Induline is also a new aniline colour, and may be used as above. It is a dark powder, and gives an agreeable pale bluish-purple stain; and, if used after carmine or picrocarmine, the cell body and intercellular substance will be preferred by the induline, and the nuclei and connective fibres by the others. It dissolves in warm water or dilute alcohol. Maroon, phosphine, and cerise are new to histology.

Treble Staining.—Methylanilin violet, and iodine, malachite or methyl green, combined, give beautiful results. I first worked with aqueous solutions, which yielded good preparations, but now use an alcoholic mixture in the following way. Make a saturated solution of violet in strong alcohol, and filter. Do the same with the green, leaving some granules in excess at the bottom of the vessel; this solution is a greenish-blue. Filter and add the violet solution to it, drop by drop, till the mixture is the colour of Prussian blue, which soon occurs. If a large quantity be made for future use, add a little strong carbolic acid solution, about three drops per ounce of the solution, to prevent decomposition, and to retard the acetic change in the alcohol, which would soon spoil the dye. Filter about twenty drops into a watch glass, and dilute with spirit, and immerse sections for five to ten minutes; wash off excess in ordinary water, or better, drain off on filter paper, and set in saturated solution of acetate of potash, and mount in a mixture of equal parts of pure glycerine and acetate of potash. This gives good preparations for several weeks; but the dyes may be fixed by placing the sections, for three to five minutes, in a mixture of equal parts of a saturated aqueous solution of tannin, to which a little carbolic acid has been added, and distilled water. Then wash in water, and transfer, for the same time, to a mixture of rather more than one part of tartar emetic, (potassio-tartrate of antimony), and rest distilled water; wash, and put in strong pure methylated spirit for five to ten minutes; draw off excess of spirit on filter paper, and put for five minutes in oil of cajuput, cloves, juniper, aniseed, or turpentine, and mount—after drawing off excess of oil—in Canada balsam or dammar. The tannin and antimony solutions should be filtered into a watch glass before using, as also should be the dyes. Preparations hardened in spirit, or Müller's fluid, answer best; but chromic hardened sections will do, if previously soaked for twenty to thirty minutes in methylated spirit. One part of a saturated aqueous solution of xanthate of soda, and one of distilled water, will partly fix violet for passing through spirit and clarifying oil, if this be done quickly; but I have not found it to answer so well as the tannin and antimony. The xanthate solution is yellow, and has an odour of decomposing cheese. If this process be successfully carried out, and I have not found it to fail if the steps be carefully executed, very striking results are obtained. Connective and elastic tissues and cell protoplasm are stained violet; nuclei, nucleoli, young cells, and leucocytes are greenish-blue. The nuclei of unstripped muscle-fibres, and the nuclei of the sarcolemma of striped fibres, are blue; blood is rusty brown. The young cells of tumours, especially cancer and sarcoma, are greenish-blue, thus producing a treble stain—violet, blue, and greenish-blue. Sections of lymphatic glands are very pretty, the leucocytes being blue, and the rest violet; and, if tumour cells be present, they are greenish-blue, and readily made out. I have observed that some cells have an intermediate tint, due probably to their protoplasm having commenced to undergo the cancerous change.

Double Staining.—Roseine and green, fixed as above, have given me very satisfactory preparations in sections of tumours, the former selecting the stroma, and the latter the nuclei, but especially the young cells, some of which are also stained with the roseine. The tannin and carbolic solution, if used rather stronger, will often fix these colours without the antimony; and, in sections of tongue and skin, good results and multiple staining may be obtained by first staining in Itanvier's picrocarmine, and putting sections at once in the tannin fluid, then in roseine, and in the tannin again before and after the green; then draw off excess of green on filter-paper, and pass through the antimony, and wash before placing in methylated spirit. Staining in picrocarmine, and passing the sections at once into a mixture of iodine and malachite green, gives multiple staining in several tissues, if the dyes be fixed as above.

