Similarly, it would help to facilitate this exchange of views and a realization that both sides form a team if the local health officer could have some attachment to his local hospital and be welcomed in their common-rooms and committees as one of themselves.

I must apologize for presenting so many figures, but it was essential to a proper understanding of what is the burden of ill-health which it is the duty of our National Health Service to try to reduce. My main thesis is that it is only by a "teaming-up," as they say in America, of the curative and preventive sides that progress can be made.

I wish to express my indebtedness to Mr. Benjamin and Mr. Gore, of the Statistical Section, and to Mr. Trendell, of the Library and Information Section of the Public Health Department of the London County Council, for valuable help with the figures and references.

REFERENCES

- ¹Hospital and Community, II. Ayrshire. Nuffield Provincial Hospitals Trust (1949).
- ²Annual Report of Chief Medical Officer, Ministry of Health, 1933.
- ³Sickness in the Population of England and Wales in 1944-7. Percy Stocks. Studies on Medical and Population Subjects, No. 2, General Register Office (1949). London.
- ⁴Collins, S. D., *et al.* (1950). *Publ. Hlth Rep., Wash.*, No. 65, p. 1235. U.S. Public Health Service, Federal Security Agency.
- ⁵*Minist. Lab. Gaz.*, May, 1950.
- ⁶Civil Estimates, 1950-1. Class 5, Health. H.M.S.O.
- ⁷L.C.C. Maintenance Estimates, 1950-1. L.C.C. Publication No. 3685.
- ⁸Drolet, G. J. (1949). *N.Y. St. J. Med.*, 29, 2956.

USE OF CORTISONE IN DISEASES OF THE EYE*

BY

F. S. LAVERY, M.D., M.Ch., D.O.M.S.

Lecturer on Ophthalmology, University College, Dublin

L. E. WERNER, M.B., B.Ch., D.O.M.S.

D. O'DONOGHUE, M.B., B.Ch., D.O.M.S.

PHILOMENA M. GUINAN, M.B., B.Ch., D.O.M.S.

AND

J. MACDOUGALD, M.B., B.Ch., D.O.M.S.

The dramatic results obtained by Hench *et al.* (1950) in the treatment of rheumatoid arthritis by the systemic use of cortisone gave rise to the hope that cortisone would be a helpful therapeutic agent in those ophthalmic conditions that seem to have an allergic origin. It had also been found that certain ophthalmic diseases were benefited in patients who were being treated for rheumatoid arthritis with systemic cortisone (Moore *et al.*, 1951).

When this investigation was begun (July, 1950) there were no publications available to us dealing with the local use of cortisone in the treatment of ophthalmic lesions. It was therefore necessary, in the first place, to find out by clinical trial the optimum dosage and the most suitable method of administration. We found that the instillation of a drop of cortisone acetate suspension into the conjunctival sac did not produce any irritative reaction. As a number of therapeutic agents which are used in the local treatment of ophthalmic conditions

have their maximum therapeutic effect when injected subconjunctivally this method of administration was next tried, and likewise produced no irritative symptoms when administered in the concentration and volume mentioned below.

The cortisone used was generously given free by Dr. James M. Carlisle, Medical Director of Messrs. Merck & Co., to the Medical Research Council of Ireland through Professor Henry Moore; for this investigation it was in the form of cortisone acetate ointment (25 mg. per g.) and a 2.5% suspension in saline (25 mg. per ml.) for instillation, both being bland when introduced into the conjunctival sac.

