and chronic inflammation. But really this was precisely as he (Mr Hutchinson) had stated the facts. A disease which clinically ran a more or less malignant course showed to the microscope only inflammation products. Whether the disease was called a local cancer or not, depended entirely upon whether a histological or a clinical definition of cancer was adopted. Dr. Coupland had suggested that, when recurrences of cancer after operation were delayed for very long periods, they still did not prove anything more than local origin, since the germinal plasma might possibly remain long latent. This was probably true, but there need be no anxiety on the part of the advocate of the local origin to adopt it to the exclusion of that of separate and spontaneous production. No doubt, constitutional tendency was, in some persons, of considerable strength; and this, together with the abundance of local causes, might well explain occasional multiplicity of new growths, whether simultaneous or after long intervals. He recollected the case of a lady for whom many years ago he excised an eye, on account of melanotic sarcoma. She remained well eight years, and then died of epithelial carcinoma of the vagina and uterus. He did not regard it as an instance of dormant cells, but rather of independent production of a second growth. When the disease, after a long interval, reappeared in the original site, or in the proximal lymphatic glands, then probably Dr. Coupland's suggestion would be the correct one.

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

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(Continued from page 153.)

Extract of Opium.—The experiments with this preparation may be more cursorily given; for, in the main, the results obtained were similar to those which the morphia gave. A 10 per cent. solution of the watery extract was employed. The quantities required to arrest the heart in diastole gave, for the six experiments, an average of 3.26 c.c.; whilst the 5 per cent. solution of the hydrochlorate of morphia, it will be remembered, gave 14.16 c.c. as the average toxic dose. This, of course, would make the opium rather more than twice as poisonous as the morphia. There can, however, be little doubt but that this discrepancy is due to the extract of opium solution being acid, for in an even very feebly acid solution, the ventricle ceases to beat. The quantity table hence loses its value; and, indeed, the qualitative results are vitiated from the same cause, although, with the exception that inhibition was more marked than with morphia, the agreement was tolerably close; thus latent period and "period of diminished excitability" were similarly affected; the behaviour to continuous faradisation was likewise similar; and the results, both of dilution of the poisoned fluid and of substitution of the same by fresh blood, were also similar. The "exhaustion" or "recovery" effect described under morphia was exceedingly well shown, much more perfectly than in the case of morphia; and it was possible, by placing the stimuli, to get either a descending or ascending staircase of contractions.

There remains for description the bromide of potassium. The experiments with this drug were made about ten to twelve months previously, and the results given in a paper in the *Medico-Chir. Trans.* for 1882, from which the following is taken.

The heart is arrested in diastole. The average quantity requisite for this was 2.13 c.c. of a ten per cent. solution; this is equivalent to 0.213 grammes of the salt, or 3.28 grains. Inhibition, though less marked than with chloride and iodide of potassium, is still a characteristic feature. Contractility is diminished from the outset, no stage of stimulation preceding; in the end, there is complete abolition of the power to contract. The duration of the contraction is not increased; on the contrary, a pointing of the apex of the trace occurs; this is uniformly the case with potassium salts.

Experiments subsequent to those above mentioned have shown that the "period of latency" is considerably increased, as also is

the "period of diminished excitability." The excitability for continuous faradisation is lessened for bromide of potassium, as it is for the other potassium salts examined (*op. cit.*).

Dilution of the circulating poisoned fluid with an equal volume of fresh blood was tried in three cases with restoration of good spontaneous beats. Replacement with fresh blood would, of course, have been yet more effective.

To discuss the results obtained, we note that, in contradistinction to the somewhat large group of systolic arrestors, these three drugs, chloral, morphia, bromide of potassium, arrest the ventricle in diastole; this, we know, will result from a toxic dose administered to the organism in its entirety; but these experiments show further that these drugs are depressants, when applied directly to the substance of the ventricle; and they demonstrate that, contrary to what one would be led to infer from Labbé's statement, chloral is capable of arresting the isolated ventricle.

The question as to whether the quantitative results here obtained will help us with reference to the toxic dose required for the entire organism, must clearly be answered in the negative. The working of the entire organism is an accurate and delicate adjustment of numerous functions; and, as the strength of the rope is the strength of the weakest part, so the power of resistance of the entire organism is the power of resistance of the most delicate part of the complex structure. The structure of the great nerve-centres is, as a rule, the weakest point, and hence, in general, systemic death results, whilst the peripheral structures still functionate more or less perfectly.

Here, in these experiments, the drug is pushed on to the complete extinction of the peripheral structure, *i.e.*, to a degree beyond, though it is impossible to say by how much beyond, the death point of the entire organism. The curious action of curare in selecting, not the nerve-centres, but the muscle-endings of the motor nerves, shows that it is not always the nerve-centres which first succumb, and stays one from inference as to the relationship of the death-points of central and peripheral structures. Still, much may be learnt from comparative action on a peripheral structure, and, in particular, a definiteness in the results obtained quite impossible else.

