that angioma of the choroid may be the connecting link between these two diseases.

Calcification of the ocular tissue (capillaries, angiomata, internal limiting membrane and ganglion cells) was a feature of the case.

Reference is made to the allied anomalies—von Recklinghausen's disease, the Treacher Collins—von Hippel-Lindau disease and Bourneville's disease.

A brief description is given of an angioma of the retina recently found in a case of Bourneville's disease.

We are greatly indebted to the Council of the Ophthalmological Society of the United Kingdom for the loan of the blocks of Figs. 1, 2, 6, 9, 11, 12 and 13, which illustrated the paper by A. Garrow and A. Lowenstein in the *Transactions*, Vol. LXII.

REFERENCES

- ANDERSON RINGLAND.—Hydrophthalmia, Cambridge, 1939.
 BALLANTYNE, A. J. (1930).—*Brit. Jl. of Ophthalm.*, Vol. XIV, p. 481.
 ——— (1940).—*Brit. Jl. of Ophthalm.*, Vol. XXIV, p. 65.
 DUMPHY (1935).—*Amer. Jl. of Ophthalm.*, Vol. XVIII, p. 714.
 GARROW and LOEWENSTEIN (1941).—*Brit. Jl. of Ophthalm.*, Vol. XXV, p. 509.
 HEINE (1905).—*Deutsche med. Wochenschr.*, No. 21.
 VAN DER HOEVE.—*Trans. Ophthalm. Soc. U.K.*, Vol. XLIII, p. 534, 1923; and Vol. LII, p. 380, 1932.
 LINDEMEYER (1932).—*Klin. Monats. f. Augenheilk.*, Vol. LXXXVIII, p. 339.
 LOEWENSTEIN and STEEL (1941).—*Amer. Jl. of Ophthalm.*, Vol. XXIV, p. 731.
 ROBSON, BLACKWOOD and COOKSON (1941).—*Brit. Jl. of Ophthalm.*, Vol. XXV, p. 431.
 SALUS (1920).—*Klin. Monatsbl. f. Augenheilk.*, Vol. LXIV, p. 433.
 SPIELMEYER (1922).—*Histopathologie des Nervensystem*, J. Springer, Berlin.

IONTOTHERAPY

(Ionic Medication, Iontophoresis, Ionisation)

AS AN AID IN OPHTHALMIC THERAPEUTICS

BY

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LONDON

IONTOTHERAPY in ophthalmology is far from being a new form of treatment, but the old methods were somewhat laborious and the results not over encouraging. No doubt there were reasons for this and my experience suggests that too strong currents, too strong solutions and too long applications, were among the causes of disappointment. Furthermore, the very feasibility of the treatment has been doubted and even denied.

Iontotherapy, by its etymology, expresses treatment by ions electrically administered, and this describes in brief what this paper elaborates. Ionic medication is a euphonious alternative with a similar meaning. Iontophoresis, a term widely used abroad, expresses the carrying of ions from one point to another, but it is not one that comes readily to the English reader. Ionisation is a term which has for long been associated with destructive processes and in consequence is unlikely to convey the idea of the healing processes here described.

By using a set deriving its power from small batteries and ensuring that the milliamperemeter needle never indicates more than two milliamperes, the undesirable effects of too strong currents can be prevented at source.

An experience of weak solutions will rapidly remove all temptation to use stronger ones, as the weak ones prove their own efficacy, convenience and freedom from complications.

The apparatus with the dry batteries is contained in a case measuring 8in. by 6in. by 3½in., the sloping front panel of which carries a dual-purpose meter and the controls. The meter is calibrated to record on the lower scale the voltage of the battery and this can be instantly checked by pressing a Test Button which connects the meter as a voltmeter. Situated centrally below the

meter is an output control rheostat combined with an on/off switch. Switching on by a clockwise movement brings into operation the meter as an 0—3 output milliamperemeter. This also starts an electric ticking device for timing purposes. The instrument is so constructed that positive ions, such as Calcium and Zinc, are normally introduced into the eye and is provided with a reversing switch for introducing negative ions such as salicylates. Modifications of Erlangers hand and treatment electrodes with their flexible leads and plug connections complete the apparatus.

