

the venom. 5. Exhaustion of the heart is probably predisposed to by the strain put upon the organ in having to work for a long period against an abnormally high blood pressure.

We are now in a position to explain the sudden rapid fall of the curves of heart-beat rate and of blood pressure which ushers in death at the close of one of these long experiments. An over-strained and weakened heart is suddenly and violently called upon to bear a further burden, for respiration has ceased and the medullary centres are acutely asphyxiated. As a consequence there is a violent excitation of the cardio-inhibitory and vaso-motor mechanisms. The heart is slowed and at the same time has to work against a suddenly increased pressure and it gives way. In fact, we have the phenomena of asphyxiation in their entirety. The vessels of the splanchnic area are affected *pari passu* with those of the body generally and they in no wise act independently. The vaso-motor mechanism remains active throughout and is, as we have seen, profoundly affected by changes in the venosity of the blood.

6. Cobra venom, when injected in large doses and especially when given intravenously, causes: (1) a sudden fall of blood pressure; (2) a subsequent rise, provided that the dose has not been too large; and (3) a final fall to zero. The early fall is undoubtedly due to inhibition of the heart. It has been clearly shown that this is mainly brought about by the direct action of the poison on the vagal centres in the medulla oblongata, as it occurs before the accompanying failure of respiration has had time to act. Moreover, it is seen whilst artificial respiration is being actively carried on and can be checked in these circumstances by division of the vagi. On the other hand, there can be no doubt that asphyxiation of the vago-inhibitory centre intensifies and maintains the inhibition which direct influence of the venom on the vagal centre produces. The spontaneous recovery of respiration or the application of artificial respiration has a powerful influence in mitigating the action of the venom on the vagal centre. In the same way artificial respiration, and to a less extent the spontaneous recovery of respiration, appear to act beneficially on the poisoned respiratory centre. Even if the heart is cut adrift from all central vagal impulses, whether direct or indirect, by the division of the vagi there yet remains evidence of a continued inhibition which must be attributed to the direct action of cobra venom on the terminals of the vago-inhibitory mechanism. This action would appear to be a direct one but there is every probability that it is indirect as well, in other words, that it acts through asphyxiation of the vagal terminals as well as by the poisoning of these parts by the circulating poison. There is, however, another factor which must not be lost sight of—viz., a direct exhaustion of the heart muscle as the result of irregular over-stimulation.

7. When the secondary rise of blood pressure which follows the primary fall takes place it is due to the same factors which determine its occurrence when small doses have been injected. It remains to explain why it is sometimes absent, brief, or ill marked. The explanation is simple: it is merely a question of cardiac failure. We have seen that the direct inhibitory action of the venom through the vagal centre is capable of overcoming the tendency which the blood circulating through the heart muscle has to throw that muscle into death in systolic tone. Were it not for these two rival forces to some extent equilibrating each other cobra poison would kill by its direct action on the heart muscle. When the doses are comparatively small, or when the vagi are cut or thrown out of gear by atropin, we find the tonic cardio-muscular influence of the venom in evidence, but when the dose of venom is large, and especially when it is given intravenously (the vagi remaining intact), the inhibitory action overpowers the muscular excitation and failure of the heart occurs. If the inhibition is sufficiently well marked no amount of arteriolar spasm that occurs will compensate it, consequently the blood pressure falls. When the dose of venom is a very large one the direct muscular stimulation may be so intense as to overcome the maximum inhibitory impulse and then the heart dies in systole with a quickened beat and is found after death as hard as a contracted post-partum uterus. In such circumstances any increase in the force of the heart is temporary, for the beat is probably a very partial one, the heart passes through a stage of excitement into one of increasing systolic tonus in which the contractions are very limited in extent.

THE TREATMENT OF INCONTINENCE OF FÆCES BY THE SUBMUCOUS INJECTION OF PARAFFIN.¹

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INCONTINENCE of fæces may arise from many and very varied causes but from the point of view of surgical treatment the cases may be broadly classed into two groups. 1. Those cases in which the sphincter ani still retains some amount of power but not sufficient to close entirely the anal orifice. It is conceivable that if by introducing paraffin into the submucous tissue on the inner surface of the sphincter we narrow the lumen of the bowel at this situation and thereby diminish the work which the sphincter has to perform, even a weakened sphincter may be able firmly to occlude the remaining lumen and so to render the patient continent. 2. Those cases in which the sphincter is completely paralysed, as in many nervous diseases, or has been entirely removed as after the operation of excision of the rectum. Various plastic procedures have from time to time been advocated with the object of surrounding the anus in such cases with muscular fibres diverted from their natural function, the chief muscles concerned being the gluteus maximus and the levator ani. Attempts have also been made to produce a valvular action of the rectal wall, such as by dissecting out the rectum, twisting it on its long axis, and refixing it, or by producing a sharp curvature or kink in its lower portion—attempts which are frequently unsuccessful. In two cases of incontinence of fæces belonging to this second group, one of which was associated with rectal prolapse, I have obtained great benefit from the submucous injection of paraffin into the lower portion of the rectum, as originally suggested by Gersuny of Vienna in 1899.