Parallel Work

It is of interest that other investigators, working independently, have come to similar conclusions about dosage and mode of administration and adjudge the therapeutic value of cortisone, in the main, much as we do. The first report was by Henderson (1950). Steffensen *et al.* (1950) record the use of a saline suspension of cortisone administered topically (4 volumes of isotonic saline to 1 volume of the original crystalline cortisone suspension) in four ophthalmic cases. These cases had, in addition, received systemic treatment with A.C.T.H. and cortisone. One of these, a case of luetic interstitial keratitis, showed continued improvement with the use of cortisone topically after the systemic treatment with cortisone had been suspended. Woods (1950) reports upon the use of cortisone locally in eight cases. Only one of these received systemic cortisone in addition. He concludes that cortisone administered locally in the conjunctival sac has a profound effect in the control of external ocular inflammation, the beneficial effect being uniformly observed after two to four days' intensive treatment, but that it has not yet been demonstrated that cortisone has any effect on the exudation in the vitreous. Koff *et al.* (1950) report that, out of nine patients with acute or acute recurrent iritis treated with subconjunctival injections of cortisone, eight were decidedly improved. They injected 0.2 to 0.4 ml. (25 mg./ml.), the injections being repeated in 48 to 72 hours where necessary.

Present Investigation

As our investigation was a clinical one, and as most of the cases were being treated by the local use of cortisone, it was considered that laboratory tests would not be of assistance in helping to regulate the dosage.

The use of cortisone locally in ophthalmic conditions has advantages. When used locally, such small quantities are required that the cost of the hormone is not a serious obstacle and no side-effects need be feared. The impression gained was that the method of choice is in the first instance by subconjunctival injection followed

*Third Report of the Cortisone Clinical Subcommittee (Professor Henry Moore, Chairman and Clinical Director, Professor W. J. E. Jessop, and Dr. D. K. O'Donovan) to the Medical Research Council of Ireland. Three circumstances led to this work being undertaken: (a) the first case of rheumatoid arthritis treated by our cortisone team also suffered from severe episcleritis; on the fifth day of intramuscular cortisone treatment the episcleritis had completely disappeared; (b) a short time after that observation Henderson's work in the Mayo Clinic on the use of cortisone in ophthalmic diseases became known to us; and (c) the free gift of cortisone preparations for use in ophthalmic diseases became available to us. Consequently, the Cortisone Clinical Subcommittee of the Medical Research Council of Ireland requested Drs. Lavery, Werner, O'Donoghue, Guinan, and Macdougald to undertake the study described in this article under its general direction.

by the instillation of cortisone drops every two hours during the day and the insertion of some of the ointment into the conjunctival sac last thing at night, the subconjunctival injection of cortisone being given every second day. The number of subconjunctival injections required varies from case to case, and local treatment should be continued until the inflammatory condition has subsided or until it is apparent that no response is being obtained. If a relapse occurs the treatment should again be instituted.

The subconjunctival injections were found to be entirely painless if local analgesia had been previously produced by the application of a pledget of cotton-wool that had been soaked in 2% butacaine sulphate ("butyn") at the site of the intended injection.

Only one patient complained of a smarting sensation being caused by the eye drops; the bland and soothing effect of the ointment and drops was remarked upon by many.

Notes on the treatment of 83 cases are set out below.