Considered thus, we learn, first, the qualitative similarity of action of chloral, morphia, and bromide of potassium; they are depressants, and they are so by inhibition, and by direct diminution of muscular contractility. Compared, we note that, whilst inhibition is a well marked factor for both chloral and bromide of potassium, it is but slight for morphia. Compared further, we note that, for both chloral and bromide of potassium, the action on muscular contractility is depressant from the onset, whilst morphia presents a fairly well marked stage of stimulation, or of heightened muscular contractility, preceding the stage of depression. Further, with reference to morphia, must be noted the really enormous dose required to destroy contractility, *i.e.*, the slight action of the drug on the cardiac tissues. We may here state, moreover, that "contractility" was not appreciably affected till late in the action of the drug, whilst then the decline was rather rapid; in other words, the resisting power was maintained till a considerable percentage dose of the poison was reached. These results are in complete conformity with the statement, previously noted, that morphia affects but slightly the peripheral structures, nerve and muscle; and comparison in respect of quantity will place both chloral and bromide of potassium as far more poisonous to peripheral structures than morphia.

The isolated heart of the frog, we have stated, manifests a twofold activity, *viz.*, contractility and rhythm; chloral and bromide of potassium we find threatening in both of these directions—there is the direct weakening of the contractile power, there is the tendency to inhibit. Is the presumption unlikely that nervo-muscular action generally, which rhythm and contractility may serve to typify, will be similarly affected qualitatively, and that the action of bromide of potassium and of chloral will be generally depressant to nervous and muscular tissues; also that the qualitative relation above seen to hold for the three drugs will apply generally? If so, a more extended inference as to the relative value of the three drugs in question will be possible; but, even if one limit oneself to the consideration of the local cardiac action, it must be evident that a drug such as morphia—which, in the doses employed in medicine, must be practically without local influence on the heart, or which, to a very small extent of this action, must be stimulant rather than depressant in nature—is to be preferred over drugs such as chloral and bromide of potassium, which in their smallest doses appear to be depressant, and which are employed therapeutically in far larger doses than morphia.

Clinically, the dangers of bromide of potassium and of chloral have been recognised; and thus, in our text-books, we find the statements that the presence of grave adynamic symptoms contraindicate chloral and bromide of potassium. Opium, on the other hand, in such adynamic states, frequently appears to lend actual support. The results of definite experiment we find to accord with the results of clinical experience; and the value of the former lies in that they confirm, and by their definiteness must tend to enforce, the teachings of the latter.

The choice of a drug is, however, no simple matter; an advantage here may be outbalanced by a disadvantage there; and practical men may object that they would gladly give opium, but that the disordered stomach, blunted appetite, inactive liver, and torpid intestines, more than outweigh the advantages of opium administration. This clearly is a matter for consideration in the individual case under treatment; and the decision will have to be according as one or other element, asthenia, or derangement of the digestive, etc., powers, is most to be feared.

These objections to opium, on the one hand, and chloral and bromide of potassium, on the other hand, raise the question as to whether, in very many cases, a drug, at present rather extensively used, especially in America, viz., bromide of sodium, might not with advantage be substituted in their place. The salts of sodium generally contrast very markedly with those of potassium; for the chlorides, bromides, and iodides of these two metals, the lowest figure would represent the potassium as ten times as active as the sodium. These precise numbers refer to action on the ventricle of the frog's heart;* but on all hands the evidence is forthcoming that, whilst salts of potassium are very poisonous, those of sodium are very slightly so. One of the marked points of contrast between the two sets of salts is to be found in respect of inhibition; potassium salts inhibit the frog's ventricle strongly, sodium salts scarcely at all. Here, however, we are considering drugs as to their cardiac effect; and, in respect of this, sodium bromide would rank far ahead of bromide of potassium, chloral, or opium, as to innocuousness. The objections holding for opium would not apply here, for sodium salts are generally very little disturbing to the tissues. With these advantages the general verdict of clinical experience is to the efficacy of bromide of sodium as a hypnotic, and, indeed, as a substitute for bromide of potassium; and should this position but be maintained, it is clear that bromide of sodium will be in very many cases the sedative above all others to be selected.