To prevent disappointment, I must point out that often sections which look pale by daylight (especially the violet and green preparations) are very clear by artificial light if the illumination be good. I think this is due to the combination of the red and yellow rays of the light with the stained elements of the tissue, and also to the fowness of the violet rays in ordinary oil lamplight, and in gaslight.

Other agents will partially or completely fix some of the anilines, such as arsenious, acetic, hydrochloric, and carbolic acids; hypophosphite of soda, stannate of soda, and silicate of soda, to which a

little hydrochloric acid has been added, and should these be tried in special cases. Acids extract aniline blues, and acetic acid has the same effect on violet, but gives good temporary preparations. Saturated aqueous solution of acetate of potash fixes roseine, saffranine, soluble blue, and partly fixes fuchsine, when these colours are used alone, so that they can be passed through spirit and clove-oil. I have found that dilute aqueous solutions of induline, methyl green, and rosins, stand spirit and absolute alcohol without fixing, if used alone.

Dahlia, which is monophenylosanilin, and some of the other violets, are very serviceable in dyeing the connective substances, as they distinguish the plasma cells from the ordinary connective tissue-cells, rather more clearly than the other anilines; the bodies of the cells are stained a pale violet, and nuclei darkly, while the plasma-cell body is dark violet, and nucleus remains clear. As the violets do not, in weak solutions, stain the intercellular substance, they may usefully be combined with some dyo that does, such as French archil, murexide, phosphine, picrocarmine, rosine, etc.

Erythrosin, or rosin and green, give a very effective double stain. The following proportions make a good staining fluid. Erythrosin or red eosin, one part (there are a yellow and blue shades of eosin as well); iodine, methyl, or malachite green, sixty parts, dissolved in thirty per cent. solution of warm alcohol. The epithelial nuclei are a bluish violet, the connective nuclei greenish blue, and cell-body and stroma of tumours red.

If sections of skin be stained in methyl green and induline, or *vice versa*, it will be found that the Malpighian layer is stained a greenish blue, the corium cells and nuclei violet red, nuclei of subcutaneous tissue-cells and the nuclei of vessels and nerve-sheaths are rose-colour. Calberla introduced these dyes (*Morph. Jahrbuch*).

By using ordinary water for washing, and strong methylated spirit for dehydrating and passing into the clarifying oil, without putting in absolute alcohol, time, expense, and trouble are saved, and the curling up of large thin sections avoided; further, if in mounting in Canada balsam or dammar, a drop of spirits of turpentine be put on the cover-glass, and this gently lowered on to the sections, no air-bubbles will form. This practical hint is well worth recollecting. In a further communication, I will draw attention to some other methods of dyeing and fixing the dyo in tissues, and in the meantime hope that the above directions will prove of service.

AN EXPERIMENTAL INVESTIGATION OF THE ACTION OF CHLORAL, OPIUM, AND BROMIDE OF POTASSIUM.

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FOR the purpose of lessening nervous and nervo-muscular action, the above three drugs are perhaps the most frequently employed in medicine. From the physiological evidence forthcoming, it would appear that the action of chloral, in therapeutic doses at any rate, is more especially on the cerebrum; that that of opium similarly employed, is likewise more especially on the cerebrum, but to a more marked degree than obtains for chloral, for whilst chloral, in doses sufficient to produce sleep, is of very little value as an analgesic, opium is, of all other drugs, perhaps the most powerful analgesic. Other differences are to be found. Thus, both drugs threaten by their depressant action on the centres at the base of the brain; but the dangerous paralytic stage is, with opium, preceded by a well-marked stage of stimulation of those centres, as indicated by the slow and full action of the heart and respiration, and the strongly contracted pupils, during the second stage of opium poisoning. A similar stage of stimulation is held to occur with chloral, but it is much less marked. Opium, again, has a marked effect on the centres of the spinal cord, at least in the lower animals, as is seen best in the frog, in which convulsions precede paralysis; these convulsions having been shown by Kölliker to be of spinal origin. With regard to the peripheral structures, both opium and chloral are stated to be without effect on motor nerve or muscular tissue; though with reference to opium the evidence is somewhat conflicting.