CASE 1.—The patient, a male, aged 58 years, was admitted to the Manchester Union Hospital with the history that three years previously he had undergone two operations elsewhere for fistula in ano, as the result of which the fistula was cured but he was completely incontinent of fæces. Two subsequent plastic operations were performed to relieve this condition, but were unsuccessful, and he had had absolutely no control over his stools for three years. On examination no trace of a sphincter could be discovered, the anus extended in a posterior direction almost to the coccyx and was surrounded by several dense scars, the result of former ulceration. Under anaesthesia I injected paraffin in several places into the submucous tissue of the rectum, commencing as high up as I could reach and working towards the anus. In all, upon two occasions, the rather large amount of 52 cubic centimetres of paraffin was introduced, its melting point being 111° F. This patient was shown at a clinical meeting of the Manchester Medical Society three weeks after the operation and I last heard of him nine weeks afterwards, during which interval he had had complete control over his motions and had never soiled his linen upon a single occasion.

CASE 2.—The patient, a boy, aged seven years, had been an inmate either of the Manchester Union Hospital or of the Swinton Schools attached thereto for the last five years, suffering from complete incontinence of fæces associated with a large rectal prolapse dating from infancy. During the past four years he had undergone linear cauterisation on two or three occasions, excision of the elliptical folds of the mucous membrane, and, finally, excision of the lower portion of the prolapsed rectum, all of which were unsuccessful in curing the prolapse, and had no effect upon the incontinence. The anus was abnormally large and lax and easily admitted four fingers, while there appeared to be an entire absence of sphincteric action. At first I injected only six cubic centimetres of paraffin submucously, but even this small amount certainly prevented the prolapse from descending with anything like its former frequency. On a subsequent occasion I introduced 27 cubic centimetres in three successive tiers, each tier consisting of three

¹ A portion of a paper communicated to the Manchester Medical Society on Feb 3rd, 1904.

nodules of three cubic centimetres each and the prolapse has never since recurred, while the incontinence was very considerably improved. As, however, he still occasionally soiled his linen at night I decided to narrow the enlarged anus, which I did by a plastic procedure similar to Tait's flap-splitting operation for the repair of an incomplete laceration of the female perineum and this operation, performed 12 weeks ago, has resulted in complete relief. The boy is still under observation and his general condition has considerably improved since he acquired full control over his motions. An interesting point in this case was that when the patient was under the anæsthetic on the last occasion, before commencing the plastic operation I attempted to draw the former prolapse forcibly down but could not do so.

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THE THERAPEUTICS OF THE ICHTHYOL COMPOUNDS: WITH SPECIAL REFERENCE TO ICHTHOFORM AND ICHTHARGAN.¹

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EXACTLY a year ago I had the honour and privilege of bringing before your notice my experiences with ichthyol in the treatment of pulmonary diseases.² When I was asked to give you something on the same lines this session I thought I could not do better than follow up my former paper by saying a few words about the various compounds of ichthyol. As some of you may know, I have devoted much time and careful research to the investigation of ichthyol and its preparations, so convinced am I that in it we possess a most valuable therapeutic agent the properties of which depend not so much on its containing a fairly large amount of sulphur in its composition as on its being a very powerful anti-inflammatory agent. This fact I have tried to bring to the notice of the profession in a short paper on the subject which I recently contributed to the *Journal of Tuberculosis*.³ I may, perhaps, be allowed to quote the concluding sentences of that paper: "I am no believer in the theory that ichthyol owes its action to its antiseptic property nor in the view that its beneficial effects are entirely due to its action upon nutrition. We must go further afield and regard ichthyol in its true light as a vaso-constrictor and as an anti-inflammatory agent. This is its true action and the only one which is of much value in the application of the remedy to cases of pulmonary tuberculosis. Thus regarded ichthyol becomes a remedy of the greatest importance and one worthy the support of the profession everywhere." Ichthyol, I need hardly remind you, is a natural product that has been chemically treated. It is, in fact, a hydrocarbon oil obtained from a fossiliferous mineral, and this, after being acted on by sulphuric acid, gives us ichthyol-sulphonic acid. It is the ammonia salt of this acid which is known commercially as ichthyol. The history of the discovery of this hydrocarbon oil is of the greatest possible interest but it is somewhat outside the scope of the present paper.