The fact that drugs can be introduced into the body by an electric current has been dramatically demonstrated by such experiments as killing rabbits with the characteristic symptoms of strychnine poisoning, the introduction of strychnine being brought about from the positive pole by the employment of strychnine sulphate. This was first done by Boccaleri and Massieri in 1888. A more impressive experiment was described by Leduc in 1900 and this he regarded as definitely establishing the electrolytic introduction of ions into the living organism. Two rabbits were linked together in series in the following manner; the positive pole, by which the current enters, was charged with strychnine sulphate and applied to the first rabbit; this rabbit was connected with a vessel containing saline and so to the second rabbit to which the negative pole, charged with cyanide of potassium, was applied. A current of 80 milliamperes was then passed: the first rabbit died in convulsions and the second with symptoms of cyanide poisoning.

Another experiment of interest is that described by Erlanger where he caused cataract in a guinea pig by means of barium, a solution of barium chloride being applied to the positive pole.

Iontotherapy may be applied directly to the cornea or to the bulbar conjunctiva, to the closed lids or to the everted lids, according to indications.

Most authorities express the view that drugs administered in this way penetrate only the most superficial layers and are immediately carried off into the general circulation; many infer that on this account the local effects cannot be great. If this opinion were correct, it would surely safeguard us against any local accumulation of a drug in the eye leading to excessive dosage. It would, however, be unwise to rely on any such dispensation: one of the most remarkable features of therapy of this kind is the prolonged action of the drug: this is well shown in the case of adrenalin, where a very weak solution causes an exsanguination remarkable for its degree and persistence, and in the case of zinc, where one must be prepared for pain to come on about an hour after treatment: it seems improbable that these consequences would manifest themselves after all traces of the drug had left the part.

In an article on the electrolytic destruction of growths Leduc says that the majority of destructive ions remain and accumulate around the point of introduction.

But my object in writing these pages is not to question or to amplify the findings of the many physicists and physicians who have studied and described the electric phenomena associated with ionic medication: it is to draw attention to the unique assistance which this form of treatment offers in the therapy of all sorts of ophthalmic conditions and to its consequent importance to physician and patient. In this way I may add my contribution to the experience of others.

It must be clearly stated that I would recommend iontotherapy only as an addition to our armamentarium, and in no sense would I set out to replace any of our tried and trusted methods. Particularly would I emphasize that discovery of the cause remains the crux of the satisfactory treatment of all secondary inflammations; but that in no way reduces the value of the empirical treatment of such an inflammation during investigation of its aetiology, nor of the value of iontotherapy in clearing up an inflammation of which the cause has been removed.

Let me cite a few examples from many cases of *conjunctivitis* treated by this method. A hospital dispenser was sent to me by the R.S.O. with a double acute conjunctivitis. I administered calcium, adrenalin and prontosil by the method described: next day her eyes had recovered and there has been no recurrence. A professional man, who had an acute conjunctivitis in one eye, had similar treatment with a similar result. A case of acute pneumococcal conjunctivitis with much haemorrhage sent to me by Dr. F. was completely cured in five days. Before the introduction of prontosil and such drugs, Dr. C.M. sent me a bad case of bilateral gonococcal conjunctivitis in a man; treatment with calcium, adrenalin and silver nitrate achieved an excellent result within ten days. These were primary infections.

A woman sent by Dr. S. had a severe double conjunctivitis of **some** six weeks standing; it was associated with a series of small lid abscesses. Treatment brought about a most welcome improvement but she relapsed: bacteriological investigation revealed an abundant growth of haemolytic staphylococcus in eye, nose and throat. A vaccine was prepared and administered but to no purpose. We therefore concluded that this was either a case of bacterial allergy or, more probably, a protein allergy with a superimposed infection, and Dr. S. sent her to Dr. George Bray. His investigation revealed a sensitiveness to dust and to dogs; she kept a dog to which she was greatly attached. Treatment by injections of the desensitising preparation supplied by Dr. Bray

produced a rapid and dramatic cure. A man, a patient of Dr. C., had a very acute conjunctivitis of both eyes: treatment was again helpful but he relapsed: investigation showed a sub-acute, right maxillary sinusitis: this was drained and I then had no difficulty in restoring the eyes to normal. These last two examples were secondary infections.