Passing to the bromide of potassium, the physiological evidence would show that this salt acts powerfully on all parts of the nervous system, both central and peripheral nervous structures; but that the central nervous system, brain and spinal cord, is more rapidly and deeply affected than the peripheral structures, nerve and muscle.

The action on all these tissues is depressant, paralytant; it is not, however, characteristic of potassium bromide alone, but holds for potassium salts generally, and must be described as a potassium effect.

With reference to the action of these three drugs on the heart, this organ is found arrested in diastole after systemic death, and this in the case of each. The evidence as to the mode of arrest by chloral is conflicting, Rajewsky stating that the arrest is quite independent of the inhibitory nerves, whilst the experiments of Labbé would lead to the inference that chloral influenced the heart through the centres at the base of the brain. Labbé further states that when powdered chloral is placed on the heart of the frog, there results a marked slowing, but no arrest of its action.*

Opium would appear to influence the heart's action very strongly through the vagi, but, in addition, Gscheidlen states that the intrinsic motor ganglia of the heart are first stimulated, then paralysed (*op. cit.*, p. 220).

Potassium bromide and potassium salts generally have been clearly shown to exert a direct paralyzing action on the heart.

Thus, then, chloral arrest is doubtfully of intra- or extra-cardiac origin, but it is not muscular. Opium, apart from its extra-cardiac action, affects the heart directly, but a stage of stimulation precedes the stage of paralysis. Bromide of potassium, as a potassium salt, is a direct cardiac paralytant, without apparently any preceding stage of stimulation.

This being so, it became of interest to attack the simpler problem of the action of these three drugs on the isolated frog-heart, or rather on the ventricle of the frog-heart. Such apparatus, after a longer or shorter interval following its removal from the body, begins to beat spontaneously and rhythmically, and accordingly its action may suffer modification in these two directions, viz., of contractility and of rhythm. The former is clearly muscular in its nature, the latter is more probably nervous in character.

Mode of Experimentation.—The ventricle was secured to the double cannula of a Roy's apparatus by means of a ligature, tied as nearly as possible in the auriculo-ventricular groove. The blood mixture with which the heart was fed, consisted of a solution of four grammes of dried bullock's blood in 100 c.c. of a saline solution (this latter consisted of five parts saline solution 0.6 per cent., and two parts of water). In each experiment, 100 c.c. of the blood-mixture were taken.

The contractions of the ventricle were recorded by means of a lever on the blackened surface of a revolving cylinder. At regular intervals of time, each quarter revolution of the cylinder (about two minutes), the drug was added to the whole mass of blood. The dosage was kept uniform, and was such as previous experiment had found necessary to stop the heart within about an hour. The common English frog (*rana temporaria*) was throughout employed. The experiments were performed during the month of October 1882. For the purpose of stimulating the heart, break shocks alone were employed.

Chloral Hydrate.—The strength of the solution employed was 10 per cent.; the reaction to test-paper was faintly acid.

The heart was arrested in diastole. The following table gives the quantities of the drug required in each experiment to effect this arrest:

				Quantity.
October 2nd,	temperature of room 16° C.,	solution strength 10%,		5.2 c.c.
" 2nd,	" "	" "	" "	4.2 c.c.
" 3rd,	" "	" "	" "	4.5 c.c.
" 4th,	" "	17° C.,	" "	4.8 c.c.
" 5th,	" "	16° C.,	" "	4.5 c.c.
" 5th,	" "	17° C.,	" "	4.5 c.c.
				27.7 c.c.

Average quantity = 4.6 c.c. = 0.46 grammes = 7.09 grains.

With regard to inhibition, the frequency of the spontaneous contractions lessened in every instance under the influence of the drug; this effect appeared early, and, in the majority of the cases, it amounted, practically, to a complete inhibition of spontaneous contraction in the end stages.