Table of Cases

Diagnosis	No. of Cases	Result
Interstitial keratitis ..	9	Symptoms relieved within 24 hours in 8. Six of these had had other treatment, without result, for weeks before institution of cortisone. Rate of clearing of corneal opacification much hastened by cortisone. Only one case did not respond. Treatment was carried out for from three weeks to two months. None of the eight cases which responded relapsed over a period of several months
Other types of vascular keratitis—two associated with acne rosacea	8	Symptoms relieved in six cases, but in only one case was there improvement in visual acuity. Two cases did not respond to treatment
Keratitis and iridocyclitis associated with herpes ophthalmicus	1	Rapid relief of symptoms. Visual acuity, which had fallen to 6/18, came up to 6/9 after two weeks' cortisone treatment. No relapse over a period of three months
Superficial punctate keratitis	1	Not improved. This was the case that complained that the drops produced a smarting sensation
Corneal burns:		
Lime	4	Two of the lime burns were fresh cases; in these treatment appeared to have no effect. In the other two treatment was begun late; corneal opacification was lessened and one showed improvement in visual acuity from "hand movements" to 3/60 in two weeks. No improvement in visual acuity in alkali acid burn cases
Alkali	1	
Acid	1	
Disciform keratitis ..	1	Marked and rapid improvement. Area of corneal opacification reduced to a quarter of its former size. Period of treatment required was two weeks. No relapse up to five months after cessation of treatment
Mucous membrane pemphigus with ocular involvement	1	Condition still active, blisters being present on buccal mucous membrane. Symptoms rapidly relieved with clearing of symblepharon from cornea. Owing to clouding of cornea, no improvement in vision occurred in spite of continuance of treatment for a further five weeks after initial relief of symptoms
Corneal ulcers ..	12	In one case, a dendritic ulcer, healing occurred in 48 hours; this case had been resistant to other treatment for three weeks. In three the lesion healed within four days, subjective symptoms having been abolished within eight hours. In eight cases, beyond producing some relief in subjective symptoms, the condition did not appear to be influenced by treatment
Corneal dystrophy ..	1	Objectively, the corneal condition appeared to be unimproved, but the visual acuity increased from 3/60 to 6/60. No further improvement in visual acuity occurred. It seems that local cortisone treatment did not have any beneficial influence
Follicular conjunctivitis	1	Rapid relief of symptoms. Follicles resolved in two weeks. No relapse had occurred up to five months later

Continued from previous column

Diagnosis	No. of Cases	Result
Episcleritis	1	The two areas of inflammation which were present disappeared after five days' treatment. No relapse had occurred up to four months later
Scleritis	4	No improvement in three. In the fourth case raised intraocular tension was associated with the condition; a subconjunctival injection of cortisone brought the tension down from 40 to 29 mm. Hg (Schitz) in eight hours; no myotic was used. Intraocular tension again rose to former level in 48 hours, when it was controlled by myotics
Sympathetic ophthalmia	2	First case came under treatment at beginning of condition on 3/10/50; the keratitis punctata disappeared after three days' intensive local cortisone treatment, and five months later showed no recurrence. The other case, which came under cortisone treatment when condition had been long established, was improved; this case is discussed in detail below
Reaction to retained lens cortex after extracapsular extraction of cataract	2	Rapid removal of symptoms and of injection of affected eye. One case, which had six weeks' treatment, relapsed three months after suspension of treatment. In the other case a permanent good result was obtained after two weeks' treatment
Intraocular infection following extracapsular extraction of cataract	1	On second day after operation wound infection was present and there was pus in anterior chamber. Hourly instillation of cortisone drops begun forthwith. Cortisone ointment used at night. Penicillin injected subconjunctivally daily and every four hours intramuscularly. On fourth day of treatment wound was clean and pus in anterior chamber had been absorbed. It is not possible to estimate what part, if any, cortisone played in achieving this result
Iridocyclitis following intracapsular extraction of cataract	1	Three days after operation the eye which had been operated upon showed marked ciliary injection and vitreous haze. No response to usual treatment. After two subconjunctival injections of cortisone the eye became almost white and clearing of vitreous opacities was noticed
Iridocyclitis	22	In eight, rapid relief of symptoms and much improvement in visual acuity; these were all early cases; none relapsed over a period of six weeks to three months; seven showed some relief of symptoms; seven appeared to be uninfluenced by the treatment. Details of two cases showing value of early cortisone treatment are given below
Eales's disease ..	4	In one case, which before cortisone treatment had been stationary, visual acuity improved from 1/60 to 6/60 in two weeks. Other three cases were uninfluenced by treatment
Exudative choroiditis ..	3	One case had local treatment only; the lesion cleared up, but it is doubtful whether treatment had any effect in bringing about resolution. The other two cases had systemic cortisone treatment as well as local treatment, and are discussed below
Macular exudate and vitreous opacities associated with arthritis in a child	1	Unimproved on subconjunctival injections over two months
Retinal detachment secondary to tuberculous uveitis	1	No improvement in vision or in retinal condition. Eye became white after one month of local cortisone treatment, but again became injected three months later. Local cortisone treatment has been resumed

A survey of the above 83 cases shows that 27 were much improved, 22 were moderately improved, and 34 were unimproved by local cortisone treatment.