Chronic conjunctivitis is, of course, particularly likely to be secondary to such conditions as refractive errors or nasal infections, but there are times when attention to these things does not bring about a cure and there are times when no such cause can be found. In these cases one can rely with confidence on iontotherapy to bring about very considerable betterment, if not a cure. In *asthenopia* with irritability, photophobia and blepharospasm in varying degree, the case is similar: there may be a cause, discoverable or not: there are those which yield so wonderfully to convergence training: but there are many in which routine methods have disappointing results. The fact that sundry drastic treatments for *asthenopia* have had their advocates proves the difficulty which prompted them. In such cases amelioration is the rule and so marked may it be that I have had one case—a patient of Dr. C. who, last year, was able to keep her eyes open in the sunlight for the first time for many years. The possibility of allergy must always be borne in mind but, apart from this, the more protracted and intractable the history of a case of conjunctivitis may be, the more surely will relief be found in treatment by iontotherapy. Such words conjure up the spectre of trachoma; but it is not of trachoma that I am writing. Of the treatment of early trachoma by ionic medication, I have but the smallest experience and would not speak: but I have seen enough to recommend treatment by iontotherapy most heartily for those old chronic cases with vascularisation of the cornea and recurrent ulcers.

The cure—or shall we say the disappearance—of certain hyperaemic states following treatment by iontotherapy has caused me to wonder whether some of these chronic congestions are really inflammations at all, whether indeed, they are not simply bad habits on the part of the local vascular system which, after a certain period of hyperaemia, is unable on its own to reduce the blood traffic to normal and which is maintained to some extent by the unwonted stimulation of its own excessive transudate. Undue persistence in the use of heat may also play its part, for we have all seen lids which have become persistently hyperaemic following months of fomenting. It would appear unreasonable to anticipate that the continuation of heat application beyond a certain point is likely to produce anything other than adverse and stagnating effects.

There is no condition one can have to treat which is more unpromising than *corneal scars* and on this account it is of interest to note that treatment by ionic medication is capable of bringing about surprising improvement in many cases. Generally speaking, the more recent the case, the greater the improvement. The most remarkable case I have had under my care was a large leucoma of three years standing. It was so large and dense that only a small amount of peripheral vision was possible: following treatment at varying intervals over the course of a year, the leucoma was reduced in size to somewhat less than that of the pupil so as to admit of vision of 5/60 and 1/9.

In cases of *corneal ulceration*, carbolicisation affords an anchorage which should always be sought in suitable cases, and the greater the storm the more urgent the seeking. The sulphonamide group of drugs given by the mouth are apt to ease the situation tremendously. But the mighty diversity of corneal conditions, of their causes and of the appropriate treatment, is so great that particularisation in this paper is impossible, and I must content myself with a few general observations. In the active stage of many ulcers iontotherapy affords the best treatment, and in many more such treatment alone would be adequate: during recovery from an ulcer iontotherapy will expedite resolution and reduce residual scarring: it may even prevent it, altogether. Infiltration, primary or secondary, can be reduced and sometimes completely removed; pain is alleviated: the filling up of a crater is assisted and expedited: vascularisation is reduced and persistent vascularisation may be prevented: friable scars may be made strong. This form of treatment is of special value after perforation of the cornea, primary or secondary.

The calming, analgesic and decongestive effects of iontotherapy are well seen in the treatment of *herpes ophthalmicus*. This is a disease which is very variable in its gravity, duration and complications, and consequently it is hard to say what course a particular attack would have taken had a certain line of treatment not been adopted. Two cases seen in the early stages, with ulceration, pain and photophobia obtained immediate relief, and with continued treatment recovery was rapid and uncomplicated.

Another case is of special interest. Mr. L., a dental surgeon, sent to me by Mr. I., came on October 5, 1939. Several weeks previously he had had a supra-orbital herpetic eruption which had been mistaken for furunculosis and for this condition he had been treated. For a couple of weeks his sight had been failing and was now limited to seeing large objects at close range. The cornea was cloudy, keratic precipitates were abundant, the eye was hard (secondary glaucoma), and vitreous opacities could be

appreciated. Treatment at first was with acetylcholine and calcium and later by calcium and adrenalin with eserine and continued with variations. On October 10 vision was 6/24, tension was normal, the cornea only slightly hazy and the keratic precipitates much less. By November 16 vision was 6/9. Occasional fresh deposits of K.P. were found at intervals and it took six months for the cyclitis to disappear entirely; the vitreous cleared almost completely. I saw him from time to time during the following year in the course of which he played a lot of cricket and had no trouble whatever; $v=6/5$.

