loin, and if I am not mistaken the first one diagnosed as suprarenal growth prior to operation. I refer, of course, to growths in the adrenal itself, not to growths of adrenal origin embedded in the kidney.

REFERENCE.

¹ BRITISH MEDICAL JOURNAL, June 27th, 1908.

SOME EXPERIMENTS WITH IONIC MEDICATION.

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THE subject of ionic medication is so technical as to involve in considerable difficulties those not continually applying it. One source of error that the beginner is very apt to fall into is that of not recollecting which pole should be used to drive in each particular ion: for instance, I recently came across a case in which a surgeon ordered the ionization of cocaine and employed a nurse to do this for him: both he and the nurse agreed that the cocaine should be placed on the negative pole. Now, as basic radicles, including alkaloids, are driven in at the positive pole and acid radicles at the negative pole, the result of this, of course, was that, cocaine hydrochloride being the salt used, no cocaine was driven in at all, but only chlorine ions. Another error is exemplified by a simple experiment which the author has performed upon himself, which can easily be repeated and which will also serve to emphasize some of the essential points of the treatment. A pad of cotton-wool soaked in cocaine hydrochloride was placed on the forearm over a square window cut in a piece of oil silk; this was connected with the positive pole: a similar pad was placed on the other forearm with an oil-silk window of exactly the same size and connected with the negative pole: the size of the window in the oil silk was 3×3 cm., and the current used was from 10 to 15 milliamperes for ten minutes, the time being reckoned after the needle had first reached 10 milliamperes. It was found at the end of this time that the skin in the square area covered by the *positive* pad was completely anaesthetized, while no anaesthesia whatever was obtained beneath the *negative* pad, showing that the cocaine had been introduced from the anode (or positive pole), not from the kathode (or negative pole). Now, anybody who repeats this experiment will find that the anaesthetic effect of cocaine ions so administered is extremely transitory, passes off in a few minutes, and is followed by hyperaesthesia and hyperaemia, which persist for some days and which are succeeded by brown pigmentation. Obviously, therefore, this method is a bad one for local anaesthesia.

A further experiment was performed with cocaine; this drug was first driven in (from the anode, of course) over an area of 2×1 cm. An attempt was then made to extract the cocaine from half this area by covering half the patch and reversing the current, but this was not successful, the reason being either that cocaine is deposited in the tissues in an insoluble form, or else that the ions of sodium, potassium, etc., which abound in the tissues, are extracted in preference to the heavier cocaine ions.

In order to determine as far as possible the path which various ions took when they were introduced into the tissues, a series of experiments was performed on animals.

The method used was as follows: The part to be treated (generally the animal's back) was first of all shaved. After a few days had elapsed to allow any abrasions due to the action of parasites or to minute lesions incidental to shaving to heal thoroughly, the animal was anaesthetized by chloroform or ether. A thick pad of pure cotton-wool was thoroughly wetted with a solution of the salt containing the ion to be tested and a piece of metal gauze connected to the source of current placed over it. The whole was then completely enveloped in a piece of oil-silk in which a window 2×1 cm. had been cut on the side opposite to the gauze, and this window placed against the skin: a similar pad was prepared and connected with the other pole. By this method there was no possibility of

short-circuiting even if the pads touched. In order to obtain uniformity one-twentieth normal solutions were used in all cases, so that they all had the same number of molecules per unit volume, that number being sufficient to provide an adequate supply of ions. For convenience the pad on the right side of the back was always connected with the anode.

The current was obtained from a shunt rheostat across a constant current main. The resistance handle was moved rapidly until the ammeter registered 6 milliamperes; the resistance had to be varied to keep the current constant during the experiment. The current was allowed to flow for a definite time, and in the case of some of the ions the effect of passing the current for different lengths of time was observed. The skin containing the ionized patches was then removed and in most cases the subcutaneous tissue and muscle beneath it also, the animal being killed by an overdose of the anaesthetic. An attempt, where possible, was then made to stain the ions *in situ* by immersing the tissue in a solution which caused the formation of a coloured compound with the ions in the skin. When this method could not be used the tissue was merely fixed and hardened in alcohol and stained in various ways. In all cases the tissue was properly hardened and embedded in paraffin and microscopical sections were made. In one experiment in which it was desired to observe the late effect of the action of zinc ions the animal was allowed to recover and was killed at a later date.

The experiments were performed on cats, rabbits, a monkey, and a dog.