The contractile power of the muscular tissue was also affected. This effect was manifest, subsequently to inhibition, in the lessening height of the contractions caused by stimulation. When the full amount of the drug had been added, contractility was completely, or all but completely abolished. Reduction of contractility

was not preceded by a stage of stimulation, i.e., of increased action, the height of the trace lessening from the very outset. The breadth of the trace, i.e., the duration of the beat, increased somewhat during the later stages, as compared with the duration of the beat at the start. The period of latency was increased, but not to any marked extent. The state of diminished excitability of the muscular tissue, which invariably attends the stage of active contraction, was lessened in duration under the influence of chloral.*

The excitability of the heart for a rapid and prolonged succession of shocks (e.g., for continuous faradisation) lessens, however, under the influence of chloral; and the fusion of beats which such continuous faradisation may be made to effect with the normal heart, gradually disappears for the heart poisoned with chloral. From the statement preceding this last as to the effect on the "period of diminished excitability," it might have been expected that continuous faradisation would yield a completer fusion instead of a less complete. Whatever be the explanation, whether the effect of exhaustion be a factor or not, the facts are as stated. It must be borne in mind, however, that the continuous faradisation which the hammer of the induction apparatus allows, represents a rapid succession of shocks, and also that both make and break shocks alternate in such, i.e., shocks differing not only in strength but also in direction. In testing the effect on the period of diminished excitability, break shocks alone were employed.

A feature in the action of chloral yet remains to be noted. If, after contractility has been considerably lessened—i.e., the height of the trace has been much diminished—a stimulus be thrown in, and then, at the moment of completed systole, another stimulus be made to follow, the muscular tissue will respond to this second stimulus by a further contraction, starting from the condition of systole as from a condition of rest. A third or fourth stimulus, thus placed, will often similarly be effectual, and the trace mounts up, staircase fashion, till at times the original height of beat is almost recovered. This "piling" or "mounting up," as the phenomenon will be subsequently referred to as, was constant for chloral, and occurred up to the very end or close on this—i.e., so long as contractility persisted; it was, however, best marked in the middle stage, or just subsequent to this.

The chloral experiments were completed by observations on the effect of dilution. In four out of the six cases, when the poisoning was complete, the poisoned blood was replaced by the original quantity, 100 c.c. of fresh blood. In one case, no recovery occurred after two and a half revolutions of the cylinder (about twenty minutes) had been allowed to pass; in another, there was a mere trace of recovery after a similar period; in another, after a like time, but faint recovery; in the fourth, after close on three rounds, but very faint recovery. In all these cases, the circulation of the blood mixture was rapid, so that the tissue was thoroughly washed out with the circulating fluid.

To sum up shortly the chloral effects, we find that the cardiac tissue is directly affected by the drug, and that the ultimate expression of this action is diastolic arrest; that, preceding this event, the action of the drug is manifested by the slowing or complete arrest of the heart's beats; and that, simultaneously with this, but independently of it, the contractile power of the muscle-substance is affected, down to complete extinction. This depressant action sets in at once; there is no primary stage of stimulation. Limiting, now, the consideration to a single contraction, we find that the period of latency grows, but not to any marked extent; but that the "period of diminished excitability", attendant on the stage of active contraction, lessens under the influence of chloral; and, therefore, that, in a sense, the muscle is rendered more irritable—a condition analogous, perhaps, to that spoken of clinically as irritable weakness. It is true, the effect of continuous faradisation does not seem quite in accordance with this; but this latter is evidently a more complex phenomenon, and, therefore, less decisive on this point. The phenomenon of "piling up" must further be remembered, as it will serve as a point of contrast.

Hydrochlorate of Morphia.—A five per cent. solution was employed; it gave a neutral reaction to test-paper.

The heart was arrested in diastole.

* See Wood's *Therapeutics*, p. 336. For a general physiological consideration of these three drugs, and for references as to the experimental work done, consult the same author under the headings, Opium, Chloral, Bromide of Potassium, and potassium salts generally.