With regard to the *sclerotic* there are few conditions where an ophthalmic surgeon may find success more difficult and more uncertain of attainment than in *episcleritis* and *scleritis*; yet there is no condition where iontotherapy produces a more marked and more immediate improvement. Episcleritis may disappear in a night and never return: persistence or a recurrence points conclusively to an underlying cause (this may be the appendix as in a case of Dr. J.). As Juler has recently emphasised many cases of scleritis and sclerosing keratitis are tuberculous. Apart from attention to a discoverable cause no text book advocates any line of treatment with particular enthusiasm, and, when the cause is tuberculous, the success of treatment of an eye lesion will be influenced by the presence or absence of other active foci. Even in these cases ionic medication is likely to be of the greatest value, keeping the eye open, free from pain and watering to a gratifying degree and preserving the sight for an indefinite period. A case of *tuberculous sclerosing keratitis* with cyclitis referred to me by Dr. B., in October, 1941, had just been the subject of a report from a London Ophthalmic Hospital so pessimistic that her doctor told the patient that he thought enucleation would be the best way to deal with the situation. The whole cornea was hazy, congestion extreme, there was much mutton fat keratitis punctata, the eye could scarcely be opened and watered profusely. Light could not be tolerated and sight appeared to be lost. Treatment during the last year has resulted in a gradual improvement, not without setbacks but on the whole very steady. At present there is no congestion, no keratic precipitates, a cornea only slightly scarred, an active pupil, no photophobia and vision is 6/6. For some months treatment was given once a week and later once a fortnight; she has had no other treatment.

In a given case of *iritis* one endeavours to treat the cause, the local congestion, and the consequences of that congestion. The first is all important, but both before and after that has been dealt with, iontotherapy will help us to relieve pain, reduce congestion and avoid complications. While the cause is active the results

of treatment vary in different cases and the value of heat is in no way to be underestimated: not infrequently no cause is found and in such cases iontotherapy will usually effect a cure: for residual, chronic and recurrent iritis ionic medication is of the greatest value; the eye opens up, congestion is relieved and posterior synechiae may be broken down. A point of special interest in the treatment of iritis is the mydriatic power of adrenalin acting on an iris simultaneously exsanguinated by the same drug, and reinforced by the subsequent instillation of atropine. In this way it is possible to break down posterior synechiae which would offer a discouraging aspect when treated by the more usual methods. When cyclitis is present with keratic precipitates or opacities in the anterior vitreous the employment of ionic medication is equally opportune. The measure of its value and the choice of drugs, time and mode of application vary with the case and cannot be closely prescribed. There are few conditions more distressing to patient and practitioner than irido-cyclitis and my experience indicates that a greater and not a less reward awaits those who give to iontotherapy an important place in treatment.

Iontotherapy generally and with adrenalin in particular is apt to cause a slight temporary rise in ocular tension and in the glaucomatous subject this might be serious. It is necessary therefore, as when considering the use of a mydriatic, that one should be constantly alive to the possibility of a patient being glaucomatous. With regard to the treatment of *glaucoma*, one must tread very warily, but I have found that a very little medication with acetylcholine followed by instillation of eserine causes extreme miosis and a fall in tension, especially if leeches can be applied subsequently. As glaucoma, in my view, is a local expression of a more general disorder, I do not anticipate that a permanent cure can be effected by any form of local treatment. In one case I treated one eye by trephining and one by ionic medication; the result was good in each case and remained so after eight years (Mrs. B.). I have also treated one case of monocular acute glaucoma in this way and succeeded in reducing the tension to normal in three to six hours; this has been done three times in the same patient for recurring attacks at intervals of a few months.

The question of the treatment of the posterior parts of the eyeball is likely to be more controversial than that of the anterior, but my experience has shown that these parts also are readily influenced by ionic medication.

