	..

Date.	Appearance.	Urea.			Phosporhic Acid.			Chlorine.			Dose.
1865.		gram.	grains	prop.	gram.	grains	prop.	grm.	gr.	p'n.	grain.
Dec. 11	Cld. at bottom	28. 6	441	22.	2.76	42.5	2.125	6.76	104	5.2	
" 12	Large deposit	28.29	436	24.6	2.58	39.8	2. 25	5.98	92	5.2	
	..	31.88	492	30.4	2.67	41.	2. 54	6.	92	5.7	
	..	35.65	550	35.	3. 2	49.	3. 1	5.79	89	5.6	
	..	37.48	578	..	3.56	55.	..	7.42	114		
	..	28.29	436	..	1.95	30.	..	4.72	73		
	..	8.19	142	..	1.61	25.	..	2. 7	41		
Dec. 13	Cloud. at bottom	27.95	431	26.	2.74	42.2	2. 55	6.	92	5.5	1-200
" 14	Floculent cloud	28.88	445	27.4	2.68	41.2	2. 55	..	..	..	1-200
" 15	Large precipitate of phosphates	38.06	587	26.	3.16	48.7	2. 16	8. 8	135.6	6.	1-200
" 16	Turbid throughout	27.96	431	23.8	2. 7	41.6	2. 3	..	..	..	1-200
" 17	Cloud. at bottom	32.14	496	28.7	2.63	40.5	2. 35	8.36	129	7.1	1-200
" 18	Clear, cloud. at bottom	28.76	443	25.5	2.76	42.5	2. 45	6.74	104	5.9	1-200
" 19	Clear, faint cloud. at bottom	30.45	470	21.	2.64	40.7	1. 82	7.06	109	4.8	1-200
" 20	Clear, cloud. at bottom	30.90	476	28.2	2.72	42.	2. 49	..	..	..	1-200
" 21	Not quite clear	33.	509	33.5	..	..	..	..	..	..	1-200
" 22	Large deposit	..	..	..	..	..	..	..	..	..	1-200
	..	30. 9	476	26.	2.75	42.4	2. 31	7. 4	114	6.2	
	..	32. 1	496	28.7	2.63	40.5	2. 35	8. 3	129	7.1	
	..	38.06	587	..	3.16	48.7		8. 8	135		
	..	27.95	431	..	2.63	40.5		6.	92		
	..	10.11	156	..	.53	8.2		2. 8	43		

Date.	Temp.	Moist.	Pulse.	Sleep.	Work.			Amount.		S. G.	Reactn.
					hrs.	hrs.	min	c. ct.	oz		
1866. Jan. 4	46.2	damp	..	7	4½	..	50	1100	38.7	1029.5	alk.
,, 5	36.5	dry	74.	7½	4½	5	110	1383	48.7	1028	alk.
,, 6	37.	dry	78.	6¼	3½	..	80	1655	58.2	1019	acid
,, 7	..	..	..	8¼	..	..	20	1176	41.4	1026.5	acid
,, 8	37.	damp	75.	8	5	..	60	1111	39.1	1026	acid
,, 9	34.7	damp	77.	7½	6	..	70	989	34.8	1031	ft. acid
,, 10	33.1	damp	73.5	7¼	8	..	65	1005	35.3	..	..
,, 11	24.1	fine	78.5	7¾	5	..	55	1305	45.9	1026.5	ft. acid
,, 12	26.5	fine	88.	8	4½	5	90	1398	49.2	1027	acid
,, 13	..	..	82.5	7¾	3½	..	50	987	34.7	1029.5	acid
,, 14	..	..	..	8½	..	..	20	980	34 5	1031.5	neut.
,, 15	33.5	damp	78.	8¼	5	..	60	1156	40.7	1227.5	ft. acid
,, 16	..	..	77.2	7½	4½	..	65	1002	35.3	1027	ft. acid
	34°.3	..	78	7¾	5	5	72				
Daily mean, excluding Sunday's urine,						..		1190	41.9	..	..
Sunday's,	..	..	..	..	..	..	..	1078	37.9	..	..
Maximum,	..	..	..	..	..	..	..	1655	58.2	..	..
Minimum,	..	..	..	..	..	..	..	980	34.5	..	..
Difference,	..	..	..	..	..	..	..	675	23.7	..	..
Jan. 17	39.7	damp	79.2	7¼	4½	..	60	1073	37.7	1029.5	ft. acid
,, 18	44.2	dry	77.6	6¾	6¼	..	90	1202	42.3	1025.5	ft. acid
,, 19	43.1	damp	83.	8½	4½	5	90	1266	44.5	1025.5	alk.
,, 20	40.5	damp	76.	7	4	..	60	1164	40.9	1024.5	acid
,, 21	..	..	..	10½	.	..	..	990	34.8	1027.5	neut.
,, 22	40.1	dry	76.5	8	5	..	60	1119	39.4	..	..
,, 23	42.	dry	78.	7	7	..	50	1029	36.2	..	..
,, 24	40.2	dry	78.	8¼	4½	..	60	992	34.9	..	..
,, 25	44.4	dry	76.5	7¾	4	..	60	1193	42.	..	..

Date.	Appearance.	Urea.			Phosphoric Acid.			Chlorine.			Dose.
1866.		gram.	grains	prop.	gram.	grains	prop.	grm.	gr.	p'n.	grain.
Jan. 4	Clear, cloud. at bottom	37.56	580	34.1							
" 5	Phosphate at bottom	40.79	630	29.5	4.92	75.9	3.92	9.8	151	7.	
" 6	Slightly turbid throughout	33.97	524	20.5	3.60	55.5	2.18				
" 7	Clear, faint cld. at bottom	36.05	556	30.6	3.42	52.7	2.91				
" 8	Clear, faint cld. at bottom	34.41	531	31.	2.34	36.1	2.11				
" 9	Clear, faint cld. in lower half	33.62	518	34.2	2.98	46.	3.02				
" 10	..	30.75	474	30.6	2.51	38.7	2. 5				
" 11	Pale, clear	33.27	513	25.5	3. 2	49.3	2. 7				
" 12	Turbid, pale orange yellow	40.38	623	26.	3.45	53.2	2.47				
" 13	..	32.57	502	27.5	2.98	45.9	3.02				
" 14	Clear	32.34	499	33.	2.98	45.9	3.05				
" 15	Slightly turbid, phosphate	34.68	535	30.	2.84	43.8	2.46	8.79	135.6	7.6	
" 16	Clear, cloud. at bottom	27.65	419	29.6	2.54	34.1	2.54	..	..	..	1-50
	..	34.46	531	28.8	3.14	48.4	2.74				
	..	34.19	527	31.7	3. 2	49.3	2. 9				
	..	40.79	630	..	4.92	75.9					
	..	27.65	419	..	2.34	36.1					
	..	13.14	111	..	2.48	39.8					
Jan. 17	Somewhat turbid	30.25	466	28.2	2.89	44.5	2. 7	8.36	129	7.7	1-25
" 18	Do.	31.01	478	25.1	2.76	42.5	2. 3	8.98	138.5	7.4	1-25
" 19	Not quite clear	31.65	487.5	25.	3.22	49.6	2.55	9. 4	146	7.4	1-25
" 20	Turbid, flocculent phosphate	30.26	466.9	26.	..	..	..	7.	108.4	6.	1-25
" 21	Clear, cloud. at bottom	29. 7	458.2	30.	2.90	44.7	2.93	5. 8	90	5.8	1-25
" 22	..	34.68	475.1	31.	3.20	49.3	2.86	4. 7	73	4.2	1-25
" 23	..	29.32	451.4	28.5	2.76	42.5	2.69	8. 4	30	8.1	1-20
" 24	..	..	..	27.6	3.03	46.7	3.06	6. 1	94	6.1	3-50
" 25	..	34. 6	533	29.	3.14	48.4	2.64	7. 3	113	6.1	3-50

Date.	Temp.	Moist.	Pulse.	Sleep.	Work.			Amount.		S. G.	Reactn.
					hrs.	hrs.	min	c. ct.	oz.		
1866. Jan. 26	46.5	dry	77.6	7¾	3	4	90	1327	46.7	..	..
" 27	45.5	dry	77.	7	2	2	85	1515	53.3	..	..
" 28	..	..	..	9	..	..	..	827	29.1	..	..
" 29	34.8	damp	70.5	8¾	4	..	90	1177	41.4	..	..
" 30	33.1	damp	76.2	7	4	..	120	1537	54.1	..	..
" 31	38.7	damp	76.5	7¼	5	..	60	977	34.4	..	..
Feb. 1	45.5	damp	65.5	7¾	4½	..	60	1177	41.4	..	..
	41°.4	..	78.6	8	4½	4½	74				
Daily mean, excluding Sundays,					..	..		1196	42.1	..	..
On Sundays,	..	..	..	..	..	..	..	908	31.9	..	..
Maximum,	..	..	..	..	..	..	..	1537	54.1	..	..
Minimum,	..	..	..	..	..	..	..	827	29.1	..	..
Difference,	..	..	..	..	..	..	..	710	25.	..	..
Feb. 2	44.7	dry	72.5	7¾	3¾	4½	110	1341	47.2	..	..
" 3	39.7	dry	74.	7¼	5½	..	25	1440	50.	..	..
" 4	..	..	..	8¾	..	..	20	915	30.2	..	..
" 5	40.1	wet	67.	8½	2½	..	80	1204	42.2	..	..
" 6	41.9	wet	72.5	8	4½	..	60	1196	41.4	..	..
" 7	39.9	wet	67.	7	3	..	100	1203	30.2	..	..
" 8	36.1	damp	73.	7¾	4	..	60	1315	46.3	..	..
" 9	39.1	damp	73.	7½	4½	1½	120	1446	50.9	..	..
" 10	39.	damp	70.	7¾	1	2*	30	1145	40.3	..	..
" 11	..	..	..	7¾	..	..	60				
" 12	38.1	dry	79.	8¾	2½	2*	40	1685	59.3	..	..
" 13	36.5	dry	72.	7½	2	..	90	1246	43.8	..	..
" 14	28.3	snow	69.	7¾	4	..	50	1129	39.7	..	..

* In railway.

Date.	Appearance.	Urea.			Phosphoric Acid.			Chlorine			Dose.
1866.		gram.	grains	prop.	gram.	grains	prop.	grm.	gr.	p'n.	grain.
Jan. 26	..	33.44	515	25.2	3.39	52.3	2.56	5. 6	86	4.2	3-50
" 27	..	28.78	444	19.	3.29	50.7	2.39	..	..	..	3-50
" 28	..	26.71	412.1	32.3	3.08	47.5	3.73	4. 8	74	5.8	3-50
" 29	..	32.36	499.3	27.5	3.00	46.2	2.55	5. 7	89	4.8	7-100
" 30	..	38.88	599.9	25.3	3.56	54.9	2.32	7. 7	120	5.	4-50
" 31	..	29.31	452.2	30.	2.90	44.7	2.97	5. 5	85	5.6	1-10
Feb. 1	..	33.54	517.5	28.5	3.23	49.8	2.75	7. 8	120	6.6	1-10
	..	31.63	488	27.4	3.09	47.6	2.73	7.	108	5.8	1-16
	..	28. 2	435	31.	2.99	46.1	3.29	5. 3	82	5.8	
	..	38.88	600	..	3.56	55.	..	8.98	138		
	..	26.71	412	..	2.76	42.5	..	4. 7	73		
	..	12.17	188	..	.80	12.5	..	4.28	65		
Feb. 2	..	32.85	506.8	24.5	2.91	44.9	2.18				
" 3	..	31.32	483.2	21.75	3.31	51.	2. 3				
" 4	..	27.45	423.5	30.	3.68	56.7	4.02	7. 7	119	8.4	
" 5	..	33.11	510.8	27.5	3.04	46.9	2.52	7.	108	5.8	
" 6	..	31.09	479.7	26.	3.18	49.	2.66	6. 6	102	5.5	
" 7	..	27.66	426.7	23.	2.77	42.7	2. 3	8. 4	130	7.	
" 8	..	35.50	450.7	27.	3.12	48.1	2.61	6. 2	96	4.7	
" 9	..	34.70	535.4	24.	3.16	48.7	2.41	8. 5	132	5.8	
" 10	..	34.35	516.9	30.	3.35	51.7	2.93	5. 3	82	4.6	
" 11											
" 12	..	33.01	509.3	19.	2.91	44.9	1.73				
" 13	..	30.52	470.9	24.5	3.15	48.6	2.53	6. 7	103	5.3	
" 14	.	31.26	482.3	27.7	3.07	47.3	2.72	5. 5	85	4.6	

Date.	Temp.	Moist.	Pulse.	Sleep.	Work.			Amount.		S. G.	Reactn.
1866.					hrs.	hrs.	min	c. ct.	oz.		
	38°.5	..	71	8	3½	3	65				
Daily mean, excluding Sundays,					..	..		1304	45.9	..	..
On Sundays,					..	..		915	32.2	..	..
Maximum,					..	..		1685	59.3	..	..
Minimum,					..	..		915	30.2	..	..
Difference,					..	..		770	29.1	..	..
Feb. 15	35.3	damp	70.2	7¾	5	..	65	1329	46.7	..	..
" 16	35.3	..	79.	7¼	5½	4½	100	1812	63.8	..	..
" 17	34.2	dry	88.5	7	½	..	225	1118	39.3	..	..
" 18	..	..	..	9	.	..	30	920	32.3	..	..
" 19	35.1	damp	73.5	8¼	5⅛	..	60	1158	40.7	1026.5	..
" 20	38.6	dry	76.5	7½	1⅜	3½*	50	1430	50.	1023	..
" 21	37.8	dry	72.5	7¾	4½	..	60	1249	40.4	1027	..
" 22	39.6	damp	..	7½	3½	..	90	1302	45.8	1025	..
" 23	42.8	damp	74.	8	3¾	5	80	1296	45.6	1025	..
" 24	38.	dry	70.5	5½	4	2†	90	1245	43.8	1025	..
	37°.6	..	75.6	7½	3¾	4¾ / 2¾	85				
Daily mean, excluding Sundays,					..	..		1326	46.6	..	..
On Sundays,					..	..		920	32.3	..	..
Maximum,					..	..		1812	63.8	..	..
Minimum,					..	..		920	32.3	..	..
Difference,					..	..		892	31.5	..	..
Feb. 25	..	..	..	7½	..	..	20	925	32.5	1031	..
" 26	38.8	snow	70.5	8	4	..	60	1287	45.3	1022	..
" 27	36.3	dry	72.	8	4½	..	90	1228	43.2	1025	..
" 28	31.2	snow	69.5	7½	5	..	60	1305	45.9	1026	..