* This, perhaps, requires further explanation. Contractile tissue generally is, during the stage of active contraction, relatively insusceptible of stimulation, i.e., of responding to further excitation by contraction. This state of diminished excitability attends, of course, the ventricular contraction, and it has a definite duration. Drugs are capable of lessening, or of increasing, the duration of this period. Thus, potassium chloride increases this period, as does also ammonium chloride in the later stages, sodium chloride, on the other hand, lessens somewhat the period.

The following table gives the quantities used in effecting this :

	Quantity.
October 18th, temp. of room 17° C., solution strength 5%, 14.0 c.c.	
" 19th, " 17° C., " " 18.0 c.c.	
" 19th, " 17.5° C., " " 14.0 c.c.	
" 20th, " 18° C., " " 15.0 c.c.	
" 20th, " 17.5° C., " " 12.0 c.c.	
" 21st, " 16° C., " " 14.0 c.c.	
	85.0 c.c.

Average quantity = 14.16 c.c. = 0.708 grammes = 10.92 grains.

The effect on spontaneous action was, as compared with chloral, but slightly marked; in the end stages, the beats grew much less frequent, it is true, but, on the whole, the effect was but slight.

The contractile power of the muscular tissue was ultimately abolished; but, in this process, two points are noteworthy. The first, that it was not till the later stages that this effect became pronounced: thus, with an average toxic dose of 14.16 c.c., the effect on the height of the trace was not marked till 9 c.c., or more, had been added, the subsequent effect being frequently somewhat sudden; the second, that a primary stage of increased force of beat preceded the decline. With a ventricle emptying itself at the start, it is not possible to show this, since, though it empty itself more rapidly and more forcibly, it still does not do more than empty itself, and the height of the trace remains unaltered. It was possible, however, in some of the cases, where contraction was not to the full at the commencement, to demonstrate a distinct, though slight, increase in the height of the beat.

The duration of the beat was in every case increased, and the increased breadth of trace was a constant and early manifestation; it, as a rule, went on increasing somewhat up to the very end.

The period of latency was very greatly increased, and this before any notable effect on the height of the trace was observable. In like manner, the "period of diminished excitability" was very considerably increased, and this also whilst the height of the trace was apparently unaffected. The effect of continuous faradisation was quite in accordance with these results, the excitability, or readiness of the heart to respond to this mode of stimulation, lessening markedly as the dose of morphia increased.

In contradistinction to the chloral phenomenon of "piling up," no such effect was witnessed with morphia; indeed, the excitability of the muscle was so much lowered, that a stimulus thrown in at the moment of completed systole was quite ineffectual. This lowered excitability extended, moreover, to the period of diastole, and even beyond this to a greater or less extent into the period of pause; so that, when the toxic effect was well marked, a stimulus thrown in early, after a contraction had been completed, remained without effect. A yet more interesting phenomenon was observed, viz., that if, subsequent to a preceding contraction, such early stimulation did cause response, this was comparatively feeble; whilst, after the lapse of a longer interval, the same stimulus caused full contraction. Normally, *i.e.*, with the undrugged heart, a stimulus, if not effective during the period of systole, is effective during a part, if not the whole, of the period of diastole; and, during any part of the pause following a contraction, an effective stimulus will always yield a full contraction; but here, under the influence of morphia, we see that the change, whatever its nature, occurring when the phenomenon of contractility is manifested, is one requiring the element *time* for a change in an opposite direction, *i.e.*, for the restoration of the state preceding the moment of contraction. Normally, then, the processes of change and counterchange are too rapid to admit of demonstration; but in morphia we have a drug which, by lengthening out the process of counterchange, enables us to demonstrate the existence of these processes.

With regard to the effects of dilution, in two cases good recovery followed replacement of the poisoned blood by 100 c.c. fresh blood; the recovery was, however, a slow one as compared, for instance, with the rapid recovery which is observed when a heart poisoned with a potassium salt is washed out with fresh blood-mixture. In one case, simple dilution of the poisoned fluid with an equal bulk of saline, 0.75 per cent. yielded fair recovery, but the recovery here was likewise very slow, requiring about twenty minutes. Of the two cases where fresh blood was substituted for the poisoned, in one, faint recovery occurred at the end of one revolution of the cylinder (8 to 9 minutes); at the end of another revolution, the contractions were good. In the other case, dilution was first tried, and this being ineffectual, substitution was made; in about 10 to 11 minutes from the moment of substitution, there was good recovery.