In conclusion, it remains for us to consider briefly one or two points, and to show that the statements with reference to the effect of the drugs on "latent period" and "period of diminished excitability" bear on the question of depressant action. Clearly this is so; for, if a stimulus be longer manifesting itself, this, all other things being equal, corresponds to a lessened or depressed condition of the tissues; and the same applies to the "period of diminished excitability;" for if, *ceteris paribus*, the cardiac muscle is longer recovering from the effects of an antecedent contraction—longer returning to a condition of excitability—that, again, is a form of depressed function. Both of these forms of depressed activity are observed to a very marked degree for morphia; whilst yet spontaneous action may be but little affected, and whilst the height of the contraction may have scarcely appreciably suffered. These morphia effects are very noteworthy; for it would thus appear that certain functions of the tissues may be very profoundly modified, whilst yet others suffer but slightly. They must also be remembered for the sake of contrast with the bromide of potassium and chloral; the former produces effects like those of morphia, but these do not become apparent till the value of the beat has suffered appreciably; the functions of the tissue, at such time, are therefore more profoundly depressed, the vitality is more affected. The opposite effect of chloral on the diminished excitability may be remembered as a point of contrast with the other two salts, if its further meaning be not very apparent. The dilution-experiments are of considerable interest; for, whatever the nature of the changes taking place in the tissues, and constituting toxic action, we perceive that, of the three drugs, chloral is the one from which recovery is least ready, whilst potassium-bromide is that whose effect is most readily removed. The recovery-experiments are those from which we learn most here, for they indicate that the degree of change constituting toxic action in such cases cannot be very profound; indeed, the functions of the tissues at such times are more properly considered as simply suspended: they return

with the restoration of the antecedent conditions. Chemical action, of any degree of intensity or stability, would scarcely be compatible with this ready restoration. The further consideration of this point cannot, however, now be entered on.

A CASE OF RECURRENT HÆMATINURIA.*

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Local Secretary Collective Investigation Committee.

I HAVE the pleasure of bringing before your notice to-day a case which was of great interest to me for some months, and one that is comparatively speaking unusual, and therefore not unworthy of our consideration. It is a case of Recurrent Hæmatinuria, a term perhaps novel, but I think justified by the history and symptoms.

The disease hæmatinuria has been described under various names by different writers on the subject, *e.g.*, Intermittent Hæmatinuria, by Harley and Dickinson; Paroxysmal Hæmatinuria, by Greenhow; Intermittent or Paroxysmal Hæmatinuria by Sir William Gull, Legg, Begbie, and our countryman, William Roberts. The object of the different writers in their nomenclature has been to convey the idea of the presence in the urine of hæmatine or hæmato-globuline; and that occurring paroxysmally or being of an intermittent character, such intermittency varying in the several cases related, from a few hours to a few days. But, in the case I will lay before you, the hæmatinuria only occurred for a few days in every four weeks: so that the term "intermittent" or "paroxysmal" is hardly appropriate, and I have designated it recurrent or remittent, as I think one of those terms conveys the peculiar nature of the case better than the others mentioned.

T. J., aged 10, an intelligent well-developed and healthy looking lad, had been suffering, September 27th, 1877, for some days from a partial suppression of urine, so little being passed that his mother became alarmed, and owing to its continuance called me in. He had slight puffiness of the face, especially under the eyes, no dropsy or swelling of the feet, complained of no pain in the lumbar region, or in fact anywhere; the conjunctivæ were quite clear, and there was nothing icteric in his complexion, and no swelling of or pain over the liver. The urine was high-coloured, and contained albumen to the extent of one-fourth.

The only cause that could be ascribed for the symptoms was, that he had a few days previously got a wetting while sailing some model yachts, a pastime of which he was fond, and, as may be imagined, he often became wet and was repeatedly sitting for hours with wet feet.

As the suppression was the leading symptom, he was ordered to bed; fomentations were applied to the loins, and an effervescent citrate of potash mixture given, with benefit; but, before the kidneys were restored to their normal activity, he was seized on the 29th with convulsions, which, under chloral-hydrate in ten-grain doses, every two hours, were stopped.

On October 5th, his urine became of a very dark colour, almost suddenly, but was voided in natural quantity; and with this he complained of great pain over and around the umbilicus, but none over the loins, even on firm pressure. In three days after this a most extensive crop of petechiæ appeared on the legs and thighs, but not on the body, more marked on the legs and knees than on the thigh, and on the knees being almost scarlet and seemingly coalescing, so that when closely examined they resembled minute arterioles on the skin. After their appearance, the urine began to regain its normal colour, although darker; and subsequently to this return towards the normal state of the urine the petechiæ disappeared, but the pain around the umbilicus continued along with flitting pains in the joints, particularly the shoulders and knees, but unaccompanied by any swelling.

The urine during the attack was of a dark mahogany colour (No. 9 Vogel), was alkaline, of specific gravity 1022, and albuminous to the extent of three-fourths to one-half, and contained, under the microscope, some granular matter, oxalates, and one or two faint granular tube-casts, but no blood-corpuscles. He was given Easton's syrup, in the hope that the iron, by its hæmostatic powers, would prevent

* See *Médecine-Chirurgicale Transactions*, vol. lxx, concerning the action of the salts of potash, soda, and ammonia on the frog's heart.

* Read before the North Wales Branch.