* Reading and examination. † Examination.

Date.	Appearance.	Urea.			Phosphoric Acid.			Chlorine.			Dose.
		gram.	grains	prop.	gram.	grains	prop.	grm.	gr.	p'n.	gr. mg.
	..	31. 9	492.	25.4	3.14	48.4	2.57	6.8	105	5.2	
	..	27. 4	423.	30.	3.68	56.7	4.	7.7	119	8.4	
	..	35. 5	450.	..	3.68	56.7	..	8.5	132		
	..	27.45	423.	..	2.77	42.7	..	5.3	82		
	..	8.05	27.	..	.91	14.	..	3.2	50		
Feb. 15	..	32.71	504.7	24.6	3.50	54.	2.64	8.	108	6.	3-200.1
" 16	..	39.00	601.7	21.5	3.31	51.	1.83	9.	140	4.9	3-50.4
" 17	..	34.97	539.5	31.2	3.24	50.	2. 9	7.	108	6.2	3-50.4
" 18	..	35.71	551.	39.7	3.40	52.4	3. 7	6.	94	6.5	3-50.4
" 19	..	33.84	522.1	29.2	3.17	48.9	2.74	6.5	100	5.6	3-50.4
" 20	Not quite clear	35. 2	543.1	24.6	3.23	49.8	2.26	8.4	130	5.8	9-100.6
" 21	Not perfectly clr.	35.86	553.3	28.7	3.62	56.8	2. 9	7.3	114	5.8	9-100.6
" 22	..	36.05	556.2	27.6	3.33	51.3	2.56	7.6	118	5.8	9-50.12
" 23	..	39.87	615.1	30.7	3.36	51.8	2. 6	7.7	119	5.9	3-10.20
" 24	..	34.47	531.8	27.6	3.43	52.9	2.76	7.8	121	6.2	21-40.35
	..	35.77	552.	26.9	3.36	51.8	2.69	7.5	117	5.6	
	..	35.71	551.	39.7	3. 4	52.4	3. 7	6.	94	6.5	
	..	39.87	615.	..	3.62	56.8	..	9.	140		
	..	32.71	504.	..	3.17	48.9	..	6.	94		
	..	7.16	111.	..	.45	8.	..	3.	46		
Feb. 25	Clear, cld. at bottom	31.30	482.9	33.8	3.55	54.7	3.84	6.1	95	6.6	
" 26	Do.	34.31	529.4	26.7	3.03	46.7	2.36	8.5	131	6.6	
" 27	Cloud. at bottom	32.11	495.4	26.1	3.07	47.3	2. 5	8.5	131	6.9	
" 28	Clear, cld. at bottom	34. 8	536.9	25.9	3.13	48.2	2. 4	9.3	145	7.1	

Date.	Temp.	Moist.	Pulse.	Sleep.	Work.			Amount.		S. G.	Reactn.
					hrs.	hrs.	min	c. ct.	oz.		
1866.											
March 1	33.2	snow	75.	6¼	5	.	90	1488	52.3	1022	..
" 2	35.7	dry	70.	5¾	5	5	95	1209	42.2	1026.5	..
	38°.2	..	71.4	7	4¾	5	69				
Daily mean, excluding Sundays,					..	..		1303	45.9	..	..
On Sundays,					..	..	..	925	32.5	..	..
Maximum,					..	..	..	1488	52.3	..	..
Minimum,					..	..	..	925	32.5	..	..
Difference,					..	..	..	563	19.8	..	..
March 3	33.5	damp	..	6½	3¼	..	50	1057	37.2	1031	..
" 4	..	..	..	8	..	..	20	1090	38.3	1030	..
" 5	..	..	74.	8¼	4½	..	70	1371	48.2	..	.
" 6	33.4	damp	70.	6¾	4¼	..	60	1221	43.	..	..
	33°.4	..	72.	7½	4	..	50				
Daily mean, excluding Sundays,					..	..		1216	42.8	..	..
On Sundays,					..	..	..	1090	38.3	..	..
Maximum,					..	..	..	1371	48.2	..	..
Minimum,					..	..	..	1057	37.2	..	..
Difference,					..	..	..	314	11.	..	..
March 7	33.8	snow	68.5	9½	4	..	60	1102	38.8	..	..
" 8	36.	damp	67.5	7½	3½	..	80	1228	45.	..	..
" 9	40.2	dry	66.	7¼	5½	4½	80	1313	46.2	..	..
" 10	39.8	dry	67.	9¼	5	..	40	890	31.3	..	..
" 11	..	..	..	10	..	.	20	1123	39.5	1031.5	..
" 12	42.2	dry	65.5	9¾	3½	..	50	1259	44.3	..	..
" 13	41.2	dry	64.	7½	3½	..	120	1488	52.3	..	..
" 14	37.4	dry	68.5	5½	2	..	80	1607	56.5	..	..

Date.	Appearance.	Urea.			Phosphoric Acid.			Chlorine.			Dose.
1866.		gram.	grains	prop.	gram.	grains	prop.	grm.	gr.	p'n.	gr. mg.
Mar. 1	Clear, cld. at bottom	35.81	621.6	24.1	3.75	57.8	2.52	6.4	100	4.3	
" 2	..	35.33	545.1	29.2	3.05	47.	2.53	7.0	109	5.7	3-200.1
	..	34.07	524.	26.1	3.26	50.3	2. 5	7.6	118	5.8	
	..	31. 3	483.	33.8	3.55	54.7	3.84	6.1	95	6.6	
	..	35.86	621.	..	3.75	57.8	..	9.3	145		
	..	31.30	483.	..	3.03	46.7	.	6.1	95		
	..	4.56	138.	..	.72	11.	..	3.2	50		
Mar. 3	..	34.14	526.8	32.3	3.40	52.4	3.22	3.1	49	2.9	3-50.4
" 4	..	..	..	..	3.48	53.7	3. 2	..	..	..	3-50.4
" 5	..	37.96	585.5	27.6	3.05	47.	2.23	6.2	96	4.6	3-50.4
" 6	..	35.80	552.3	29.3	3.06	47.2	2.52	5.5	77	4.	3-50.4
	..	35.96	555.	29.5	3.25	50.1	2.82	4.8	74	3.9	
	..	..	..	..	3.48	53.7	3. 2				
	..	37.96	585.	..	3.48	53.7	..				
	..	34.14	527.	..	3.05	47.	..				
	..	3.82	58.	..	.43	6.7	..				
Mar. 7	..	29.38	453.3	26.6	2.44	37.6	2.22	7.5	116	6.8	9-100.6
" 8	..	37. 6	580.1	30.6	3.10	47.8	2.41	10.	155	8.1	6-50.8
" 9	..	37.51	578.7	28.5	3.30	50.9	2.52	9.3	145	7.	6-50.8
" 10	..	30.57	471.6	34.3	3.09	47.6	3.47	4.3	67	4.8	3-20.10
" 11	Somewhat turbid	39.73	613.3	35.3	3.30	50.9	2.97	7.2	113	6.4	3-20.10
" 12	..	34.21	527.8	27.1	2.41	37.1	1.96	7.1	111	5.6	9-40.15
" 13	..	37.31	575.6	25.	3.27	50.4	2. 2	7.1	110	4.3	63-200.21
" 14	..	35.43	446.6	22.	3.21	49.5	2.	6.5	101	4.	3-10.20

Date.	Temp.	Moist.	Pulse.	Sleep.	Work.			Amount.		S. G.	Reactn.
1866.					hrs.	hrs.	min	c. ct.	oz.		
Mar. 14	38°.6	..	66.3	8½	4	4½	66				
Mean, excluding Sundays,				..	..	..		1421	50.	..	..
On Sundays,				..	..	..		1123	39.5	..	..
Maximum,				..	..	..		1607	56.5	..	..
Minimum,				..	..	..		890	31.3	.	..
Difference,				..	..	..		717	25.2	..	..
March 15	36 .	damp	65.5	8	3½	.	80	1090	38.3	..	..
" 16	40.1	damp	64.	8	2	4½	90	1184	41.7	..	..
	38°.	..	64.7	8	..	..	..				
Mean,				..	..	..		1137	40.	..	..
March 17	41.4	dull	71.	7¼	1½	*1½	200	1258	44.2	1023	..
" 18	..	..	..	9½	..	..	30	1200	42.2	1022	..
" 19	39.6	damp	63.5	9	3½	.	100	1855	65.3	..	..
" 20	34.2	dry	61.	5¾	6	..	50	1293	45.5	..	..
" 21	35.6	snow	67.	8½	3½	..	85	1523	53.6	..	..
" 22	37.6	snow	68.	8¼	3½	..	90	1655	58.2	..	..
" 23	37.8	wet	71.	6¾	2½	1¼	80	1194	42.	..	..
" 24	37.3	damp	73.	8	3	*2½	110	1219	42.9	..	..
" 25	..	..	..	9	..	..	..	1080	38.	..	..
	37°.6	..	68.	8	3½	1¼	105				
Daily Mean, excluding Sundays,				..	..			1428	50.2	..	..
On Sundays,				..	..	..		1140	40.1	..	..
Maximum,				..	..	..		1855	65.3	.	..
Minimum,				..	..	..		1080	38.	..	..
Difference,				..	..	..		775	27.3	..	..

* Examination.

Date.	Appearance.	Urea.			Phosphoric Acid.			Chlorine.			Dose.	
1866.		gram.	grains	prop.	gram.	grains	prop.	grm.	gr.	p'n.	gr.	mg.
	..	35.21	543	24.7	3.01	46.4	2.46	7.3	114	5.1		
	..	39.73	613	35.3	3. 3	50.9	2.97	7.2	113	5.6		
	..	39.73	613	..	3.30	50.9	..	10.	155	..		
	..	29.38	453	..	2.41	37.1	..	6.5	101	..		
	..	10.35	160	..	.89	13.8	..	3.5	54	..		
Mar. 15	..	35.77	551.9	32.8	3.18	49.	2.92	5.4	84	5.	9-20.30	
" 16	..	34.60	533.8	29.2	3.05	47.	2.58	6.1	95	5.1	9-20.30	
	..	35.18	542	30.9	3.11	48.	2.75	5.7	89	5.		
Mar. 17	Turbid	35. 5	547.7	28.2	3.09	47.6	2.46	7.2	112	5.7		
" 18	Turbid	30.66	473	25.5	2.65	40.8	2. 2	1.5	24	1.2		
" 19	..	43.70	674.2	23.5	3.06	47.2	1.65	12.6	195	6.7		
" 20	..	29.83	460.2	23.	2.43	37.4	1.88	7.9	123	6.1		
" 21	..	35.14	542.2	23.	2.61	40.2	1.71	5.9	91	3.8		
" 22	..	43.28	667.8	26.1	3.24	50.	1.96	8.4	131	5.		
" 23	..	38.34	591.4	32.1	3.25	50.	2.72	3.8	60	3.1		
" 24	..	40.00	617.2	32.8	2.99	46.1	2.45	5.4	84	4.4		
" 25	..	36.00	555.8	33.3	3.38	52.1	3.14	5.6	86	5.1		
	..	36. 9	569	25.8	2.95	45.5	2.24	6.4	100	4.4		
	..	33.33	514	29.2	3.23	49.8	2.83	6.4	100	4.4		
	..	43.70	674	..	3.38	52.1	..	12.6	195	..		
	..	30.66	473	..	2.61	40.2	..	1.5	24	..		
	..	13.04	201	..	.77	12.	..	11.1	171	..		

RECAPITULATORY TABLE.