[To be continued.]

NOTES ON A CASE OF FORCIBLE REMOVAL OF THE UTERUS.

By LEONARD CANE, M.D.Lond., B.S.

A NOTE in the JOURNAL (page 389) draws attention to a case which occurred in 1845, where the uterus, the lower part of the small intestines, and the greater part of the large intestine were torn away at a labour. The notes of the following case, where the uterus with some of its appendages was torn away by a midwife, may be interesting.

Mrs. B., aged 29, in delicate health, had her first child about five years ago; the infant was healthy. Then she had two miscarriages, probably due to syphilis; then, about two years ago, a living child, which showed signs of syphilis. She was expecting her confinement about the end of November. On October 26th, 1882, I was sent for to see the patient, who lived about four miles in the country. She stated that, without any known cause, she was suddenly taken with "labour-pains," and had a great deal of "loss." The pains had ceased when I saw her, and she was about the house, but stated that there was still some hæmorrhage going on. On examination, I found the os uteri sufficiently open to admit the tip of the forefinger, and there was a slight amount of hæmorrhage going on. There being no signs of imminent labour, and as she did not expect to be confined for a month, I gave an opiate, told her to remain quiet, and to send at once if anything came on. On October 28th (two days afterwards) I received a message that Mrs. B. died during the night, and that only a neighbour and the village midwife were present. I went to the place, calling upon the midwife on my way to learn particulars. She said that she found Mrs. B. fainting, and with great loss, that the child was born when she got there, but that there was a "false conception," which came away after the child.

I then proceeded to the patient's house, and saw the woman who was present. She told me that, after my visit, on the 26th, the loss stopped, and that, though Mrs. B. seemed very faint and weak, there appeared to be nothing wrong with her. About midnight on the 27th, severe labour-pains came on, and, before she could get any one there, the child was born. There was no one in the house at the time, but she sent the husband as soon as possible for the midwife. She would say nothing further than that soon after the arrival of the midwife, Mrs. B. died suddenly. Mr. Beecroft, a retired surgeon living in the village, was sent for by the midwife, but he did not arrive until after Mrs. B.'s death.

The woman had saved the "after-birth, and what came away with it." On examining this I found, in a basin full of blood and water, the placenta, which was much broken up on its uterine (attached) surface, and had apparently been torn on removal. Besides this there was a substance which proved to be the inverted uterus. On re-inverting this, the whole uterus was found to be torn away, the rupture passing through the vaginal wall in front, about an inch from its reflexion on to the cervix uteri. Behind, it was torn away at the reflexion of the peritoneum from the uterine walls. The broad ligaments were torn, the rupture passing through one ovary, the other ovary was still attached to the uterus. The uterus appeared to be healthy, whilst the ovaries were normal. The inner surface of the uterus, from which the placenta had been detached, was ragged, and small portions of the placenta were still adherent. Unfortunately, the specimen was not preserved.

With the assistance of Dr. W. E. Paley, and Dr. Kirkwood, I made a *post mortem* examination of the body on October 30th. The remainder of the left ovary was in its proper place, the organ being torn in halves. On its surface was a small adherent blood-clot. The uterus, with the rest of its appendages was missing. Nothing else abnormal was found.

The history obtained from the two women at the inquest was very unsatisfactory, and nothing further could be learnt from either of them. They denied using much force, and would say nothing about anything coming after the child. The midwife stated that Mrs. B. was fainting when she arrived; that she cut the cord, took away the child and removed the after-birth, which came away quite easily.

An open verdict was returned.

In addition to the case mentioned in the JOURNAL, Neale's *Digest* (1868-1) mentions two other cases, to be found in the *British and Foreign Med.-Chir. Review*, vol. i, 1856, p. 535, and in the *Medical Times and Gazette*, vol. ii, 1863, p. 728.