The ions experimented with were:

Acid Radicles (from Kathode).	Basic Radicles (from Anode).
Hydrogen	Hydroxyl
Sulphide	Calcium
Ferrocyanide	Zinc
Ferricyanide	Copper
	Ferrous
	Ferric
	Mercuric

It would be as well in the first place to describe a very important experiment bearing on the whole question of the ionic treatment of joint diseases. A monkey was anaesthetized by chloroform, and a pad soaked in potassium ferricyanide was placed over the front of its knee, the area which the solution touched being limited by a window cut in a piece of oil-silk. This pad was connected with the negative pole, that attached to the positive pole being placed on the back. A current of 10 milliamperes was passed for thirty minutes, and then the animal was killed. Before its death, however, the knee was removed by cutting through the thigh and the leg, and was placed in a solution of ferrous sulphate. A control experiment was performed in which a pad of potassium ferricyanide was fixed on a monkey's knee for the same length of time, no current being passed, and the knee was subsequently treated in exactly the same way. The next day the knee was opened, and it was found in the case in which the current was used that the skin, subcutaneous tissues, and patellar tendon over which the window had been placed were stained an intense blue from the interaction of the ferricyanide ions and the ferrous sulphate, and further that this blue extended right into the joint, there being a stained patch on the cartilage which penetrated right down to the bone. In the control the blue did not even penetrate the skin. This definitely proves that it is possible to introduce the ions of some substances directly into a joint, even into the cartilages; at any rate of a comparatively superficial joint like the knee.

Very few ions driven in at the kathode, that is to say, acid radicles, can be traced in this way, but it is possible in various ways to trace certain of the basic radicles driven in at the anode.

The penetration of different ions varies enormously, and it is possible to tell from the movements of the needle of the milliammeter whether a drug is entering the tissues freely or not. In using two ions which penetrated the tissues freely, it was found that if the handle of the shunt resistance was moved to a certain point and left there the milliamperage gradually increased, which means that the resistance of the skin had diminished so that the ions were entering in greater number. With ions which

* In most of the experiments this was found the most convenient current to use.

precipitated in the epidermis, as described subsequently, the milliampère actually decreased after the first few moments, showing increased skin resistance and a lessened number of ions entering; to maintain the milliampère at all, the handle of the shunt resistance had to be continually moved in order to raise the voltage. In the case of ions subsequently proved to be deposited in the deeper layers of the skin, an intermediate effect was obtained, the current rising first and falling afterwards.

Hydrogen and hydroxyl ions cannot themselves be stained, but it was found that hydrogen ions caused the tissues to have an increased affinity for basic stains, the whole of the tissues under the ionized patch being deeply coloured by them, and the nuclei not picked out in the usual way. On the other hand, hydroxyl ions (introduced at the positive pole) produce the reverse effect, the tissue under the ionized patch failing to take basic stains. The staining in the hydrogen ion patches was even, and no granules could be detected. The effects persisted some time, as in one case the animal was allowed to recover, and the patches excised two days afterwards, when they still exhibited the same phenomena.

Attempts to stain sulphide ions by immersing the tissue in metallic salts, such as mercuric chloride, failed. Similarly, metallic ions could not be stained by immersing the tissue in solutions of sulphuretted hydrogen or potassium sulphide.

Ferrocyanide ions can be traced through the skin and subcutaneous tissue into the muscles; they are seen in large quantity in the capillaries of the subcutaneous tissue. All the tissues are stained blue, but the stain is not quite diffuse, as some parts seem to be picked out and stained more than the rest; the hair follicles and sebaceous glands are to a large extent avoided, and apparently the absence of staining of these is because the fat which they contain is a non-conductor of electricity. The taking up of the ions by the subcutaneous capillaries gives the deep layers of the subcutaneous tissue a more intense colour than the superficial layers. Ferrocyanide ions give a very similar appearance to that obtained with ferrocyanide ions.

Copper ions were easily demonstrated by fixing the tissue with potassium ferrocyanide. They were deposited entirely in the epidermis, not even reaching the corium, and the deposit extended a short way down the hair follicles.

With ferric ions, the tissues being fixed in a solution of potassium ferrocyanide, precisely similar results were obtained. With ferrous ions, on the other hand, the appearances were almost identical with those given by ferrocyanide ions, with the exception that there was a rather more abundant deposit in the epidermis.

Calcium ions were found to be deposited in and beneath the corium, only a small quantity going through the corium, even when a large current was passed for a long time. The deposit takes the form of minute granules which stain very intensely with a basic dye.