Date.	Temp.	Pulse.	Sleep.	Exercise.	Amount.		Urea.			Phosphoric Acid.			Chlorine.		
					C C.	Oz.	Gram.	Gr.	Prop.	Gram.	Gr.	Prop.	Gram.	Gr.	Prop.
1865. Nov. 14—Dec. 12	43°.6	68	8	..	1048	36.9	31.88	492	30.4	2.67	41	2.54	6.	92	5.7
Dec. 13— ,, 22	41°.2	64.3	7½	5 —4¾—73	1189	41.8	30.90	476	26.	2.75	42.4	2.31	7.4	114	6.2
1866. Jan. 4—Jan. 16	34°.3	78	7¾	5 —5 —72	1190	41.9	34.46	531	28.8	3.14	48.4	2.74			
,, 17—Feb. 1	41°.4	78	8	4½—4½—74	1197	42.1	31.63	488	27.4	3.09	47.6	2.73	7.	108	5.8
Feb. 2— ,, 14	38.5	71	8	3½—3 —65	1304	45.9	31.90	492	25.4	3.14	48.4	2.57	6.8	105	5.2
,, 15— ,, 24	37.6	75.6	7½	3¾—4¾—85	1326	46.6	35.77	552	26.9	3.36	51.8	2.69	7.5	117	5.6
,, 25—Mar. 2	38.2	71.4	7	4¾—5 —69	1303	45.9	34.07	524	26.1	3.26	50.3	2.51	7.6	118	5.8
Mar. 3— ,, 6	33.4	72	7½	4 .. 50	1216	42.8	35.96	555	29.5	3.25	50.1	2.32	4.8	74	3.9
,, 7— ,, 14	38.6	66.3	8¼	4 —4½—66	1421	50	35.21	543	24.7	3.01	46.4	2.46	7.3	114	5.1
,, 15— ,, 16	38.	64.7	8	2¾—4½—85	1137	40	35.18	542	30.4	3.11	48	2.75	5.7	89	5.
,, 17— ,, 22	37.7	66	8	3½ .. 62	1517	53.4	37.49	578	24.7	2.88	44.4	1.9	8.4	129	5.5
,, 23— ,, 24	37.5	72	7½	2¾ .. 95	1206	42.4	39.17	586	32.4	3.12	48	2.58	4.6	72	3.7

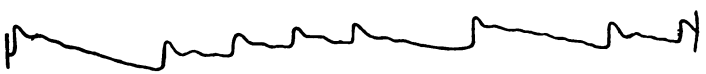
CASE OF POISONING BY INFUSION OF DIGITALIS.—RECOVERY.

DANIEL G., aged fifty-two. Admitted into Royal Infirmary, October 4, 1865. The patient, who is a tall and powerful man, had an attack of pleurisy more than three months before admission, and, after the acute symptoms were relieved, he was unable to resume his occupation of using the fore-hammer on account of shortness of breath, loss of appetite, and general weakness. On applying to a medical man, it was discovered that there was effusion into the left pleura, reaching up to the third rib; and after being treated by mercurials, &c., for some time, he was admitted into the hospital, and the effusion was found to be still at the same level. On admission, there was dulness over the left front from base of lung to above the level of third rib, and on left back partial dulness from above the scapula to its inferior angle, and thence downwards absolute. There was frequent cough, but no expectoration. The apex beat was most distinct at left side of zephoid cartilage. Heart sounds natural; pulse 70, of moderate strength; tongue furred; appetite moderate; bowels regular; urine in good quantity, natural in character. He was at first ordered acetate of potash, 20 grs., three times a-day; but this producing little benefit, he was ordered half-an-ounce. Infusion of digitalis three times a-day.

After being ordered infusion of digitalis, he at first measured it, but soon began to guess it, and had gradually increased the amount. Shortly after doing this, his appetite began to fail, and, at the same, he had a bad taste in his mouth, and his tongue felt very dry. He felt also a dull sickening pain over the stomach, rising up the line of the sternum to the throat. Occasionally this was like to make him sick. He felt weaker every day. This was about the middle of November, about three weeks before the symptoms attracted attention. He went on gradually increasing the dose. When he lost his appetite he also got occasional headache, and, along with the pain in epigastrium, he had palpitation. His bowels were costive. About the third week of November he vomited once or twice after meals when seized by a severe fit of coughing. The vomiting he attributes entirely to the cough. These symptoms grew worse, and he felt weaker and weaker, and less able to walk. About the 1st or 2nd of December he noticed his sight becoming dim, and when he looked at his own hands, or another per-

son's face, they seemed blue. The pain in the stomach was now almost constant; but the headache was not much worse—it was worst in the afternoon. On the morning of the 5th December he complained of weakness and want of appetite. His pulse was found weak and very irregular. At the visit in the middle of the day the cardiac action was found increased, and the pulse distinctly dichrotic. The general rhythm was about two beats in one second, and then an interval of about two seconds. The pulse was 58—somewhat feeble. The pupils were natural and skin moist. Urine deposits a considerable amount of lithates, otherwise normal. He got three ounces of brandy before I saw him, which I did about 5.20 P.M. At that time the cardiac impulse was very abrupt and felt strong, the impression to the hand being exactly what I had felt in experimenting with dogs. The pulse was 66, but very irregular. I took the following tracing with the sphygmograph :—

6 P.M.—December 5.—Right radial ; patient lying.



From this we see that the pulse is irregular and intermittent. The *ligne d'ensemble*, or line which would connect the tops and bases of each beat, instead of being straight, is curved, showing that the arterial tension is more influenced than usual by respiration. The pulse is dichrotic, this being especially marked in the last pulsation on the tracing. This dichrotism is not perceptible, or only to a very slight extent in subsequent tracings, showing that the tension of the pulse, when the present tracing was taken, was not only low in itself, but much below the ordinary arterial tension of the patient.* He got 3 oz. more brandy, and a diaphoretic mixture (spt. ammon. aromaticus), which lessened the dimness of vision.

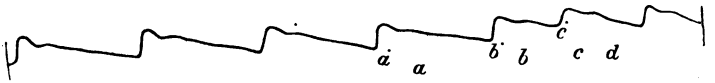
December 6.—Tracing taken from right radial about 6 P.M.
Patient lying.

* Comparing the suddenness with which the wave attains its maximum height, and its sudden descent, with a tracing after recovery, we see that the cardiac systole is very much more abrupt and short than normally.

The *ligne d'ensemble* is much more nearly straight than yesterday, showing that the arterial tension is less variable. Pulse very slow, and irregular as to time; but while yesterday it was as it were a quick pulse with occasional intermissions, or perhaps it might be termed a quick pulse, becoming occasionally a slow one, to-day it is a slow pulse with an interpolated beat or beats; or a slow pulse, becoming occasionally, and for a brief period, a quick one.

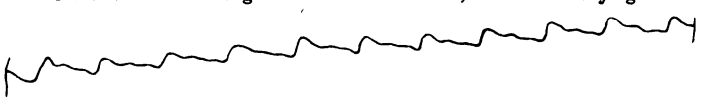
The arterial tension is distinctly higher than yesterday, the line of ascent being more oblique, the top of the curve, instead of being sharp, is rounded, and the line of descent gradual instead of sudden, and only the faintest trace of dichrotism.

December 7.—Tracing taken from right radial at 1 P.M. Patient lying.



The pulse is still irregular, and its characters are almost identical with that of yesterday. We see the distinct interpolation of a beat in the case of the pulsation *b*, which, if the line of descent prolonged to the same length as that of *a*, would reach to the point *d*. If we join the bases *a'* and *b'* of the lines of ascent of the waves *a*, *b*, and *c*, and prolong the line, we find that it passes through the point *d*, and also that the distance between *a'* and *b'* is the same as between *b* and *d*, showing that the rate of lowering of the arterial tension is the same in both; or, in other words, that the blood has been escaping with the same degree of rapidity through the capillaries in both cases. So, when the next wave *c* was impelled into the arteries before its usual time, the base *c'* of the wave *c* found the arterial tension greater than usual, and in consequence is on a higher line. We notice also, that though the amount of blood sent in by this wave, as indicated by its height, is less than usual, yet, coming so close upon the last, it has raised the arterial tension higher than usual, as is shown by the height of the top of *c* being above that of the others.

December 8.—Tracing taken at 3 P.M. Pulse, 93. Patient lying.



This tracing was taken about half-an-hour after patient had had his dinner, and the rapidity of the pulse is probably due to this.

The pulse is much more regular, and the *ligne d'ensemble* nearly straight. The line of ascent is comparatively abrupt, and then presents an ascending plateau. This latter is probably due to loss of elasticity of the arteries from commencing senile degeneration, which it is evident that patient has, from the nature of the tracings after his return to health. The line of descent is tremulous.

The dimness of sight and pain in epigastrium has been gradually diminishing. This afternoon he had rigors, and went to bed complaining of intense frontal headache.

December 9.—Tracing from right radial, 8 P.M. Patient lying.
Pulse, 64.

Pulse much slower than yesterday. *Ligne d'ensemble* of bases pretty nearly straight. The waves vary slightly in height and length, each third one being smaller, and the line of descent straighter, than the others. This is probably due to the influence of respiration. The ascent is comparatively oblique at first, and after ascending some way becomes still more so, and the line of descent gradual, showing high arterial tension. To-day the headache is better, and the shiverings have not returned.

December 10.—Being Sunday, I did not examine the case.

December 11.—12.30 P.M.

Ligne d'ensemble is not quite straight. The line of ascent almost perpendicular, then a well-marked ascending plateau. From the little modification that the cardiac impulse has undergone, one would be inclined to say that the elasticity of the arteries was more impaired than usual.

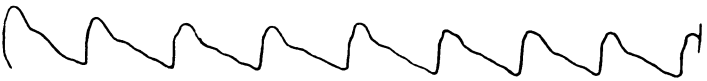
Headache almost gone; patient much better.

December 12.—Tracing taken at 1.50 P.M.

Plateau less marked; tops more rounded.

December 13.—Appetite slightly improved; still slight headache; pulse, 60; quite regular; seems now to have returned to its normal state completely.

Tracing taken at 6.30 P.M.; pulse then 66.



December 14.

Tracing, at 5.45 P.M.; pulse, 56; respiration, 20.

Tension slightly higher than yesterday, and pulse slower.

December 15.—Patient was sitting up, but went to bed, and had been lying about forty minutes before the present tracing was taken.

1.28 P.M.; pulse, 60; respiration, 24.

In this there is a nearly horizontal plateau, and the tension is considerably affected by the respiration.

December 16.—Tracing taken at 6 P.M.; pulse, 64; respiration, 23; headache to-day only occasional.

Patient still complains of headache, which up to this time has been constant.

December 17.—Sunday.

December 18.—Between 1 and 2 P.M.; pulse, 63; respiration, 27½.

Appetite improving. For the last two days headache has not been so bad.

December 19.—Appetite still improving; headache only occasional. The headache over the right or left parietal bones and frontal bone, chiefly about the parietal protuberances; never on the vertex or occiput. It goes from side to side—being to-day over the left, and yesterday over the right, parietal bone. Some pain in back to-day.

Tracing taken at 6 P.M.; pulse, 73; respiration, 26½.

Pulse rather quicker; tension rather less.

December 20.—Tracing at 5.30 P.M.; pulse, 68; respiration, 32.

My observations were now stopped, as I was going to the country; but, from the constancy of the characters of the pulse during the last four days, we may suppose that it had now returned to its normal condition.

EXPERIMENTS ON THE INFLUENCE OF DIGITALIS

ON THE

PRESSURE OF BLOOD IN THE ARTERIES.

In order to determine the influence exerted by digitalis, or digitaline, on the arterial pressure, the carotid of a dog was exposed; the nozzle of a hæmadynamometer inserted, and the height to which the column of mercury rose was noted. After waiting a short time to see if the pressure was constant, digitaline suspended in water, or infusion of digitalis, was injected into the jugular vein, and the pressure again noted.

The instruments which were commonly used consisted of a glass flask, partly filled with mercury, into which two tubes dipped, and were held firm by being cemented air-tight into a brass cap. The mouth of the flask is closed by an India-rubber stopper, through which were passed a brass tube, provided with a stopcock, and having a funnel at its upper end, and a curved glass tube, by means of which the instrument was connected to the artery. This brass nozzle is small at the end, and grows rapidly wider, and is roughened at the small end to prevent its being dragged out of the vessel by giving a better hold to the ligatures securing it. By means of a piece of glass tubing, with a bulb upon it, and India-rubber tubing, the nozzle was connected to the hæmadynamometer. A clip was placed on the tubing, so as to restrain the flow of blood at pleasure. The whole apparatus having been filled up to the end of the nozzle with a solution of bi-carbonate of soda, to prevent coagulation of blood, poured in by the funnel, the stopcock was turned, and the apparatus ready for use. A graduated scale was applied to the tubes, to show the height to which the mercury rose. As the volume of mercury in the flask was so much greater than that in the tube, no corrective was employed for the lowering in the flask as it rose in the tube, as would have been necessary had a simple bent tube been used. An apparatus of this kind, with a plain tube, gives trustworthy indications so long as the pressure is constant; but when it is variable, the indications

become fallacious from the mercury at each oscillation, acquiring a rapidity which carries it above and below the true maximum and minimum points.

To obviate this, the compensating tube of Marey was used. This consists of a tube, whose bore is reduced to a capillary size near the lower end. The mercury can only pass through this very slowly, and the influence exerted by each oscillation on the height of the mercury in it being very small, the true mean pressure of the blood is thus obtained.

EXP. I.—*Nov.* 25, 1865.—The dog experimented on was a pointer of the usual size. It was tied down to a table, and chloroform administered while the carotid was being exposed.