In a series of 14 consecutive cataract extractions by one of us there occurred post-operative reactions of an unusual kind, manifested by "red-eye," increased conjunctival secretion, and, in some cases, mild cyclitis. In the next six cases which came for cataract extraction the effect of a prophylactic subconjunctival injection

of cortisone was tried. The injection was given as soon as the operation was completed. In four out of the six cases the post-operative course was uneventful. In the first of the two remaining cases the eye which had been operated upon remained white for six days after the operation; on the seventh day circumcorneal injection appeared. A further subconjunctival injection of cortisone was given, with the result that the eye again became white and no relapse occurred. In the second of these two cases vitreous was lost upon completion of the section and the lens was removed with a vectus. Severe cyclitis developed, and did not yield to a second subconjunctival injection of cortisone on the seventh post-operative day. This series of cases suggests that cortisone may be of value as a prophylactic against post-operative reaction in ophthalmic surgery.

As will be seen, dramatic results were obtained in eight out of nine cases of interstitial keratitis. It may be of significance that in the one case which failed to respond the blood Wassermann reaction was negative (two tests) at the time the cortisone treatment was begun, while in the other eight cases it was positive. This patient had had interstitial keratitis in his other eye 11 years previously, and at that time the blood W.R. was positive before antisyphilitic treatment was instituted.

Details of two cases which show the value of the early institution of the cortisone treatment are as follows.

Case 1. Iridocyclitis

A woman aged 26 was first seen on March 7, 1940, when she had a severe iridocyclitis in her left eye. The visual acuity of the eye was reduced to 3/60. General investigation was negative except for a strongly positive Mantoux reaction to 1/10,000 old tuberculin. She was treated with protein shock produced by intravenous injection of T.A.B., large doses of sodium salicylate by mouth, and 1% atropine drops locally. After six weeks' treatment the condition subsided, with a resultant visual acuity of 6/12. On November 24, 1950, the iridocyclitis had recurred in the left eye. Extensive keratitis punctata was present, and there were inflammatory cells in the vitreous. Vision in the left eye was again reduced to 3/60. Two subconjunctival injections of cortisone, with a day's interval between them, were given, and cortisone drops were instilled every two hours during the day. On November 28 the affected eye had quieted down, the keratitis punctata started to shrink, and the vision had improved to 6/18. On December 4 only vestiges of the keratitis remained, and the vision was 6/12, which, it will be noted, was the degree to which it had reached after the 1940 attack had subsided. The local treatment with cortisone was discontinued on January 9, 1951. When last seen on January 31 there were no signs of a recurrence of the condition, and vision was still 6/12.

Case 2. Iridocyclitis

A man aged 26 was first seen on December 1, 1950. He gave a history that vision had begun to fail eight days previously. Vision in the right eye was 6/18, in the left eye 6/36. Both eyes showed the presence of fine keratitis punctata and vitreous haze. Subconjunctival injections of cortisone were given to both eyes on December 1, and he was put on 1% atropine drops. On December 6 vision in the right eye was 6/12, in the left eye 6/24; subconjunctival injections of cortisone were given to both eyes. On December 13 vision in the right eye was 6/12, in the left eye 6/18; keratitis was much less and vitreous haze had diminished; subconjunctival injections of cortisone were repeated. On December 22 vision in the right eye was 6/9, in the left eye 6/18; media clearer, very little keratitis present; subconjunctival injections of cortisone were repeated. On January 10, 1951, vision in right eye was

6/6, left eye 6/9; no keratitis present and media clear. No relapse had occurred up to February 22.

In four cases, in addition to local treatment, cortisone was administered intramuscularly. Details of these cases are as follows.