Unfortunately the attempts to demonstrate zinc ions failed; one would expect from the macroscopic results to obtain very similar preparations to those of calcium ions, as in each case the skin presents an opaque white appearance after the ionization.

Attempts to stain mercuric ions also failed, but from the behaviour of the current they apparently penetrated the tissue readily.

These experiments are admittedly very incomplete, although they serve to demonstrate some important facts with regard to the science and practice of ionization.

I cannot conclude without tendering my best thanks to Dr. Goodbody for kind advice and assistance during these experiments, and to Dr. Bellamy for cutting the numerous sections in the last experiment.

A COMMISSION, appointed to advise the authorities in regard to the new German Criminal Code, has recommended that duelling with rapiers, provided that certain conditions are fulfilled for the protection of life, should not be made a punishable offence. The *Muench. med. Woch.*, in noticing this recommendation, remarks that duelling among students will in future lack the stimulation of being forbidden. Our contemporary therefore anticipates that this antiquated method of exercising muscles, pluck, and skill will become still less fashionable than it has been within recent years.

A CASE OF URÆMIA TREATED BY MORPHINE.

BY

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SUGGESTIONS in the textbooks in regard to the use of morphine in acute uræmia are usually so unconvincing that I thought my experience in a recent case might prove useful.

On July 23rd of this year I was called to see W. L., a warehouseman, aged 56. He was sitting by the fire, wrapped in blankets; his face was puffy and dusky in colour, and his legs very oedematous; his whole body was also oedematous, though not extremely so. There did not appear to be any effusions into the serous cavities.

He had been feeling vaguely out of sorts for some weeks and, latterly, particularly short of breath and easily tired. A week before I saw him he had consulted his club doctor, who had prescribed for him. He had seen him again three days before my visit. He gave a history of a severe attack of scarlet fever seventeen years previously; eleven years ago he was told he had Bright's disease, but the doctor whom he then consulted told him he was cured of it.

The patient was too ill to examine very thoroughly at my first visit: the pulse was about 90, and very full; the cardiac impulse was about 1 in. outside the nipple line, with a blowing systolic murmur; the second aortic sound was accentuated, I had not my sphygmomanometer with me, so I do not know what his tension was, nor did I, unfortunately, take it with me before his acute symptoms started. He was complaining of constant eructation of wind and occasional vomiting; he had headache, but no ocular symptoms. The urine was almost solid with albumen on boiling.

The patient was put to bed, and diaphoretics, aperients and warm packs ordered. Next morning he expressed himself much better. The sickness and eructation of wind and vomiting had stopped, and the oedema had already to some extent receded. In the evening his son came to tell me that the vomiting had recommenced, and that he was not so well. Shortly after midnight I was sent for, and on going to see him I found that he had got out of bed and fallen on the floor; he was somewhat incoherent and could not raise himself; being a big, heavy, man, it was not an easy matter to lift him back into bed. I was inclined to think that he had probably had a fit and fallen out of bed. His pulse was still very full, though not rapid, and as I thought that convulsions seemed imminent, I tried venesection and inhalation of amyl nitrite. The venesection was not a success, only about 5 oz. of blood being abstracted. He became quiet and seemed inclined to sleep, so I left him, but ordered him another hot pack.

At 8.30 the same morning I was again sent for; I was told that he had had five fits since 7 p.m., and could not be kept in bed. I found him unconscious and extremely restless, cyanosed, and incessantly throwing himself about from side to side of the bed. Having had so unsatisfactory an experience of venesection, I did not attempt it again, but gave him a hypodermic of morphine sulphate $\frac{1}{4}$ grain with atropine sulphate $\frac{1}{10}$ grain, and told his friends to get a cylinder of oxygen and administer it continuously. I called to see him again about an hour after the injection, and he was sleeping fairly quietly and had not had another fit.

At 2 p.m. I called again; he had just had another very severe fit—the first since the hypodermic injection. He was unconscious, deeply cyanosed, with a slow, full pulse, and heaving himself up and down and from side to side of the bed as if in a struggle for breath. He did not keep in one position for more than two or three seconds, and the oxygen could not be administered because of his extreme restlessness. The dyspnoea was extreme and the veins extremely engorged. I now immediately venesected him, and with the utmost ease withdrew at least 25 oz. of blood. This improved his colour considerably and to a certain extent his restlessness. He was still restless, however, and I was so anxious about the condition of his heart that I thought quiet must be obtained at almost any cost, so I gave him another hypodermic of morphine sulphate gr. $\frac{1}{4}$.