Time.	Mercury. Min. & Mx.	Mean.	Pulse.	Resp.	REMARKS.
P.M.	Inches.				
2.25′	...	...	...	...	The first incision was made, Dr Gamgee kindly performing the experiment for me.
2.51′	...	...	...	...	Nozzle introduced into carotid.
2.55′	4—5	...	...	...	Stopcock turned on—the mercury rose immediately.
2.57′ 45	5*	...			
2.59′	...	4.4			
2.59′ 30	4.95	4.25			
3. 2′	4.8—4.9	...	..	...	Slight irregularity of heart. Never sinks when animal struggles below 4.6 ; never rises above 4.9 during struggle, but fell immediately.
3. 5′	...	4.4	...	...	
3. 5′	5	...	...	...	
...	...	...	...	...	1 centigramme of digitaline suspended in distilled water.
3. 9′	...	...	...	...	The first part injected into jugular vein.
3.13′ 15	4.8	...	...	...	The fourth part injected.
3.14′ 20	...	...	...	...	Injection completed.
3.17′ 40	...	...	...	...	Pulsation faint — tube probably plugged.
3.20′	4.7—4.8	...	...	...	Not above 4.8.
3.22′ 15	4.85	...	...	...	Oscillations barely perceptible.
3.26′	..	..	..	...	Cardiac pulsations, 100—extremely irregular both in number and force.
3.29′ 30	...	...	...	...	A solution of another centigramme of digitaline was now injected into the cellular tissue of the upper part of right thigh—completed at 32′ 10″.

* Little oscillation. Probably clots already present.

Time.	Mercury. Min. & Mx.	Mean.	Pulse.	Resp.	Remarks.
P.M.	Inches.				
3.31′ 40	...	...	...	...	Heart's action weaker, and more irregular.
3.35′	...	...	...	...	It was ascertained that there was obstruction at some point in the apparatus, and on examination, the nozzle, and the greater part of the India-rubber tubing, were found filled with clots. These were removed, and the instrument again readjusted at 3.44′.
3.45′ 45	3.2—6	...	...	...	Oscillates, with extreme irregularity.
3.47′	4.3—4.4	...	...	...	Hardly perceptible.
3.50′ 45	...	...	...	...	Clip placed on India-rubber tube, and nozzle twice cleaned by suction.
3.53′ 30	3.8—5.7	...	...	...	The mercury soon again became stationary, and after another ineffectual attempt to clear the
4.	...	...	90*	...	apparatus, the nozzle was finally withdrawn at 4 P.M., and the wound stitched up. The femoral pulse was 90′, and, though still very irregular, was less so than when last estimated.

4.4′.—Dog released from the table. Seemed a little stiff at first, but soon ran about as if nothing had happened, and made water on the floor. In this experiment, instead of the nozzle which I have before described, a straight one was used of a much smaller bore, which was farther diminished by a stopcock upon it.

Exp. II.—*Nov.* 29.—In this experiment the nozzle was wider, and the apparatus was just as described at the beginning, the hæmadynamometer showing, the mean only being employed. The same dog was used which had been experimented on on the 25th. Chloroform was given as formerly.

* Less irregular.

Time.	Mercury. Mean.	Pulse.	Resp.	Remarks.
P.M.				
1.58′	...	...	...	I made the first incision.
2.5′ 30	...	...	...	Carotid exposed, and ligatured at distal end.
2.11′	...	...	...	Nozzle inserted.
2.14′	...	120	...	Clip relaxed.
2.17′	5.55			
2.19′	5.4	125	...	5.4 appears to be about the average.
2.20′ 45	5.3	...	...	External jugular vein tied.
2.22′ 30	5.15			
2.23′ 15	5.4	...	...	½ a grain of digitaline in water was injected into the jugular vein. Mercury immediately indicated 5.4.
2.25′	5.45			
	5.5—5.55			
2.25′	5.3	...	...	Suddenly fell to 5.3.
	5.5	...	...	As suddenly rose to 5.5. Then fell again.
2.26′	5.1—5.3	...	...	Heart's action extremely irregular.
2.26′ 30	4.8— 5	...	...	Still extreme irregularity in the pulsations.
2.26′ 40	4.7			
2.26′ 55	4.6—4.55			
2.27′	4.4	...	...	Breathing extremely rapid.
2.27′ 45	4.5			
2.28′ 15	4.4			
2.29′ 40	4.8	...	26	Mercury rose to 4.8. Respirations are not so rapid as they were at 27′.
2.30′	4.7	172	...	Pulse more regular.
2.30′ 15	4.8			
2.30′ 30	...	...	...	Respiration much quieter.
2.30′ 45	4.6	148	...	Pulse still regular. Oscillations slight. Column is, on an average, at 4.6, and is less violently affected than before injection.
2.32′ 30	...	200	...	Regular.
2.33′	4.3	...	...	Pupils dilated, and imperfectly contractile to light.
2.34′ 15	4.3			
2.34′ 45	4.1			
2.35′	4.			
2.35′ 45	3.8	...	...	Pulse weaker.
2.36′ 10	3.6			
2.36′ 30	3.5	180	...	Pulse very weak.
2.37′ 30	3.35	...	...	Pupils contract more perfectly. Breathing, abdominal laboured. Intercostal muscles do not act properly. Chiefly the accessory muscles of respiration act. Thorax is raised as it were as a whole.

Time.	Mercury. Mean.	Pulse.	Resp.	Remarks.
P.M.				
2.38′ 45	3.4			
2.39′ 20	3.25			
2.40′ 10	3.2			
2.40′ 40	3.3			
2.41′	3.25	154	...	Pulse weak, and rather irregular.
2.42′	3.2	...		
2.42′ 10	3.3	...	...	Thermometer in axilla of dog 96°. 5 F. Pupils smaller than at the beginning of experiment, and continue to contract on the application of light.
2.44′	3.2	...	...	Pulse cannot well be estimated. Very irregular.
2.45′ 15	3—3.1	150	...	Pulse irregular. Thermometer 99°.
2.47′ 30	3	...	21	Slimy saliva issuing from the mouth.
2.49′ 30	2.9	150	...	Pulse irregular. Thermometer 99°. 3 F.
2.53′	2.9	...	18 or 19	Dog appears to be sick, but does not vomit; the muzzle preventing him from opening his mouth at all.
...	2.95	...	...	Dog moans.
2.55′ 10	...	...	...	Groaning much increased, and louder.
2.56′ 15	2.85	155	...	Appears to be endeavouring to vomit.
2.57′ 15	3.1			
2.58′	3.2	...	...	Steadily rising.
2.58′ 10	3.3—3.5			
2.58′ 45	3.1			
2.59′	3	...	...	Gradual sinking.
2.59′ 10	2.5	...	...	Convulsions. Passage of fæces.
	2.4	...		Stoppage of heart's action.
	2.2		...	
	Down.	...		Dog dead.
3.				

After this tremors were noticed. Spasmodic twitching of the penis was noticed after heart's action and femoral pulse had ceased, and a fluid resembling, and supposed to be, semen, was emitted; but on its being at once examined microscopically, no spermatozoa were to be found, and only an abundance of large cells like mucus or pus corpuscles were seen. Post-mortem examination was made immediately. The thorax was opened, and the great veins tied. They were much engorged. At 3.16′ the thoracic viscera were removed. A great gush of fluid blood took place from the lower part of the vena cava inferior on cutting it. The veins and right side of the heart were engorged and swollen, stuffed like sausages, as Casper de-

scribes it. Right auricle distended. ℥iii. of perfectly fluid blood of a very dark colour was got from the right ventricle. At 3.21 the left ventricle was examined, and found firmly contracted, containing a clot. It was not white from contraction. The blood, on flowing from the body, coagulated in three minutes. The blood from the vena cava inferior coagulated very quickly into an extremely firm clot in the thoracic cavity. The contents of the left side of heart weighed 1 oz. $4\frac{1}{3}$ drachms.

EXP. III.—*Nov.* 29.—A full-grown sheep was experimented on—the hæmadynamometer, showing the maximum and minimum, being employed.

8.35′ P.M.—Respirations 56 per minute; the sheep being at this time tied down on the table. No chloroform was given. Carotid exposed.

Time.	Mx. & Min.	Mean.	Pulse.	Resp.	REMARKS.
P.M.					
8.49′	...	...	...	...	Distal end of carotid tied, and tube inserted.
8.56′	...	...	...	...	The clip removed; tube then broke from the artery.
9.12′	...	...	...	...	Tube replaced, and clip removed.
9.14′	3.5—5	4.2			
9.16′	3.5—5.2	4.2			
9.19′	3.5—5				
9.22′	3.5—3.6	...	78	...	Animal excited by examining the wound.
9.24′	4—5	4.3	...	..	
9.25′	...	...	...	...	$\frac{1}{2}$-a-grain of digitaline in water was injected into the cellular tissue of the thorax.
9.26′	4.1—4.6				
9.28′	4.7	...	..	...	On slight agitation.
9.30′	5	...	82	36	Breathing more laboured.
9.32′	4.2—4.4	..	80	...	Pulse steady at 80.
9.42′	3.8—4.8	4.3			
9.45′	7.5	5.4	...	...	Sheep struggling.
9.47′	4.1—4.4	...	104		Sheep struggles. After this the oscillations stopped, and clots were suspected in the artery.

Time.	Mx. & Min.	Mean.	Pulse.	Resp.	Remarks.
P.M.					
9.52′	...	...	...	...	Clip applied, and tube removed. Again applied at 10.6′, but at 10.10′ the India-rubber stopper came out, and the experiment thus interrupted was not resumed. The sheep was loosed from the table. Seemed very unsteady on its legs. There was some amount of venous oozing from the wound.
10.10′	...	...	98	39	

Exp. IV.—*Nov.* 30.—This morning the sheep seemed still much depressed, it had made a good deal of water during the night. Between 1 and 2 P.M. it was again tied on the operating table. Chloroform administered, and the other carotid opened.

Time.	Mercury. Mean.	Pulse.	Resp.	Remarks.
P.M.				
2	...	166	...	Hæmadynamometer connected with the artery.
2. 1′	...	...	21	Clip removed. Thermometer in vagina 101°. 5 F.
2. 3′	2.1—3	...	...	Till this time the mercury in the tube has oscillated between 2.1 and 3, neither steadily nor regularly.
2. 5′	...	...	...	The pupils have become contracted. At the beginning of the experiment they were dilated.
2. 6′ 40	3.5	...	...	Pretty steady at 3.5. The sheep at this
	3.6	...	..	moment made a slight struggle, and mer-
	3.7	...	...	cury rose to 3.6 at once, then to 3.7.
2. 8′	3.45—3.5	...	...	Thermometer 102°. 9 F.
2. 8′ 35	3.2			
2. 9′ 45	3.5	...	20	Steady at 3.5.
2.10′ 45	3.95	...	...	Thermometer 102°.
2.11′	3.8	...	...	Sheep appears completely free from the effects of the chloroform.
2.14′	3.05	...	...	Very feeble pulse.
2.14′ 10	3.4	...	...	During violent struggles which now take place.

Time.	Mercury. Mean.	Pulse.	Resp.	Remarks.
P.M.				
...	3.05	...	...	Then fell to 3.05.
...	3.4	...	...	During another struggle.
...	3.1	...	...	Then fell to 3.1.
2.16′ 15	3.4	...	...	An apparently convulsive movement of the head.
2.17′ 10	3.4	...	...	Pretty steady.
...	4.2	...	...	Violent struggle. Mercury rises to 4.2,
	4.3			4.3, 4.4.
	4.4			
	4.5	...	...	Another struggle.
2.20′	3.7			
...				
2.20′ 10	...	...	...	Injected the first half of 2 grains of digitaline suspended in water (into the
2.21′ 10	...	...	...	jugular vein—this from memory).
2.21′ 25	...	...	...	Injected the remainder of the digitaline.
2.22′ 10	5.2	...	...	Animal violently struggling.
...	5.5	...	...	During another struggle.
2.23′ 10	...	...	..	Pupil obviously contracted.
2.24′ 50	4.9	...	...	
2.25′	4.8	...	...	Mercury stands at 4.8. Animal struggles.
...	...	...	...	Pupil has become more dilated. Convulsive movement.
2.26′ 10	...	...	...	Another convulsion.
2.26′ 30	4.7			
2.27′	...	...	...	No perceptible pulsation in the carotid.
...	4.6	...	...	Cornea scarcely sensible to touch. Pupil more dilated.
2.28′ 10	...	...	...	Cornea insensible. Respiration just perceptible.
2.29′ 45	4.4	...	...	*Very* faint pulsation in the artery.
...	4.3			
2.31′ 30	...	...	...	Pupil widely dilated. Respiration imperceptible.
...	...	...	...	Pulse inappreciable. Thermometer 101°.
2.33′	...	..	...	Sheep allowed by all to be dead. Had made water since it was placed on the table. Mercury gradually fell.

The slow fall of the mercurial column was at first attributed to clots, but on examination none were found to account for it.

Post-mortem examination made immediately.

On opening the thorax, the veins were found much congested. The vessels were then ligatured, and the thoracic viscera removed. The left

ventricle was firmly contracted. Left auricle flaccid. The right auricle and ventricle were both distended with blood. Pulmonary artery was full and turgid; the pulmonary veins empty, or nearly so. Right ventricle contained no clot, but 2½ ounces of dark fluid blood. Left ventricle contained no clot or blood, but was markedly contracted, without any whiteness, however. Blood returning from lungs was quite fluid, and very dark. Descending aorta contained no clot, so the slow descent of the mercury could not thus be accounted for. Bladder was firmly contracted and empty.