Case 3. Sympathetic Ophthalmia

A man aged 41 was first seen on May 10, 1945, when he gave a vague history of some pitch dust having got into his right eye two days previously. A hypopyon ulcer was present in the right eye, in which vision was reduced to appreciation of hand movements. The vision of the left eye was 6/9. The condition did not respond to routine treatment. On May 18 Saemisch's section was performed. The inflammation subsided, leaving a large leucoma in the right cornea. When seen again on September 8 the right eye was injected and vision in it was *nil*; that of the left eye was 6/36. The left eye showed presence of keratitis punctata. Next day the right eye was enucleated. The condition of the left eye continued to deteriorate and intensive routine treatment was carried out.

On October 27 local cortisone treatment of the left eye was begun; the eye became white, but no visual improvement resulted. After the extraction of 10 septic teeth on November 7 the eye flared up again. Intramuscular injections of cortisone, 100 mg. a day, was begun on December 3. The vision was then 2/60. The eye rapidly became white. On December 7 the dose of cortisone was reduced to 50 mg. daily. On the 12th vision was 6/60 and there was a little clearing of vitreous cloud, but from this date gradual deterioration set in, and on January 9, 1951, the vision was 4/60 and the opacification of the vitreous had increased.

Case 4. Recurrent Choroiditis in Both Eyes

This patient was a woman aged 27. On July 26, 1950, her right eye was in a quiescent condition, but the left eye showed recurrence of gross vitreous haze with reduction of visual acuity to appreciation of hand movements. On July 27 local cortisone treatment was begun in the left eye, subconjunctival injections being given every second day for 17 days. Gradual improvement, with slow clearing of vitreous in the left eye, resulted. At the end of this period of treatment the fundus could be clearly seen and the eye was "quiet." Vision of the left eye was only 2/60, as the macula had been damaged.

On August 31 a recurrence in the right eye was demonstrated by the presence of a large active focus in the macular region accompanied by dense vitreous haze. Next day treatment with cortisone tablets (100 mg. daily) was begun. In two days the vitreous of the right eye had become much clearer and the choroidal exudate had greatly diminished. In four days the choroidal exudate could scarcely be seen; after that the vitreous continued to clear more slowly. At the end of two weeks the cortisone tablets were discontinued, and cortisone ointment was substituted, four times daily in both eyes.

On November 4 the condition recurred in the left eye, with gross vitreous haze, and no view of fundus could be obtained; vision was reduced to appreciation of hand movements. Treatment with cortisone tablets was restarted, 25 mg. four times daily, and was continued for four days, after which cortisone intramuscularly was substituted, 100 mg. daily for three days and 50 mg. daily for a further three days; the vitreous gradually cleared, until at the end of seven days' treatment a clear view of the left fundus was obtained and no active choroidal lesion was visible. Treatment was continued with cortisone ointment four times daily.

On December 4 the right eye again relapsed, with the appearance of a large choroidal exudate. On the 6th parenteral treatment with cortisone 100 mg. daily was again instituted. On the 11th the eye had again become quiet and the massive exudate was completely absorbed. Up to two months later no relapse had occurred.

Case 5. Recurrent Choroiditis

A girl aged 15 complained on October 3, 1950, of blurred vision in her left eye, which she had first noticed two weeks previously. Examination showed a large raised area of exudate in the left macular region with cells in the vitreous; vision in the right eye was 6/5, in the left eye 1/60. X-ray films of the chest, Mantoux, and Wassermann reaction were negative. Nose and throat examination revealed septic tonsils, which were removed. On October 9 initial treatments consisted of sulphonamides and intramuscular penicillin while the patient was being investigated.

On October 12 local cortisone treatment (left eye) was substituted. The exudate showed some reduction in size within 12 days, but vision was still 1/60. She was transferred to a general hospital, where parenteral cortisone was given. In four days the area of the exudate had diminished to a quarter of its former size. On November 23 the exudate had completely disappeared, leaving a scar. As was to be expected, central vision in the left eye showed little improvement, coming up from 1/60 to only 3/60.