Ichthyol, moreover, may be combined with quite a variety of active therapeutic substances. Thus we have iron-ichthyol, otherwise known as ferrichthol, calcium-ichthyol, sodium-ichthyol, and combinations with lithium, zinc, and mercury. Lastly, we have two quite recent ichthyol compounds—namely, ichthoform and ichthargan—the former being a compound of ichthyol with formic aldehyde and the latter the silver salt of ichthyol. Although I have had considerable experience with all of these time will not permit of my making more than a passing reference to most of them, reserving the greater part of my paper to a more detailed consideration of the two last named—ichthoform and ichthargan.

Iron-ichthyol or ferrichthol is a brownish-black, amorphous

powder, very light and non-hygroscopic. It is practically odourless and tasteless and is best administered in cachet or in tablet form. The amount of iron contained in this preparation is about 3·5 per cent. Aufrecht of Berlin was one of the first to publish results of clinical tests with this compound. Personal clinical experience with ferrichthol shows that it is an excellent remedy in secondary anæmia. Thus in a case of subacute rheumatism in which the red corpuscles and the hæmoglobin were reduced they returned to normal within a month under the administration of 30 grains of ferrichthol per day. Another case in which this remedy proved valuable was that of a woman suffering from carcinoma ventriculi. She was able to take ten grains of ferrichthol in the 24 hours without producing nausea, although many other iron preparations previously given had not been retained. In a case of chronic renal disease where the patient suffered from intense headache and was markedly anæmic ferrichthol proved very useful not only in improving the condition of the blood but also in diminishing the frequency and severity of the cephalic pain. In severe cases of dysmenorrhœa associated with constipation and anæmia one of the most suitable remedies is ferrichthol in ten-grain doses thrice daily. In cases of chlorosis, on the other hand, I have seen no good results follow its persistent employment. It is, therefore, in secondary anæmia that it is of most value, and here no doubt the action of the iron is largely aided by the presence of the ichthyol with which it is combined. Although I have no personal experience of its use in skin affections it is interesting to note that Unna⁴ advises its adoption in all chronic conditions, especially in urticaria and analogous skin diseases, in papular and bullous affections, and in lichen as it occurs in children. Again he finds it of service in diseases complicated either by chlorosis or by anæmia. Thus in eczemas occurring in anæmic subjects the ichthyol in combination with iron improves the circulation and so does good. No doubt iron-ichthyol has a wide sphere of therapeutic application in all diseased conditions associated with anæmia, and my own observations on its value in general diseases are fully borne out by Unna's with regard to dermatological conditions.

Sodium-ichthyol is a solid preparation and thus forms an excellent substitute for the internal administration of the ammonia salt as it can readily be made into pills. I am of opinion, however, that it is not nearly so active in pulmonary disease as is the original ammonia salt, though it is perhaps a little more readily taken by fastidious patients. In chronic gastric catarrh it has the power of checking the fermentative processes which form such a troublesome element in many of these cases. Generally speaking, where ichthyol is indicated this preparation should be prescribed, except in cases of pulmonary disease in which the original ammonia salt alone should be employed.

Calcium-ichthyol is well suited for use in dermatological practice and I have found it readily taken by children. It is not, however, in my experience such a generally useful salt as are some of the others. The zinc salt finds many indications for its use in diseases of the skin and hence its value appeals most to dermatologists. It may be used as an ingredient in ointments and in certain cases is to be preferred to the ammonia salt. Of the lithium salt I cannot now speak as, not being an advocate for the use of lithium, I have not felt it my duty to experiment much with this compound of ichthyol.

Within the last few years ichthyol has been made use of as a vehicle for certain insoluble agents such as cresol, eucalyptol, and even iodine. I have elsewhere⁵ fully recorded my experience of the use of iodine-antol, as this new combination is called, and I need not stay to consider these quite recent additions to our pharmaceutical armamentarium. Of all preparations of ichthyol two stand out pre-eminently—namely, ichthoform and ichthargan. Of these I have been making trial for some time past and it is with the greatest possible pleasure that I take this opportunity of bringing the results of my work in this connexion before your notice.

Ichthoform is an amorphous, brownish-black powder, being practically odourless and tasteless. It is insoluble in ordinary media such as water, alcohol, and glycerine. When brought into contact with dilute alkalies it gradually

¹ A paper read before the Therapeutical Society on Feb. 23rd, 1904.

² A paper read before the Therapeutical Society on Feb. 17th, 1903, and published in THE LANCET of August 8th, 1903, p. 384.

³ October, 1903.

⁴ Monatshefte für Praktische Dermatologie, 1901, Band xxxii., Heft 5.

⁵ The Medical Times, Dec. 20th, 1902.