EXP. V.—*Dec.* 20.—A large dog—a kind of bloodhound, or a cross between that and a mastiff, was experimented on. It took about 2 oz. of chloroform, which was applied on a thick towel before it was anæsthetized, though no doubt the greater part of this was lost in the application. The time when it began to get the chloroform was not noted. I cut down on and cleaned about 1½ or 2 inches of the jugular vein, and tied it. After exposing the carotid, which lay very deep, the dog was seized with convulsive tremors, which lasted a short time. Dr Gamgee then finished the cleaning of the artery, and inserted the nozzle of the hæmadynamometer. The instrument showing the mean only was used.

Time.	Mercury. Mean.	Pulse.	Resp.	REMARKS.
P.M.				
2.44′	...	...	...	Clip removed.
2.44′ 30	5.4			
2.44′ 40	...	...	...	The tube of the hæmadynamometer was forced out by the pressure.
2.55′	...	...	...	Tube re-inserted.
2.56′	5.5			
2.56′ 40	5.7			
2.58′ 30	5.7—5.9	...	...	The dog being quiet.
2.59′ 20	5.5—5.6	..	...	Dog quiet.
3.	5.7—5.75			
3. 0′ 45	5.6	...	...	Dog whines and barks as if dreaming.
3. 2′ 30	5.4—5.6			
3. 3′	5.35	...	...	Dog whines loudly.
3. 3′ 30	5.5—5.7	...	...	
3. 5′	5.9	...	...	Continues barking, as if in a dream, more loudly than before.
3. 5′ 6	5.8	...	...	During inspiration, or attempts to bark, the mercury falls. During expiration it rises.

Time.	Mercury. Mean.	Pulse.	Resp.	Remarks.
P.M.				
3. 7′	...	...	...	Still attempting to bay. By a jerk, a drop of blood got above the mercurial column.
3. 9′	5.5—5.7			
3.12′	...	156	...	
3.14′ 30	...	...	...	The injection of one grain of digitaline suspended in about 2½ fluid drams of water, into the jugular vein, was begun.
3.16′	5.9—6.1	...	...	The dog struggling and crying.
3.17′	6.3			
3.18′	5.8—6.1	...	...	The dog cries loudly.
3.18′ 30	6.4	...	...	Still crying louder than ever.
3.18′ 40	6.2			
3.19′	5.8—6			
3.20′	5.5—5.7	...	...	Continues crying.
3.20′ 20	5.35–5.55			
3.21′ 5	5.2—5.4	120	...	Pulse irregular.
3.21′ 35	5.4	...	...	During a long howl.
3.22′ 10	5.5			
3.22′ 15	5.			
3.22′ 20	5.—5.1	...	...	Respiration slow laboured, abdominal.
...	5.3	...	...	Stops crying.
3.23′	5.6	...	...	Deep slow abdominal respiration.
3.23′ 30	5.5	...	..	Breath very laboured.
3.24′	5.2	...	...	Pulse small and irregular.
3.24′ 30	5—5.15			
3.24′ 35	5.3			
3.24′ 45	5.5	...	...	The dog is quite quiet, and there is no struggle whatever to cause the mercury to rise.
3.25′	5.8			
3.25′ 15	5.9	...	...	No struggle whatever.
3.25′ 25	6	...	...	Pulse is weak and jerking. (Hæmorrhagic pulse, Maclagan).
3.25′ 40	6.1			
3.25′ 50	6.2	...	...	Action of heart violent, thumping.
3.26′	6—6.2	...	...	Dog crying. Iris is sensitive, slightly contracted.
3.26′ 40	6.3			During a deep howl.
3.27′ 20	5.8	...	...	Saphena veins tense, and femoral artery feels as if it were contracting against the heart. (Dr Maclagan).
3.27′ 50	5.9			
3.29′	5.6—5.8	...	...	Howling loudly as if suffering much.
3.29′ 30	5.5—5.7			
3.30′ 30	5.5—5.7			
3.30′ 35	5.3	...	...	From 5.3, mercury rose straight to 5.7.
3.31′ 20	5.7—5.6			

Time.	Mercury. Mean.	Pulse.	Resp.	Remarks.
3.31′ 35	5.5—5.8			
3.32′ 40	5.5	...	...	Dog struggles, howls loudly, shakes his tail, femoral pulse very small.
3.33′	5.7	...	...	During the loudest howls, the mercury only rises to 5.8.
3.34′	5.5—5.7			
3.34′ 30	5.4	...	...	During a short but very violent struggle.
3.35′	5.7	...	...	During a long struggle.
3.39′	5.3—5.5	...	...	Pupils rather more dilated.
...	5.8	...	...	During a very strong struggle.
3.40′ 55	5.9	...	...	½-a-grain of digitaline, suspended in about 1½ drams of water, was now injected into the subcutaneous cellular tissue of the abdomen.
3.41′ 35	5.4			
3.43′	5.5	...	...	Deep groans. Pulse very irregular.
...	5			
3.43′ 5	5.2			
3.43′ 10	5.4			
...	5.2			
3.43′ 30	5.5			
3.43′ 33	5.3	...	...	Great irregularity.
...	5.2			
3.43′ 40	...	...	...	Pupil somewhat contracted.
3.44′ 10	5.5			
3.44′ 20	5.2			
3.44′ 25	5.4	136	...	Pulse extremely irregular. Pupil somewhat contracted. Iris sensitive.
3.45′ 30	5.3—5.4			
3.46′ 20	5.3	...	...	The dog howls.
3.47′	4.9	...	...	In a struggle, the mercury now never rises above 5. The dog cries loudly.
3.47′ 30	4.6			
	4.7	...	...	Only rises to 4.7 during a long struggle.
3.48′ 20	...	..	...	Loud moans, deep and frequent abdominal respiration.
3.49′	4.8	...	...	Extreme irregularity of pulse. Weak moans. Deep sighing respiration.
3.50′	4.3	120	...	Pulse extremely irregular, intermits completely with inspiration. The heart seems to be going all right, and not intermitting.
3.51′ 40	4.2	...	..	Pulse less intermittent.
3.52′ 10	4.7			
3.52′ 30	4			
3.52′ 40	3.8			
3.52′ 55	4.3	...	...	Pupil less contracted. Seems normal. Sensitive.

Time.	Mercury. Mean.	Pulse.	Resp.	Remarks.
P.M.				
3.53′ 40	4.4			
3.53′ 50	4.1			
3.54′ 5	4.4			
3.54′ 10	4.1	...	10	Dog groans. Long deep howls.
3.55′ 30	4.3	...	...	There is intermitting of femoral pulse, but not of heart's action.
3.56′ 15	4.1			
3.56′ 25	4.3	...	...	Intermittency of pulse is distinctly heard during inspiration. Dog moaning.
3.57′ 30	4.2			
3.58′ 5	3.9			
3.58′ 20	3.5	...	...	Gradual fall from 3.9.
3.58′ 30	3.8	...	...	Pupils as before.
3.59′	3.4			
3.59′ 5	3.3	...	...	Dog whining.
3.59′ 40	3.8			
3.59′ 45	3.9			
3.59′ 50	3.6			
4.	4			
4. 0′ 5	4.1			
4. 0′ 10	4.2			
4. 0′ 20	4.			
4. 0′ 25	3.5			
4. 0′ 30				
4. 0′ 35				
4. 0′ 45	3.3	...	24	Gradual fall from 3.5.
4. 0′ 55	3.8	...	...	Mercury rose suddenly to 3.8.
4. 1′	4.			
4. 1′ 5	4.1	...	..	Dog whines.
4. 1′ 25	3.5			
4. 1′ 30	3.7			
4. 1′ 45	3.4	...	...	Respiration slightly convulsive.
...	3.6	...	...	Dog struggles.
4. 2′ 15	3.4	...	..	Moaning slightly.
4. 2′ 20	3.7	...	...	Falls during inspiration.
4. 3′ 40	3.2			
4. 3′ 45	3.5			
4. 4′	3.4			
4. 4′ 20	3.5			
4. 4′ 25	3.7			
4. 4′ 50	3.6	...	...	Whines and struggles.
4. 5′ 15	3.3			
4. 5′ 20	3.5			
4. 5′ 27	3.3			
4. 5′ 30	3.6			
4. 5′ 35	3.45			

Time.	Mercury. Mean.	Pulse.	Resp.	Remarks.
P.M.				
4. 5′ 40	3.75			
...	3.45	...	24	
4. 5′ 55	3.7			
4. 6′ 45	3.8			
4. 7′ 5	...	...	...	The dog snores. Pupil normal.
4. 7′ 25	3.8			
4.11′ 30	4.1	...	...	Pulse intermits during a long inspiration, and the femoral pulse gives a peculiar thrilling feeling to the finger when compressed firmly.
4.15′	...	...	...	Dog whines.
4.16′ 30	4.1	216	20	Breathing is quiet. Heart's impulse, 216 in a minute—(Dr Gamgee). 18 beats in 5 seconds. In half a minute I counted 100 beats, strong, irregular. Dr G. feels a purring tremor over the cardiac region.
4.25′	...	...	...	Loud double blowing murmur on auscultation, which, I think, is regurgitant.
4.27′	5.7	...	...	On auscultation over the carotid, no murmur is audible. Dog breathes very quietly. The double murmur varies much in intensity, the diastolic is far more prolonged. The hæmadynamometer was now stopped by a clot, so the nozzle was taken out of the artery, and the apparatus cleaned. A jet or two of blood issued from the artery before the nozzle was reinserted.
4.50′	4.	...	...	Re-inserted. Mercury stood at 4.
4.52′	4.			
4.53′	...	...	...	Convulsive movement. Head turned over. There was a clot in the artery, just at the end of the nozzle, and this was broken up by pressure.
4.53′ 20	...	...	...	Dog dead. His heart was going pretty regularly, and the beats were apparently of good strength just before the dog died. On looking at the penis, no tremors were observed, and no prostatic mucus was seen. There was a good deal of water about the point of penis, from dog's having emptied its bladder. This might have possibly concealed a drop or two, if such were there.

At 4.59 there were a kind of convulsive snorts.

Post-mortem examination made immediately.

The tongue seemed somewhat pale. On opening the thoracic cavity, the veins were found very full, and perfectly turgid. The right side of the heart was distended by dark fluid blood, and the veins on its surface were dark and full. The left heart contained a little fluid blood, and was flaccid. On the surface were one or two milk spots. The ventricle was opened before the competency of the aortic valves was tried, and then they were scarcely competent, but on examination seemed perfectly healthy. The trachea and larger bronchi contained no mucus, but there was some frothy mucus in the smaller bronchi. At 5.21′ the œsophagus contracted rhythmically when laid along with the heart and lungs on a plate. It continued to do so briskly when stimulated on its mucous surface, after being cut open.

Exp. VI.—*Jan.* 10.—A dog of middle size was laid on the table, and chloroform administered. While this was being done, the dog salivated profusely, and passed urine. The heart-sounds at the time were perfectly normal. The operation of exposing the carotid was begun at 2.57′ P.M.

Time.	Mercury. Mx. & Min.	Mean.	Pulse.	Resp.	Remarks.
P.M.					
2.57′	...	...	108	30	First incision made.
3.41′ 30	...	...	...	...	Clip removed. Mercury rose.
	5—6.5	...	84		
3.45′	5—6.5	5.65	...	20	
3.48′	5—6.5	5.65	...	...	The jugular vein was now tied. No very marked effect on the mercury.
3.55′	5—8.	6.3	...	...	The injection of 1 grain of digitaline in about 2 oz. of water was begun into jugular vein. It filled the syringe 4 times.
3.55′ 20	...	...	...	..	Injection completed. Dog moans.
3.56′ 30	4.7—8.6	6.1–6.2	..	12	
3.59′ 30	3.8—7.7	5.8	...	..	Dog cries.
3.59′ 45	4—8.	5.7			
4.	4.2—8.3				
4. 0′ 15	5—8				
4. 0′ 45	6.9—7.2				
4. 1′ 20	4.8—8.2	6.4			
4. 1′ 50	6.2—7.4				
4. 2′ 15	...	6.7			
4. 2′ 30	...	6.8			
4. 2′ 45	6.3—7.5				

Time.	Mercury. Mx. & Min.	Mean.	Pulse.	Resp.	Remarks.
P.M.					
4. 3′ 25	6—8	6.95			
4. 4′	5.2—8.2	7.	80		
4. 4′ 45	6.3—7.6				
4. 5′ 15	5.8—8				
4. 5′ 30	6—7.8	6.9	...	12	
4. 7′	6—7.8	6.7	...	...	Pulse irregular.
4. 7′ 20	6.1—7.7				
4. 8′	5.8—7.6	6.6			
4. 8′ 15	5.5—7.2	6.5			
4. 8′ 40	6.3—8				
4. 8′ 50	6.1—6.9				
4. 9′	5.8—6.8	6.4			
4. 9′ 40	5.8—7.2	6.35			
4.10′ 20	5.5—6.7	..	...	30	
4.10′ 30	5.5—7.4	6.2			
4.10′ 40	5.3—6.7	6.15			
4.11′ 40	5.5—6.5	6.			
4.12′ 5	5.5—7.				
4.12′ 25	5.3—6.2				
4.12′ 40	5. —6.7	5.8			
4.13′ 30	4.5—6.3	5.7	...	38	Pulse irregular.
4.13′ 45	4.5—6.2	...	...	...	For about 3 pulsations or so, the mercury oscillates within .2 of an inch, and then there is a sudden rise or fall.
4.14′ 40	4.5—8	5.4			
4.15′ 5	4.3—5.2	5.3			
4.15′ 10	4.5—6	5.25			
4.15′ 45	4.2—5.9	...	..	...	With inspiration.
4.16′	5—7	5.3			
4.16′ 10	4—5.8	5.			
4.16′ 35	4.2—6	5.1			
4.16′ 45	4.5—6.7	5.2			
4.16′ 50	4. —6.8				
4.16′ 55	3.3—6	5.1			
4.17′ 10	3.7—7	5.	...	...	Dog very restless. Struggles.
4.17′ 40	4—6.2	4.9			
4.18′ 10	4.5—5.9	5.1			
4.18′ 35	4.7—6.2	5.35			
4.18′ 45	5. —6	5.3			
4.19′ 15	...	...	...	...	A blowing murmur is heard with one of the heart's sounds, but it is difficult to distinguish with which.
4.19′ 45	...	5.4			
4.21′ 10	4—6	5.			
4.21′ 30	4.3—5.7	5.			