Case 6. Choroiditis

A man aged 22 was first seen on December 16, 1950, when he gave a history that about a week previously the vision of his left eye had begun to diminish. Vision in the right eye was 6/6, in the left eye 6/36. His left eye showed the presence of keratitis punctata, posterior synechiae, and such gross vitreous opacities that a view of the fundus could not be obtained. The blood Wassermann reaction was negative. X-ray films of the chest did not reveal any abnormality. The Mantoux test with 1:1,000 old tuberculin was negative. Examination of the nose and throat did not reveal any focus of infection. An X-ray film of the teeth revealed an apical abscess at the root of an upper incisor; this tooth was extracted. Locally, the eye was treated with atropine sulphate solution 1%. General treatment consisted of intravenous T.A.B. injections, "sulphatriad" by mouth, intramuscular penicillin, and a course of para-aminosalicylic acid by mouth. On January 6, 1951, the condition was unimproved; vision in the right eye was 6/6, in the left eye 6/36. Intramuscular cortisone was begun, 50 mg. daily for three days; all other treatment, with the exception of local treatment of the left eye with atropine sulphate solution 1%, was suspended. On the next two days the dose was increased to 100 mg. daily. It was then raised to 200 mg. daily for five days. On January 17 the vision of the left eye had improved to 6/9 and the opacification of the vitreous showed diminution; reduction in dosage was begun on this date, the quantity injected being reduced by 25 mg. every third day. On February 1, the date upon which cortisone treatment was suspended, the vision of the left eye was 6/5, only slight vitreous haze was present, and a clear view of the fundus could be obtained; a large area (about three disk diameters) of "healed choroiditis" was observed in the upper nasal quadrant.

Further Work

Fifty other cases of various ocular diseases have been treated by local cortisone therapy, in the main with similar results to those described above.

One case of sympathetic ophthalmia treated with intramuscular cortisone is of particular interest, and, although the case is not yet completed, a short outline is here given.

On January 15, 1951, a boy aged 11 was admitted to hospital under the care of Dr. Desmond Douglas. Ten days previously his left eye had been struck by a stick. There was a penetrating wound in the left cornea in which iris tissue was incarcerated. The prolapsed iris was excised and the corneal wound was covered with a conjunctival flap. On January 26 he was discharged from hospital; the left eye was "quiet" and the visual acuity was: right eye

6/6 and left eye 6/9. He returned for observation on February 9; slit-lamp examination of the left eye showed oedema of the corneal epithelium.

On February 19 the visual acuity of the left eye had fallen to 6/18, the margins of the optic disk were blurred, and cellular deposits were present on the posterior corneal surface; the right eye showed early bedewing of the corneal endothelium and cellular deposits on the posterior corneal surface. The boy was readmitted to hospital. The eyes were treated locally with atropine; general treatment consisted of "aureomycin" and sulphatriad by mouth and penicillin by intramuscular injection. On February 21 the left eye was enucleated; subsequent pathological examination of the excised eye showed the presence of the changes typical of sympathetic ophthalmia; the visual acuity of the right eye at that time was 6/9, and treatment with intramuscular injections of cortisone was begun, 100 mg. being given daily. On February 23 slit-lamp examination showed that the endothelial bedewing on the posterior surface of the right cornea had disappeared. On the 24th gradual reduction in the dose of cortisone was begun. On cessation of the cortisone treatment on March 10 visual acuity of the right eye was 6/6. Slit-lamp examination did not show the presence of any inflammatory signs. On March 21 slit-lamp examination showed a recurrence of endothelium bedewing of the cornea, but the visual acuity of the right eye was still 6/6. Intramuscular cortisone was reinstituted, 100 mg. daily for three days. In addition, cortisone was administered subconjunctivally every second day. On March 24 the endothelium bedewing was reduced in amount and the dosage of intramuscular cortisone was reduced to 75 mg. daily for three days and the subconjunctival injections of cortisone were discontinued. On the 30th the dosage of intramuscular cortisone was reduced to 25 mg. daily, and this dosage has been continued up to April 4. The right eye does not now show the presence of any inflammatory signs. It is intended to maintain the patient on small doses of intramuscular cortisone for a further 10 days, and a careful watch will be maintained for the first signs of a relapse.