Treatment of *retro-bulbar neuritis* due to tobacco by acetylcholine and calcium with eserine may be dramatic; it may even be possible to register an improvement in vision in little more than the time

necessary to administer the treatment. A patient of Dr. L.W., a man, had the usual colour scotoma and vision 6/18 R.L. He came on September 12; by October 4 his vision was 6/6 R. and L. I treated him five times. A patient of Dr. W.W., a woman, had a complete central scotoma for colour and vision reduced to less than 6/60 R. and L. Treatment was begun on August 8; in

FIG. 1.

Embolism of the inferior temporal branch of the Central Artery of the Retina in a girl of sixteen suffering from Chorea. November 26, 1941.

spite of a short attack of episcleritis in the left eye on the 18th, her scotoma had gone and vision returned to 6/9 R. and L. by September 9. I saw her on nine occasions.

Still more remarkable success attended the treatment of a woman aged 31, sent to me by Dr. B. She had right monocular retrobulbar neuritis, not due to tobacco and for which no definite cause was found. She was first treated on Friday, March 20, when para-central vision was 6/60; on the 21st she had lost all form and colour

sense—the lower half of her visual field was almost completely lost and the whole of the upper half was vaguely affected. There was slight swelling of the optic disc indicating that the neuritis was “coming forward.” The left eye remained normal. The right pupil was semi-dilated and almost inactive, consensually the reaction was normal. There was pain on pressing the eye backwards into the socket. The abdominal reflex was present.

FIG. 2.

The same case after treatment by Iontotherapy. February 27, 1942.

Treatment was continued; acetylcholine directly to the eyeball for three minutes at 1 m.a. followed by calcium externally (hot) with a few drops of eserine; benerva was injected hypodermically. Treatment was repeated daily for five days and improvement recorded as follows: 23rd 1/60 (half letter), 24th 1/36, 25th 1/18, 26th 1/12, 27th 1/3 and 6/36. On the 30th vision was 6/6 and on April 4th 6/5 and the greater part of 6/4. The eye appeared to be normal in all respects.

A patient of Dr. H.W.—a girl aged 16 years—who suffers from chorea, sustained an *embolism* of the inferior temporal branch of the central artery of the retina, close to the disc. (Fig. 1). She complained that the upper half of the sight of the left eye had gone black and her central vision which was aided by a cilio-retinal artery was 6/36. I decided to try treatment with intravenous heparin to prevent an extension of intravascular clotting

FIG. 3.

The same case. Field of vision taken February 27, 1942, showing loss of field remaining at the end of the course of treatment.

and medication with acetylcholine to dilate the vessels. I was fortunate in seeing the girl within twenty-four hours of the onset and I am quite sure that this fact contributed greatly to what was a surprisingly good result.

Heparin was injected on the first two occasions before treatment to the eye; acetylcholine and calcium with eserine were continued at increasing intervals for six weeks when the fundus appeared

normal, (Fig. 2), vision was 6/5 and the loss of field had been restored except for the small paracentral scotoma and peripheral segment indicated in the accompanying chart, (Fig. 3). A case of complete embolism occurring during pregnancy in a woman of 30, but not seen until a whole week had elapsed was similarly treated but showed no improvement. (Fig. 4.)

FIG. 4.

Embolism of the Central Artery of the Retina taking place during pregnancy in a woman of thirty. Causal agent? chorionic villus. Drawing made eight weeks later; total blindness in that eye. The optic disc of the other eye is illustrated for purposes of comparison.

We may anticipate that before long we will have many opportunities of proving the value of iontotherapy on a variety of war injuries and inflammatory conditions. I am convinced that by its use the prospects of many casualties will be greatly enhanced and this constitutes a special reason for the publication of the paper at this juncture.