Time.	Mercury. Mx. & Min.	Mean.	Pulse.	Resp.	Remarks.
P.M.					
4.22′	3.8—6	4.9			
4.22′ 25	3.5—6	4.7			
4.23′ 30	3.2—5.8	4.5			
4.24′	3.1—5.5	4.4			
4.24′ 10	3.2—5.2	4.35			
4.24′ 15	2.9—5.1	4.3			
4.24′ 25	3.2—5				
4.24′ 30	2.9				
4.24′ 45	3.3—5				
4.25′	...	4.25			
4.25′ 10	3.2—5				
4.25′ 15	5.6	...	...	...	Dog attempts to bark.
4.26′	4.2—5.3				
4.26′ 7	..	4.4			
4.26′ 25	...	4.5			
4.26′ 45	...	4.6			
4.27′	4.2—5.3	4.65	...	22	
4.27′ 40	4. —5.8	4.6			
4.28′	3.8—5.8	4.6			
4.28′ 30	3.3—5.4	4.5			
4.28′ 59	3.2—5.2	4.3			
4.29′ 10	3.3—5.8				
4.29′ 30	2.9—5.4				
4.29′ 45	...	4.1	...	...	Dog howling.
4.30′ 20	...	3.95			
4.30′ 55	3. —5.5	4			
4.31′	...	...	...	...	Heart's impulse strong. Loud blowing murmur, which almost seems to be with both sounds, and certainly is with one—I think the first.
4.32′ 40	3. —5.2	3.9			
4.33′	2.9	...	...	...	Very irregular.
4.33′ 10	2.8—4.7	3.8			
4.34′ 20	3.2—4	3.8			
4.34′ 40	3. —4.8		...	26	The mercury goes up suddenly, and falls as it were by several short steps.
4.35′ 40	3.1—4.5				
4.35′ 50	3.3—4.7				
4.36′ 15	2.8—4.2	3.8			
4.36′ 50	2.9—4.5	3.75			
4.37′ 15		3.7			
4.37′ 30	3.1—4.4				
4.38′ 10	...	3.65			
4.38′ 20	...	3.6			

Time.	Mercury. Min. & Mx.	Mean.	Pulse.	Resp.	Remarks.
4.38′ 40	...	...	...	...	Heart's impulse felt distinctly and apparently increased. Murmur still present. Pulse cannot well be counted, it is so quick, small, and irregular.
4.39′ 15	3.2—4.3	3.55			
4.40′ 30	3.1—4.2	...	...	18	Breathing quiet.
4.41′ 10	...	3.4			
4.41′ 20	2.8—3.7	3.3			
4.41′ 50	3. —3.7	3.15			
4.42′ 35	2.7—3.4	...	...	...	White frothy saliva flows freely from the mouth. Dog lies quiet.
4.43′ 20	2.8—3.7	3.15			
4.44′ 30	2.7—3.3	3			
4.45′	2.6—3.6	...			
4.45′ 40	2.4—3.2	2.9			
4.46′	2.5—3.3	2.9			
4.47′	2.6—3.1	...			
4.47′ 20	2.7—3.7	...	...	...	Breathing quite quiet.
4.48′ 10	2.7—3.6	...			
generally	2.8—3.2	...			
4.49′ 20	...	2.8			
4.49′ 45	...	2.75			
4.49′ 50	2.4—2.7	...			
4.50′ 10	...	3.1	..	...	Moans slightly.
4.50′ 50	...	2.65			
4.51′ 10	2.4—2.8	...	...	...	Moans, and makes slight effort.
4.51′ 40	3.56	2.8	...	...	The oscillating column stopped quite still at 3.56. The mean column steadily rose till they both attained the same height, and there they remained. Thinking that there was a clot formed, the nozzle was removed, but there was none in the instrument. The artery was then pressed to break up any clots that might be in it, though none were felt.
4.54′		...	...	...	Both have stopped.
4.57′		...	...	...	The artery opened.
4.58′		...	...	...	The dog threw back his head, made several convulsive respirations, and died.

Post-mortem examination made immediately.

On opening the thorax, air rushed in. The lungs were natural in colour,

and very much collapsed. Both sides of the heart were full of blood. The vena cava and venous system generally turgid. The veins of intestines and viscera congested. The venous blood was dark in colour. On pinching the phrenic nerve, the diaphragm contracted; and on pinching the left phrenic, the contraction was not confined to the left side, the fibres of the right half visibly and plainly contracting. On tying the vena cava inferior, and cutting it beyond the ligature, the fluid blood, which issued from the lower end into the thoracic cavity, and which was very dark coloured, coagulated in about a minute. (This is by guess, not by a watch.) The heart seems quite normal. Bladder was full. No emission of semen or mucus was observed. Half a grain of the digitaline used in this experiment had been dissolved in a small quantity of spirit for another purpose, but not used. The spirit had evaporated, and the digitaline was in a resinous-looking mass—not in powder.

Exp. VII.—*Jan.* 23.—The dog operated on was a large mongrel. It was thin and weak, and had had loose and sometimes bloody stools for some days back. It was tied down and chloroformed. I then exposed both vagi, and passed ligatures under them, so as to pull them nearer the surface, when they were wanted for section. The hæmadynamometer was then inserted into the left carotid. The mean tube seemed somewhat choked at the capillary part, so as not to work freely, and its indications were therefore not quite trustworthy.

Time.	Mercury. Min. & Mx.	Mean.	Pulse.	Resp.	Remarks.
P.M.					
2.56′ 45	3.44				
—	3.4—3.9	2.6			
2.59′	3.3—3.8	...	...	...	The mercury oscillates steadily.
3	...	...	...	...	Both vagi were cut.
...	2.5—4.5	...	...	...	Mercury fell to 2.5.
...	3.5—4.5	3			
3.1′	2.9—3.3				
3.1′ 30	2.3	3.4			
3.2′ 10	3. —4.	...	...	..	Pulse slower.
3.2′ 30	3.3—4.				
3.2′ 40	...	...	..	...	The dog's breathing is gasping.
...	4. —4.5				
...	3.3—4.2	...	...	...	Gasping.
3.3′ 30	2.8—3.5	3.4	...	...	Ala nasi are working.
3.4′	3.2—3.6				
3.4′ 20	4. —4.5				

Time.	Mercury. Min. & Mx.	Mean.	Pulse.	Resp.	Remarks.
P.M.					
3.4′ 40	3.8—4.2				
3.5′	4. —4.3	3.4			
3.5′ 10	4. —4.3				
3.5′ 40	4.2—4.5	3.4			
3.6′ 15	4.2—4.5				
3.6′ 30	4.2—4.5				
3.10′	4.1—4.4				
3.10′ 30	4.1—4.3	...	...	...	Mucus runs from nose.
...	4.1—4.4	...	..	20	Respiration becomes more jerking.
3.12′	3.9—4.3				
3.12′ 15	3.8—4.2				
3.13′ 45	3.7—4				
3.14′ 15	3.5—3.9				
3.15′	3.5—4				
3.17′	3.4—3.9	..	...	...	Cheeks puff out with every respiration. Whole chest and abdomen heaves up *en masse*.
3.17′ 15	3.4—3.7				
...	3.9—4.1	...	...	...	Breathing suddenly very gentle.
3.19′	4.25—4.3	...	...	14	Inspiration is made by a series of little jerks—expiration made at once.
3.21′ 40	...	...	...	...	Distinct blowing murmur with the sound.
3.24′ 30	4. —4.25	...	...	..	The mercury rises suddenly with expiration, and falls by a series of little jerks. Breathing stronger —a kind of coughing or snorting respiration.
3.26′ 10	...	...	...	...	Dog throws back head. Mercury falls.
...	4.2—4.3				
...	3.9—4.1				
3.28′ 20	4.2—4.3				
3.28′ 30	4. —4.25	...	...	...	Dog snorting.
...	3.5—3.9	...	...	...	Convulsive movement.
3.30′ 35	3.9—4.3				
3.31′	4.3—4.5				
3.32′ 15	4.4—4.5				
3.33′ 30	4.2—4.3				
3.37′	4. —4.2	...	...	...	Jugular vein cleaned. Dog snores.
3.38′	...	...	...	...	Jugular vein tied, and ½ grain of digitaline in water injected into it. (The time of the injection is from memory.)
...	4. —4.1				

Time.	Mercury. Mx. & Min.	Mean.	Pulse.	Resp.	Remarks.
P.M.	Inches.				
3.39′ 30	4.5—5	...	...	...	Convulsive movement.
...	4.4—4.9	...	...	...	Low sighs.
...	—5.5				
3.40′ 10	4.7—5.5				
3.40′ 30	—6				
...	—5.8	5			
3.41′	4.9—5.4	5.1			
3.41′ 10	4.9—5.7	5			
...	4.2—5.6	5			
..	4.7—5.1	...	...	...	Stops.
3.43′	...	...	...	...	Heart acts very irregularly. The sounds are like toot-toot-toot-toot-toot-toot-toot-toot-too. Heart very weak. Loud snorting.
3.47′	...	...	...	...	Convulsive movement.
3.48′	...	...	...	...	Coughing.
3.59′ 30	5.3—5.4	...	...	...	Breathing very slow. Heart thumping against the ribs. Breath laboured.
4. 5′	4.5—4.6	...	...	...	Heart irregular. Breathing, sighing. Dog put back head convulsively but gently.
4. 7′ 30	3.7—4.5	...	...	10	Respirations long, and sighing.
...	4.1—4.7				
4. 8′ 5	3.5—4.4				
4. 9′ 10	4. —4.5				
...	3.7—4.3				
4.10′ 10	3.8—4.4				
4.11′ 10	3.5—4.4	...	...	...	Breathing very quiet.
4.12′	3.6—4.3				
4.13′	3.2—4				
4.14′	3.2—4.5	...	...	...	Dog moans.
4.14′ 45	3.4—4.7	...	...	...	Convulsive movements.
4.15′	4.3—5				
4.16′ 50	3.9—4.5				
4.17′ 30	...	...	...	...	Oscillations stopped.
...	4. —4.1	...			
4.18′	4.1—4.4	...	...	...	Strong beat of heart.
...					
	3.5—4.2	...	...	...	Very irregular. Mercury ascends with expiration, and occasionally stops.
4.20′	3.5—4	...	...	...	Snoring, respiration, and a quick weak moaning.
...	3. —4				

Time.	Mercury. Mx. & Min.	Mean.	Pulse.	Resp.	Remarks.
P.M.	Inches.				
4.22′ 50	...	...	...	...	Oscillations stopped, blowing murmur at heart still present.
					After trying to dislodge the clot, without effect, the apparatus was removed.
4.35′ 30	...	...	...	...	Dog moans. Convulsive breathing. Heart strong and regular.
4.50′	...	...	...	...	As the dog did not seem about to die, and we could not wait any longer, his spinal cord was severed just between the occiput and atlas.
					Post-mortem made immediately. On opening the chest the lungs collapsed. The heart was beating vigorously. At 4.55′ the heart stopped, but could be re-excited to contract. The venous system was much congested. Both sides of the heart contained fluid blood.

Exp. VIII.—*March* 9.—A middle-sized dog was put under chloroform, and the hæmadynamometer applied to the carotid.