This case will be reported upon fully later. It seems probable that in sympathetic ophthalmia cortisone treatment may have to be continued for a considerable period after signs of activity have disappeared (as in the cortisone treatment of rheumatic fever).

Discussion

The impression gained from this investigation is that in cortisone we have a very much more powerful agent for the control of allergic reactions in the eye than has been available heretofore. As a number of eye conditions have an allergic basis, cortisone should be a very valuable therapeutic agent in their treatment. If ocular inflammatory reaction can be kept under control while the basic cause is being dealt with, or until it ceases to operate, permanent damage to the eyes may be avoided. Cortisone does not appear to have any curative effect upon the underlying disease, and hitherto irreversible pathological changes remain uninfluenced; therefore it should be stressed that the greatest benefit from the hormone treatment will be obtained when it is begun early in the course of a case. It is inadvisable to delay the use of it while prolonged or time-consuming investigations are being carried out, or while other treatments are being given a trial. As might be expected, the good effects of local cortisone are confined to conditions involving the anterior segment of the eye. In those of the posterior segment amenable to cortisone treatment, its parenteral use is indicated.

The rapidity with which massive exudates resolve after the institution of parenteral treatment is astonishing, but, as is often the case, if the cause has not been

removed relapses are prone to occur if the treatment is stopped.

It was noted above that the local use of cortisone produced disappointing results in scleritis. It seems to us that for this condition it is necessary to give cortisone parenterally. This suggestion is supported by the fact that a case of scleritis (not described in this paper), associated with rheumatoid arthritis which was being treated (by Professor Henry Moore and Dr. Mervyn Abrahamson) with intramuscular injections of 100 mg. of cortisone daily, cleared up completely in five days. The scleritis had previously been resistant to the accepted forms of treatment. On withdrawal of the cortisone, both the rheumatoid arthritis and the scleritis relapsed, but were again controlled upon the reinstitution of the treatment.

Summary

Cortisone has been used in the treatment of a variety of eye conditions (143 cases in all), mostly administered by subconjunctival injection or in the form of drops. Interstitial keratitis was particularly benefited, and iridocyclitis also improved rapidly in most cases. Treatment of two cases of sympathetic ophthalmia with systemic cortisone was successful. It is concluded that cortisone is very valuable in the control of allergic reactions in the eye, but has no effect on any underlying disease which may be the basic condition.

We express our thanks to our ophthalmological colleagues who gave us access to their cases for the purpose of this investigation.

REFERENCES

- Hench, P. S., Kendall, E. C., Slocumb, C. H., and Polley, H. F. (1950). *Arch. intern. Med.*, **85**, 545.
Henderson, J. W. (1950). *Proc. Mayo Clin.*, **25**, 459.
Koff, R., Rome, S., Kasper, R., Commons, R. R., Button, R., and Starr, P. (1950). *J. Amer. med. Ass.*, **144**, 1259.
Moore, H. L., Jessop, W. J. E., and O'Donovan, D. K. (1951). *Irish J. Med. Sci.*, **65**, 95.
Steffensen, E. H., Olson, J. A., Margulis, R. R., Smith, R. W., and Whitney, E. L. (1950). *Amer. J. Ophthalm.*, **33**, 1033.
Woods, A. C. (1950). *Ibid.*, **33**, 1325.

TOPICAL CORTISONE IN TREATMENT OF SYPHILITIC OCULAR DISEASE

BY

GORDON O. HORNE, F.R.C.P.Ed.