Summary of Treatment

To have detailed the exact treatment in every case would have been wearisome even if it were possible and would have involved much repetition. My favourite application is six parts of calcium chloride 1 in 500 with one part of adrenalin hyd. 1 in 10,000; this makes the strength of adrenalin actually used 1 in 70,000 and I have found it quite possible to get a definite adrenalin effect with a dilution of 1 in 250,000. Only on the rarest occasions do I apply treatment directly to the eye for more than two minutes all told, to the everted lids for $1\frac{1}{2}$ minutes and to the closed lids for five minutes. I recommend the use of calcium externally in practically every case; adrenalin in all cases where it is not contra-indicated, as where glaucoma is suspected or a vaso-dilator is required. Zinc sulphate, 1 in 400 a small quantity added to the calcium solution where there is a loss of epithelium or an indolent state of the mucous membrane. Silver nitrate 1 in 1,000 or prontosil soluble 1 in 10,000 when a powerful antiseptic is required. Atropine Sulphate 1 in 2,000 as an alternative to its normal therapeutic use. Acetylcholine 1 in 200 and histamine 1 in 20,000 to promote vaso-dilatation and for other purposes. Quinine, eserine, pilocarpine, iodides, salicylates, and many other drugs may be used, but a few seem to serve as well as many and those one knows better than those of which one's experience is limited. It is sound to vary the treatment both according to the case and in the treatment of an individual case. The results of treatment can be observed better when they are sufficiently spaced and as the results of treatment are so lasting it is seldom necessary to see the patient very often. On the other hand, as in the recorded case of retro-bulbar neuritis, daily treatment is, on rare occasions, indispensable.

Summary

- (1) The principal feature of treatment by iontotherapy is reduction of congestion and so of inflammation generally.
- (2) It is therefore of use in all forms of conjunctivitis.
- (3) Cases are described showing remarkable success even in the treatment of such deep inflammations as scleritis, irido-cyclitis and retro-bulbar neuritis.
- (4) These claims are based on experience gained in the treatment of some thousand cases during the last ten years, both in hospital and private practice.
- (5) Iontotherapy is likely to be of particular value in the treatment of war casualties.

BIBLIOGRAPHY

- CANTONNET.—L'ionisation de l'oeil. Technique Resultats Editions Medicales N. Malione, Paris, 1927.
- ERLANGER —On Practical and Scientific Significance on Iontophoresis in Ophthalmology. International Congress of Ophthalmology, Amsterdam, Vol. I, p. 196, 1929.
- On the Scientific and Practical Value of Ionisation in Ophthalmology. *Brit. Jl. Ophthal.*, Vol. XX, p. 213, 1936.
- Iontophoretic Medication in Ophthalmology. *Arch. of Phys. Ther.*, Vol. XX, p. 16, 1929.
- KARBOWSKI.—Iontophoresis in Ophthalmology. *Ophthalmologica*, Vol. LXLVII, p. 166, 1939.
- LE CAM.—De la valeur de l'ionisation en therapeutique oculaire (On value of Ionization in Therapeutic Ophthalmology), Thesis of Medical Faculty of University of Paris, 1926.
- LE COUILLARD.—Ionisation dans les sclerites (These de Paris, 1933).
- LEDUC.—Introduction des substances medicamenteuses dans la profondeur des tissue par le courant electrique. *Ann. d'Electrobiol.*, Vol. III, p. 545, 1900.
- MORIZOT.—Treatment des Affections Oculaires par l'ionisation. *Jl. de Med. et Chir.*, 10, 8, 32. Also 110, 329, 1939.
- ROCHAT.—On iontophoresis of mydriatics in treatment of iritis and iridocyclitis. International Congress of Ophthalmology, Amsterdam. Vol. I, p. 199, 1929.
- ROHOZINSKI.—Penetration electrolytic les substances medicamenteuses dans les milieux oculaires. Paris. E. le François, 1936.

INJURY TO THE OPTICO-CHIASMAL JUNCTION—A CASE REPORT*

BY

E. B. C. HUGHES

THIS interesting case of injury to the visual pathway presented a difficult problem in localisation and in pathology. I can find no case quite comparable to it in the literature, and it has the added advantage that the lesion has been inspected at operation.

Major H. W. B., aged 31 years, sustained a severe head injury as the result of a head-on motor crash, the site of the injury was the left frontal region, and he had a fissured fracture running down in the left frontal bone, traversing the left frontal sinus, running along the floor of the left anterior fossa lateral to the optic canal, and then passing down into the left middle fossa. The actual course of this fracture has been verified in the course of two operative procedures. No definite fracture into the left optic canal was located, either by X-Ray or by direct vision; X-Ray, however, five months after injury showed this canal to be a little irregular in outline and larger than its fellow. No fracture of the left anterior clinoid process was demonstrable by X-Ray, or seen at operation.

He was admitted to another hospital, and some thirty-six hours

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