Time.	Mercury. Mx. & Min.	Mean.	Pulse.	Resp.	Remarks.
P.M.	Inches.				
3.20′	6. —6.7	6.5			
3.26′	5.5—6.7	5.9	...	...	Mercury sinks markedly with expiration (inspiration?) Dog appears to be free from chloroform, and seems to feel pain as he groans.
...	...				
3.30′	...	...	116	18	
...	5.5—6.5	6			
3.35′	...	...	...	...	Injected $\frac{1}{5}$th of a grain of digitaline in water into the jugular vein.
3.36′	...	..	...	...	Dog micturated and voided fæces.
3.40′	5.5—7	6.4	114	14	Pulse regular and stronger than before.
...	5.2—7	6.4			
3.42′	...	..	110		

Time.	Mercury. Mx. & Min.	Mean.	Pulse.	Resp.	Remarks.
P.M.	Inches.				
3.45′	...	...	116		
3.49′ 35	...	...	...	...	Injected ¼ of a grain more.
3.50′	5.7—7.8	...	106	...	Pulse regular.
3.55′	4.8	...	...	...	Mercury went down as low as 4.8.
3.56′ 30	5. —7	...	108	...	Pulse markedly smaller, irregular, and with occasional intermissions. With respiration the mercury falls more markedly than before.
4.	5.7—7.5				
4. 4′	...	...	...	...	Pulse very markedly intermittent, and the mercury falls at each intermission as low as 4.
	4.				
4. 8′	...	...	...	...	Pulse gives one strong beat and then 3 or 4 feeble ones.
4.10′	...	...	...	...	A drop of prostatic mucus exudes from the point of the urethra.
4.16′	...	...	...	...	Pulse very intermittent. Animal shivers every minute, or even more frequently. The hæmadynamometer stopped working.
4.24′	...	...	...	...	Readjusted the apparatus.
...	5. —7.7	6.			
4.26′	...	...	104	...	Pulse intermittent.
...	5.8—7.5	6.5–6.6	...	...	Animal continues to tremble.
4.29′	...	6.65	...	...	Oscillations more steady.
4.29′ 30	...	...	..	...	Clot again formed. Almost constant tremors.

The apparatus was cleaned, and again adjusted at 4.40, but the nozzle came out, and there was a gush of blood, and as this would have thrown some fallacy into the future reading of the mercury, the artery was ligatured, the wound stitched, and the dog released from the table. It lay for a few minutes, and then began to try and get off the muzzle. When this was removed, the dog rose and walked about. It seemed rather stiff at first.

Exp. IX.—*March* 20.—The dog operated on on the 9th, having recovered, was put under chloroform, and the carotid exposed. The dog was then allowed to come out from the chloroform, which it did at 2.15 P.M. Instead of digitaline, the extract obtained from commercial tincture of digitalis was employed; the tincture being gently evaporated, and the extract then dissolved in water and injected. The hæmadynamometer giving the mean was employed.

Time.	Mercury. Mean.	Pulse.	Resp.	Remarks.
P.M.	Inches.			
2	...	104		
2.37′	5.5	...	...	Hæmadymamometer set working.
2.37′20	5.7	...	...	Prolonged sigh.
2.38′	5.1			
2.39′	5.1—5.3			
...	5.4	...	...	During a long sighing inspiration.
2.41′	5.3			
2.42′	5			
2.42′10	5.2			
2.42′25	5.5	100		
2.44′	..	...	14	Pulse slightly intermittent. Respiration very sighing.
2.44′30	5.4—5.5			
2.45′	5.9	...	...	Injection of extract equal to ½ dr. of tincture.
2.46′	4.5			
2.46′45	3.9			
2.47′	3.7			
2.47′5	3.9	...	...	Injection of extract of 1 dr. of tincture.
2.47′25	4.8	108		
2.47′40	5.4			
2.48′20	5.5			
2.49′	5.7	...	...	Under the strongest expiration.
2.49′	5.9			
2.49′15	6.			
2.49′30	6.3			
2.50′15	6.15			
2.51′45	6.	102		
2.53′	5.6—6.1			
...	5.7—5.8	...	...	When lying quiet.
...	...	...	...	At every expiration there is intermittence of pulse.
2.54′	5.9—6			
2.55′	5.6—5.7			
2.56′	5.5	76	...	Intermittence and irregularity both as to the length and strength of pulsations.
...	...	...	12	
2.57′20	5.4—5.5	98		
2.59′	5.8			
3. 0′	5.5	100	14	
3. 2′	5.8	...	...	Dog howling.
3. 3′	5.5—5.7			
3. 4′30	5.9	...	...	During a struggle.
3. 4′45	6.	..	...	During another.
3. 5′	6.1	...	...	Still another.
...	6.			
3. 7′	5.7	...	...	Steady. A clot was suspected, so the instrument was removed and examined.

Time.	Mercury. Mean.	Pulse.	Resp.	Remarks.
P.M.				
3.11′ 30	5.3	...	...	Instrument replaced.
3.12′	5.5	131	...	Heart's action against the ribs is strong.
3.12′ 15	5.7			
3.13′	5.6			
3.14′	6.5	...	...	Steady. Clot again suspected. Instrument removed.
3.16′ 40	5.8	...	...	Pulse is more regular.
3.24′ 15	...	...	...	Instrument again replaced. The mercury rises in a jerking fashion.
3.25′ 30	5.5	...		
3.25′ 45	5.8	...	...	Injected part of extract of 1 dr. of tincture. No struggle.
3.26′	5.9	96	...	Respirations few and slight, quite quiet.
3.26′ 15	4.5	100	...	Injected the remainder of the water and extract.
3.26′ 30	4.7			
3.27′	5.	...	...	Dog's breathing is loud and whistling.
3.27′ 5	5.3	...	...	During a great struggle.
3.28′	5.35—5.5	...		
...	5.1—5.3	64		
3.28′ 45	4.8—5			
3.29′	4.5—4.7	...	...	Pulse very intermittent. Dog quite quiet.
...	...	...	12	Gasping respirations.
...	4.5—4.6	...	...	Respiration much less deep.
3.31′ 25	4.7—4.8	44		
3.31′ 40	4.9	50	...	Movement of mercurial column barely perceptible.
3.34′ 50	4.95—5.	...	...	Heart's action weak.
3.35′ 20	...	80	...	Pulse feels rather a wavering than distinct beats.
3.43′ 5	...	...	...	Hæmadynamometer stopped.
3.48′ 20	3.3	116		
3.48′ 50	3.2	...	...	Dog perfectly quiet.
3.50′	3.2	180		
3.52′	3.3			
3.54′	3.2	172	...	There are variations in the quickness of the pulse without variations in arterial tension.
3.57′ 15	3.1	140		
4. 0′ 30	3.2	..		
4. 1′ 30	3.2	196		
4. 3′ 40	3.25	170		
4.15′	...	...	...	Breath feels distinctly cool on the hand.
...	...	...	...	Clot again formed. In adjusting the instrument again, the blood from the artery was noticed not to be very florid.

Time.	Mercury. Mean.	Pulse.	Resp.	Remarks.
P.M.				
4.26′ 20	2.8			
4.27′ 10	2.6			
4.27′ 30	2.8	156		
4.31′ 20	...	...	...	Injected extract of 1 dr. more. Mercury rose ·3 during injection, and then fell down ·4 below former level.
4.32′ 10	2.4			
4.32′ 40	2.4	174	...	Whistling respirations.
4.33′ 40	2.7	...	...	Dog struggling.
4.34′ 40	3.4	156	...	Quiet again.
4.38′ 30	3.	...	12	
4.40′ 10	2.9			
...	3—3.1	175		

At 4.50 the experiment stopped, and dog released from the table at 5 o'clock, the wound having been sewed up. It walked about, but was weak, stiff, and staggering, and almost immediately began to vomit, and did so several times. It died several days afterwards.

Exp. X.—*April* 5.—A large dog was operated on. No chloroform was given, as after I had seen an operation conducted on a dog without chloroform, I concluded that the uneasiness they suffered while getting it was worse than they seemed to experience from the operation. The first incision was made about 11.38, cleaned a part of jugular vein and carotid artery, and inserted the hæmadynamometer. The mean tube of the double instrument having been partly choked, and not working well, I had another made, but not being drawn to a fine enough bore, the mercury oscillated too much in it.

Time.	Mercury. Mx. & Min.	Mean.	Pulse.	Resp	Remarks.
P.M.					
12. 2′ 20	5.5—6.3	5.9–6.2	132	...	Clip restraining blood removed, mercury at once rose.
12. 7′	5.9—6.5	...	...	...	Dog moaning.
12.11′	5.5—6.5	5.9–6.2	134	...	Mercury rises with expiration, falls with inspiration.
12.15′	5.5—6.5	5.8–6.2	...	...	From groaning its respiration is quick.

Time.	Mercury. Mx. & Min.	Mean.	Pulse.	Resp.	Remarks.
P.M.					
12.20′	5.4—6.4	5.9–6.1	...	...	Maximum on a deep inspiration descends to 5, and mean to 5.3
12.24′ 30	5.4—6.4	5.9–6.1	...	...	Jugular vein tied.
12.24′ 50	6. —6.5	...	...	...	Injection of 1 syringe-full of infusion of digitalis completed.
...	5.8—6.4				
12.26′ 30	5.8—6.2	...	140		
12.27′	5.5—6.2	...	120		
12.30′	...	5.9–6.2	86	...	Pulse intermittent.
12.31′	5.6—6.3	5.8–6.2			
12.32′	...	5.9–6.3	78	...	Dog quiet, not moaning.
12.34′	...	5.9–6.3	...	14	
12.35′ 20	5.5—6.5	5.9–6.3	78	...	Oscillating very steadily.
12.38′	...	5.7–6.2			
12.40′	5.5—	5.9–6.2	...	...	Pulse varies from 22–27 in ¼ of a minute, not intermittent.
12.41′	5.5—6.3	5.9–6.1	88		
12.42′	...	...	84	...	For abont 4 or 5 beats it is very slow, and then quick for a few more. Dog has passed some prostatic mucus.
12.45′	5.5—6.3	5.8–6.2	...	...	Mean occasionally descends to 5.6, and then rises. Dog whining and whistling slightly.
12.48′	5.5—6.2	5.7–6.	90	...	Mercury descends on inspiration to 5.4, and next pulsation goes up to 6.2 8-10ths of an inch of oscillation. Then there are several small pulsations of about 3-10ths of an inch oscillation each.
12.51′ 30	...	5.8–6.1			
12.53′ 30	5.5—6	5.5–5.7	104	...	Dog whining. Average oscillation of maximum column is 2-10ths of an inch.
...	...	...	...	20	But dog whining more loudly, and respiration thus disturbed.
12.56′ 15	5.5—6	5.9–6.2			
12.58′	5.5—6	5.5–5.7	100	...	Pulse has continued irregular since that was noted first. Dog quite quiet. Maximum column goes down to 5. on inspiration.
1. 6′ 15	...	5.8–6			
1. 6′ 35	...	5.5	...	...	Injection of 1 syringe-full more.
1. 6′ 50	...	5.5–6.1			
...	5.5—6.4	5.7–6.1			
1. 8′	5.4—6	5.6–5.9	84	...	Maximum occasionally descends to 5. General oscillation is 2-10ths of an inch.

Time.	Mercury. Mx.& Min.	Mean.	Pulse.	Resp.	Remarks.
P.M.					
1. 8′ 30	...	...	...	...	Dog moans loudly.
...	4.8—6	4.9–6	...	...	During long inspiration it descended.
...	5.5—	5.5	...	...	During long expiration.
1.10′	4.5—5	4.8–5	...	...	Dog tries to vomit.
1.11′	...	7.5–7.7	...	...	During vomiting.
1.12′	5.5—6.5	6–6.3	70		
1.13′	5—6.	5.5–5.8			
1.13′ 15	...	5.5–5.7	100		
1.15′	5.	5.	124	...	Pulse regular. Again tries to vomit.
...	5. —5.7	5—5.7			
1.20′	5.3—5.5	5.—5.3	...	...	Mean oscillation of maximum column, $\frac{3}{20}$ths of an inch.
1.25′	5. —5.7	5.3–5.5	112	...	Both tubes occasionally descend to 4.9
1.26′	...	...	..	...	Again vomits.
1.27′ 15	5.5—6.	5.5–5.8	...	...	In ordinary pulsations the oscillations are $\frac{3}{20}$ths of an inch.
1.28′ 15	...	5.3			
1.29′ 15	5.2—5.6	5.3–5.6	116		
1.40′	5.3 – 5.5	5.4–5.5	116		
1.45′ 15	4.5	4.5	...	...	Injected 1 syringe-full more—mercury at once fell.
...	5.5—5.6	5.3–5.6			
1.48′	5. —5.5	4.9–5.5	118		
...	At 5.	5.	...	...	Breathing very rapidly and deeply.
1.50′	4—6	...	...	...	Tries to vomit.
1.50′ 15	...	...	...	...	Again vomits.
1.50′ 30	...	5.—7.			
1.50′ 45	...	5.—6.5			
1.52′	5—6	5.5–5.8	66	...	Oscillation of max. column, after a deep inspiration, is about 1 inch, and then about $\frac{4}{10}$ths each, after.
1.56′	...	...	...	...	No cardiac murmur. Dog whines.
2.13′	...	...	102	...	Dog loosed.
...	...	...	...	...	He walked steadily, and recovered in a few days.

The infusion used in this case was made by infusing 2 drachms of powdered digitalis leaves in 4 oz. of water.

Exp. XI.—*Nov.* 25, 1864.—At 10.12 A.M. I injected 4 milligrammes of digitaline, about 1-16th of a grain, suspended in about 30 minims of distilled water into the subcutaneous cellular tissue of the lumbar region of a Skye terrier. Three minutes after he began to lick the part, and when the injec-

tion was made, showed signs of irritation. In 4¾ minutes he seemed a little confused, and began to lick the corresponding part on the opposite side. In 5 minutes his tongue began to loll out, (which I have hardly ever observed in him before or since), and he continued restless till 7½ minutes, when he lay down, his breathing being rather hurried, and his tongue still out. In another minute he rose, and sat apparently intently listening, and as there was no particular sound at the time, I thought this probably indicated ringing in his ears. With the exception of some restlessness he seemed well till 25′ after the injection, when he sat down panting and lolling his tongue, as if he had had a smart run, though he had made no particular exertion to account for this. Soon after he seemed quite in his usual, and was none the worse.