Director, Department of Venereal Diseases, General Infirmary, Leeds

Jones and Meyer (1950), Woods and Wood (1950), and Leopold *et al.* (1951) have studied the action of A.C.T.H. and cortisone on experimental ocular inflammation. Reports of clinical trials in ocular diseases with A.C.T.H. have been made by Blake *et al.* (1950), Gordon and McLean (1950), Mann and Markson (1950), McLean (1950), and Olson *et al.* (1950); with A.C.T.H. and cortisone by Harvey *et al.* (1950) and Woods (1950); and with cortisone by Henderson (1950), Henderson and Hollenhorst (1950), Fitzgerald *et al.* (1951), Leopold *et al.* (1951), Olsen *et al.* (1951), Scheie *et al.* (1951), Steffensen *et al.* (1951), and Thygeson and Fritz (1951).

The indications for the use of these hormones were discussed by these authors in the light of their relatively short experience, and all were agreed on the dramatic effects in various inflammatory and exudative conditions of the eye, especially in those in which hypersensitivity plays a part. It appeared that the earlier the hormone was administered in the course of the disease the more dramatic and beneficial were the results. After the end

of treatment relapses occurred in some conditions, but readministration of the hormone controlled them.

Woods (1950) described the effect of topical cortisone as being as dramatic in some cases as when cortisone was used parenterally, and summarized its advantages as being: "(1) That much smaller amounts of the hormone are required, (2) that the depressant action of exogenous cortisone on the adrenal cortex might be avoided, and (3) that any effect obtained by local treatment might be more permanent, since the normal secretion of cortisone by the adrenal cortex might not be seriously interfered with by the instillation of small amounts of exogenous cortisone." He instilled one drop of cortisone suspension (25 mg./ml.) into the eye every hour during the day and every two hours during the night, but had to dilute the suspension 1:4 in two out of eight cases on account of local irritation. Harvey *et al.* (1950) found that in most of their 12 cases local instillation of cortisone was just as effective as parenteral administration of either A.C.T.H. or cortisone, but that the former method did not influence vitreous exudation or changes in the posterior uveal tract.

Steffensen *et al.* (1951) listed the conditions responding to the instillation of cortisone among 24 cases of "anterior-segment" eye disease. Thygeson and Fritz (1951) treated 14 cases of phlyctenular keratoconjunctivitis successfully with cortisone instilled into the eye or injected subconjunctivally. Leopold *et al.* (1951) listed the conditions responding to cortisone administered parenterally, by local instillation, and by subconjunctival and retrobulbar injection, based on the treatment of 142 eyes.

As most cases of inflammatory and exudative ocular disease in patients with syphilis behave as if they were manifestations of "hypersensitivity," A.C.T.H. and cortisone would be expected to be of value in their management, but the literature on the use of these hormones in syphilitic ocular disease is small. Fitzgerald *et al.* (1951) reported rapid improvement (and no relapse after four months' observation) with parenteral cortisone in a case of acute syphilitic granulomatous uveitis. Reports on cases of interstitial keratitis have been made by Woods (1950) (one case, advanced and with corneal necrosis); Fitzgerald *et al.* (1951) (one case, with chronic non-granulomatous uveitis); Leopold *et al.* (1951) (four cases, no details given); Olsen *et al.* (1951) (one case, "atypical"); and Scheie (1951) (three cases, one of which was advanced with the "salmon patch" type of vascularization).

It is difficult from these reports to assess the results in interstitial keratitis in view of the small number of cases, the differing methods of administration of the hormone, and the limited data provided, but the results on the whole were disappointing. Greater success appeared to be obtained when the hormone was used early in the course of the disease and for a prolonged period.

Clinical Trial

In this investigation cortisone has been used in five cases of syphilitic ocular disease. All the patients were admitted to hospital for treatment. The drug was used topically in a strength of 5 mg./ml. of normal saline, one drop being instilled three-hourly day and night (except where otherwise stated). Only brief clinical details are given, as the objects of this communication are (1) to confirm the beneficial effects of topical cortisone; (2) to indicate that it has an application in ocular