Exp. XII.—*Dec.* 12.—A mongrel dog had some blood drawn from one jugular for examination, about the 6th, and on the 9th, one of its carotids was exposed and the hæmadynamometer applied under chloroform, but clots formed immediately, and the experiment was abandoned. On the 12th, the dog was very weak.

At 2.5′ P.M., I began to inject ½ a grain (from memory) of digitaline in water into the subcutaneous cellular tissue in the lumbar region.

2.12′ Injection finished. The dog seemed uneasy and lay down.

2.16′ Till now, he has been rising, turning round, and lying down again constantly. He now seems unable to stand well—grumbles.

2.17′ 30 Up again, grumbles, shakes his head listlessly about, seems uneasy.

2.18′ Seems inclined to vomit.

2.19′ Shakes his head and licks his foot.

2.20′ Paws his bed.

2.21′ Opens and shuts jaws.

2.23′ Sits up. The light is shining in his eyes, and his pupils are much contracted. Seems livelier. Shakes his head and paws his bed. I was then called away, and returned at 2.35′

2.35′ Dog lying quite still, but there is a tremor all over and twitchings of the subcutaneous muscle of limbs, causing the movement of skin to be distinctly visible, but causing no movement of the limb. Breathing slow and laboured. Respirations are 8 in 65 seconds.

2.43′ Pulse 30 per minute, 2 or 3 beats coming close together during inspiration and expiration, and then an interval of 4 seconds between the beats as well as one of exactly the

same length between the end of one respiration and the beginning of another.

2.55′ Much the same—grumbling.

3. I now had to go to a class, and did not see the dog again till I returned at 5.30′. The dog was then stiff and cold. The tongue was protruded at the side of the mouth; the jaws shut; saliva on the chops; some prostatic mucus at the orifice of the urethra (not examined microscopically). Post-mortem.—Lungs were of a light pink colour, much collapsed. Vena cava and venous system generally, full of black blood, and very turgid. Right auricle and ventricle distended with black blood, which was somewhat curdled—not in firm clots. Left side of heart natural in colour; contained a little blood, also somewhat curdled. Liver congested. Gall-bladder distended. Bladder firmly contracted, and empty.

EXP. XIII.—*Jan.* 16.—A small English terrier, very thin, was taken for experiment.

2.29′ P.M.—The dog was shivering; the heart sounds normal in character, but altered in rhythm, being very slow between the rigors, but during their continuance the beats were very rapid. The shiverings lasting each for about 4 seconds, and the interval about 1 minute. There was no murmur with the cardiac sounds. In the back room in which the dog had been kept, there was a bag of digitalis leaves on which it had lain, and a good many were scattered on the floor, so that the dog may have taken some along with its food before, and this possibly may have been the cause of the curious rhythm of the heart, and of the shiverings.

2.36′ P.M.—I injected ½ a grain of digitaline suspended in rather less than 1 oz. of water into the cellular tissue at the side of the lumbar vertebra.

2.37′ 15.—The dog suddenly started up, and ran to the end of his tether.

2.37′ 40.—Sat down on haunches. 2.38′ 30.—Rose again. 2.39′.—Straddles and whimpers, and jumps about. In attitude of attention; then runs about, and again stands, apparently listening intently.

4.40′ 20.—Whines and licks the place where the injection was made. On being loosed he shook himself, ran off, and sat down. Was restless, and seemed thirsty, so I gave him some water.

2.50′.—Heart sounds as before. 3.30′.—As before; no murmur.

3.50′.—Vomiting. 4.—Purging. 4.10′.—Vomiting. 4.20′.—Again vomiting, and again at 5.30′. I then left for the night.

On the following day (the 17th) the dog lay curled up on the floor for the greatest part of the day, but could stand or walk. At 5.35′ P.M. the dog had refused food, so to kill it at once I poured into its mouth some alcoholic solution of extract of digitalis, most of which it swallowed. 5.37′.—The dog vomited some white mucus, then lay quite quiet. 5.40′.—Again vomiting. 5.44′.—Seems livelier. 5.45′.—Again vomiting. 5.46′.—Purging.

On the 18th, at 10 A.M., the dog was lying curled up; it rose once or twice, but with some difficulty, and straddled very much when standing. Gait tottering and unsteady. 10.30′.—Struggles in vain to rise. Progresses along the floor, partly on its side and partly on its belly. Ineffectual efforts to rise. Heart's action very weak, but seems more regular. Surface cold. Respirations 7¼ per minute. Pupils contracted. The dog lay so, occasionally making slight vain efforts to rise for about an hour more, and then till 3.20′ P.M. it lay as if quite dead, only very feeble respiration being seen, and the eyelids contracting when the finger touched one of them or the cornea. The caruncula lachrymalis covered almost one-fourth of the eye. At 3.20′ it was lying as if quite dead; the surface quite cold; the limbs flaccid; and the pulse inappreciable when it gave one or two yawns. At 3.23′ it gave a short, weak, low howl, and immediately after the cornea was found insensible. Post-mortem was made between five and ten minutes after death. On opening the body, a small quantity of urine trickled from the urethra, probably from pressure on the bladder, which was quite full. The lungs were of a natural colour. The heart was well filled with blood in both cavities. The venous system turgid. The heart contracted readily on irritation. At 4 P.M. the dissection was interrupted. It was resumed at 5 7′. The pericardium, when opened, contained a small quantity of serum, about one or two drachms. The heart still showed signs of contractility. At 4 P.M., the diaphragm contracted readily on irritation of the phrenic nerve; the œsophagus and thoracic duct contracted on pinching them.

Jan. 26.—One centigramme of digitaline was injected into the cellular tissue of the loins of a rabbit. It produced no apparent effect.

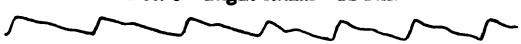
SPHYGMOGRAPHIC TRACINGS.

The following are fac-similes of sphygmographic tracings of my own pulse, taken from 6th December 1865 to 24th March 1866 :—

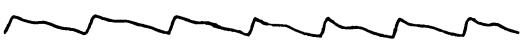
1865—Dec. 6—10.45 P.M.

Dec. 8—Right radial—12.35 midnight.

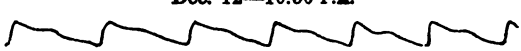
Dec. 9—Right radial—11 P.M.



Dec. 11—10.40 P.M.



Dec. 12—10.30 P.M.



Dec. 13.

Dec. 14—9.45 P.M.

Dec. 15—12 midnight.

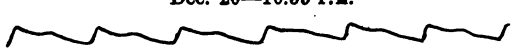
Dec. 16—11.10 P.M. Pulse 75.

Dec. 18—11 P.M.

Dec. 19—11 P.M.

Dec. 20—10.35 P.M.

1



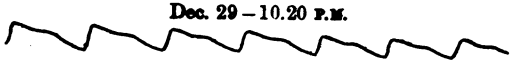
2

(1.) Not tied very tightly; (2.) Tied very tightly on the arm.

Dec. 21—10.50 P.M.

Dec. 28—10.40 P.M.

Dec. 29—10.20 P.M.



Dec 30—10 P.M.

1866—Jan. 1—11 P.M.

Jan. 2—1.5 at night.

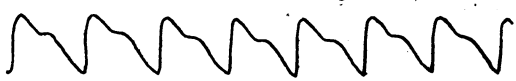
Jan. 3—11 P.M.

Jan. 4—10.45 P.M.

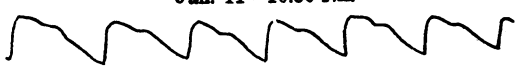
Jan. 5.—1-2 at night.

Jan. 9—11 P.M.

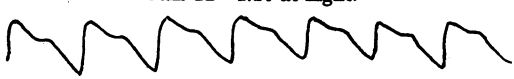
Jan. 10—11 P.M. Had had a little exercise just a few minutes before.



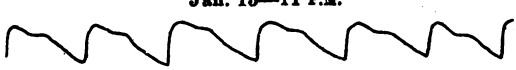
Jan. 11—10.30 P.M.



Jan. 12—1.10 at night.



Jan. 13—11 P.M.



Jan. 15—10–11 P.M.

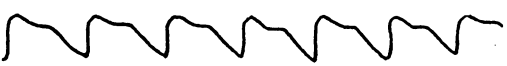
Jan. 16—10–11 P.M. Pulse 80.

Jan. 17—10.20 P.M. Pulse 82.

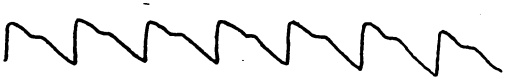
Jan. 19—12.45 midnight.

Jan. 20—10.20 P.M. Pulse 80.

Jan. 22—10 P.M.



Jan. 23—10–11 P.M.



Jan. 24—10.55 P.M.

Jan. 25—10.17 P.M.

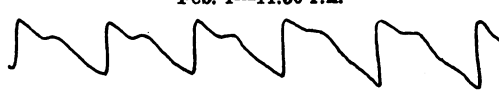
Jan. 26—12.18 midnight.

Jan. 27—11.27 P.M.

Jan. 29—11.15 P.M.

Jan. 31—10.37 P.M.

Feb. 1—11.30 P.M.



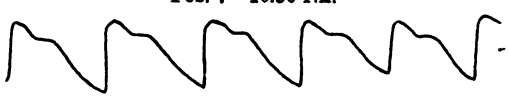
Feb. 2—1 at night.

Feb. 3—11.30 P.M.

Feb. 5—10.25 P.M.

Feb. 6—10.50 P.M.

Feb. 7—10.50 P.M.



Feb. 10—about 12 P.M.

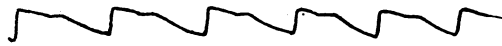
Feb. 17—10.50 P.M.

Feb. 19—10.30 P.M.

Feb. 20—11 P.M.

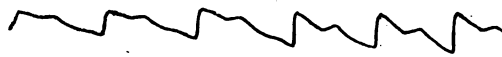
Feb. 21—11.30 P.M. Sphygmograph not so tightly tied in No. 2 as in No. 1.

1



2

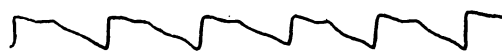
Feb. 22—11 P.M.



Feb. 23—1 at night.

Feb. 24—11.20 P.M.

Feb. 26—11.30 P.M.



Feb. 27—12.30 midnight.

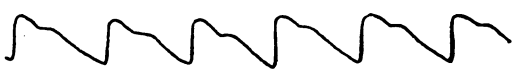
Feb. 28—10.30 P.M.

March 1—1 at night.

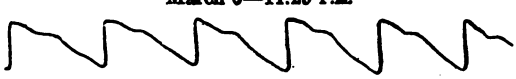
March 2—1 at night.

March 3—11 P.M.

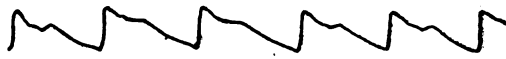
March 5—11 P.M.



March 6—11.25 P.M.



March 7—11.30 P.M.



March 8—11.30 P.M.

March 9—11.50 P.M.

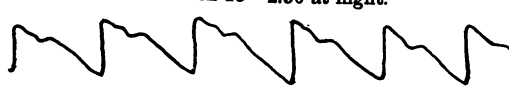
March 10—11.15 & 11.30 P.M. No. 1—11.15 P.M. The sphygmograph not so tightly tied as in No. 2.

1

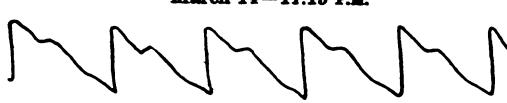
2

March 12—11.45 P.M.

March 13—2.50 at night.



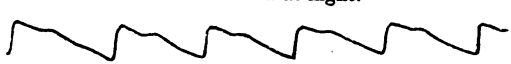
March 14—11.15 P.M.



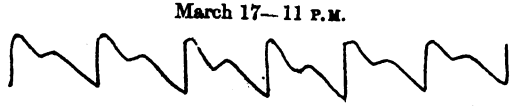
March 15—11.20 P.M.

March 16—5 A.M.

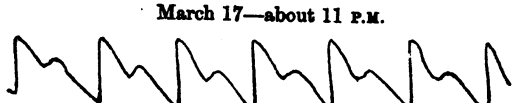
March 16—1 at night.



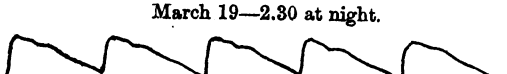
March 17—11 P.M.



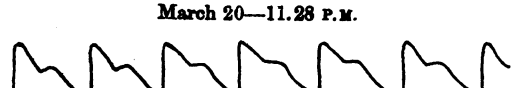
March 17—about 11 P.M.



March 19—2.30 at night.



March 20—11.28 P.M.



March 23—12 midnight.

March 24—10.40 P.M.

March 24—10.40 P.M.

LORIMER AND GILLIES, PRINTERS, EDINBURGH.