ON THE THERAPEUTIC VALUE OF TOPICAL CORTISONE ACETATE IN POST-OPERATIVE AND POST-TRAUMATIC IRIDOCYCLITIS.

a

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by

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AIM AND SCOPE OF THESIS

The aim and scope of this thesis is to record and discuss the results of an investigation into the therapeutic value of topical cortisone acetate in the treatment of post-operative and post-traumatic iridocyclitis.

INTRODUCTION

The advantages and the limitations of cortisone acetate as a therapeutic agent in acute inflammatory conditions have been widely discussed in medical literature during recent years. It is recognised that the drug has a powerful action in blocking the exudative features of any inflammatory tissue response. It is equally clear that this action is a temporary one continuing only so long as the drug is administered, that cortisone does not remove the cause of any inflammatory reaction, whether it be bacterial, anaphylactic, allergic, or traumatic, (Duke Elder, 1951a, and Woods 1950 and 1951a), and that consequently, in the treatment of inflammatory disease, cortisone generally has to be continued until the aetiology of

the condition has been discovered and removed, or until spontaneuous healing has occurred. (François 1952.)

Since the eye is functionally dependent on the transparency of its media, and since the occurence in occular tissues of an exudative reaction, of a degree which might be of little moment in another situation, may result in considerable permanent loss of vision, the fact that cortisone can frequently protect ocular tissues from the more damaging effects of such an exudative reaction, is sufficient to make the drug a potentially valuable therapeutic agent in inflammatory conditions of the iris and the ciliary body. Certain limitations on its value are however apparent. Firstly, in many cases of iridocyclitis, despite extensive investigation, the aetiology remains unknown and therefore unremedied. When cases of this type are treated with cortisone, the normal pattern of recurrences tends to take place when the drug is withdrawn. Secondly, in individual cases of iridocyclitis the duration of attack shows wide variation, and since the application of cortisone, in the acute stage of an attack, may rapidly suppress all inflammatory signs, difficulty can arise in assessing the end point of spontaneous healing.

Relapses are therefore frequent when treatment is discontinued. Nevertheless, in a disease which is normally subject to remissions, these considerations do not negative the value of the drug. At the same time they suggested to the author that in the treatment of iridocyclitis, cortisone might be expected to have its ideal application in cases in which the aetiology was known and could be removed, or was known and could be expected to be temporary. It was felt that iridocyclitis occurring in post-operative and post-traumatic cases provided an example of non-granulomatous iridocyclitis, in which the inflammatory signs could, in the absence of other demonstrable aetiology, be regarded as bearing some direct relationship to physical trauma, and as such could be expected to be temporary. It was decided therefore to investigate the therapeutic effect of cortisone acetate in a group of cases of this type.

PART I.

MODE OF ACTION OF CORTISONE AND ITS RELATIONSHIP TO POST-TRAUMATIC TISSUE RESPONSES.

Section 1. Tissue Response to Injury.

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PART I

Mode of Action of Cortisone and its Relationship to Post-traumatic Tissue Responses.

Two factors seemed of particular importance in considering the possible effects of cortisone in post-operative and post-traumatic iridocyclitis. The first was the state of the tissues in the immediate post-operative or post-traumatic period - in other words, the problem of tissue response to injury - and the second was the mode of action of cortisone.

Section 1.

Tissue Response to Injury.

Pickering (1952), discussing the mechanism of inflammation and the general background of tissue responses to injury, stated that tissues react to injury by either an "Immediate" or a "Delayed" response. The "Immediate" response is the Triple Response of Lewis - a local red reaction due to dilatation of minute vessels, a wheal due to their increased permeability, and a surrounding flare due to arteriolar dilation. This type of response

appears to be unaffected, or very little affected, by cortisone. Lewis had found his Triple Response to be identical with the histamine reaction, and he suggested that all tissue responses to injury were due to the release of an histamine-like substance from the injured cells. In cases where he found that the tissue responses to injury were delayed, he postulated an unexplained delay in the production of this histamine-like substance. (Lewis, 1927.) Later workers, however, found the "Delayed" response to injury to be different from the histamine type of response in having, as well as dilatation of small vessels and an increase in their capillary permeability, an out-pouring of cells, which were mostly polymorphonuclear leucocytes, macrophages and lymphocytes. (Pickering, 1952.) Menkin (1940a), had shown that the cell free fluid from an inflammatory exudate contained a substance, associated with the pseudo-globulin fraction of the exudate, which was capable of increasing capillary permeability and attracting polymorphonuclear leucocytes. He called this substance leucotaxin, suggested that it might be a simple polypeptide, and stated that its

main properties did not resemble those of histamine. Later, a number of polypeptides were found to have effects similar to leucotaxin and this, along with the fact that the type of cell predominating in inflammatory exudates varies in different types of injury, suggested that leucotaxin was not one substance, but a group of polypeptides possessing similar properties.

Duthie and Chain (1939) had demonstrated that the biological actions of Menkin's leucotaxin and the chemical properties of a polypeptide were possessed by peptic digests of fibrin. In 1945 Peters found that when epidermal cells were injured a protease was released, and Cullumbine and Rydon (1946) showed that digests produced by the action of the above skin protease on fibrin, contained a substance resembling leucotaxin. These investigations were extended by Spector (1951), who produced considerable experimental evidence in support of his general conclusion that when tissues are injured, enzymes (proteases) are released, which act upon tissue and plasma proteins to produce a number of peptides, collectively equivalent to Menkin's

leucotaxin. These peptides cause (a) increased capillary permeability, (b) polymorph emigration from the vessels, and (c) swelling of the vascular endothelium. They are mostly of chain-length 14 to 8 amino-acid residues. Chain-lengths of 5 are also found, and these have no appreciable effect on capillary permeability. It seems likely that following injury a number of peptides of different chain-lengths may be present, that each produces some, or all, of the above effects, in varying degree, and that inflammatory responses consequently vary in intensity.

Section 2.

Mode of Action of Cortisone.

The main effects of topical cortisone on inflamed tissues are well known. Capillary permeability is decreased, and cellular exudation reduced. In addition, the formation of granulation tissue, the fibroblastic reaction in healing, and the formation of new vessels are all inhibited. (Duke Elder, 1951b). The exact mechanism by which these effects are brought about has been somewhat uncertain. Woods and Wood (1951) stated that the effect of cortisone on ocular inflammation was probably due to a direct action on the local mesenchymal tissue. Duke Elder, (1951b) listing the effects of cortisone on inflamed tissues, stated "at which level these effects occur is unknown, - presumably, however, the hormone becomes effective at the tissue level." Woods (1950,c) quoted Turner and Hollander's suggestion that the local changes produced by cortisone were based primarily on an alteration of the mucopolysacharides of the ground substance, which was manifested by accumulation of hyaluronic acid and supression of chondroitin sulphate.

Jones and Meyer (1950) had reported that, in rabbits, cortisone inhibited corneal vascularisation following chemical injury, and they suggested that the effect was due to (a) blocking of a chemotactic influence exerted by the injured tissues on the limbal capillaries, or (b) the prevention of the response of endothelial cells to such a chemotactic influence. Kellgreen (1952) came to similar conclusions, stating that it was uncertain whether the corticosteroids prevented damaged tissues from liberating substances normally responsible for inflammatory and allergic reactions, and the processes of healing, or whether they neutralised or destroyed these substances, or protected the intact tissues against their action. He concluded that their main action must be a local one in the tissues themselves.

Woods (1952b) postulated that the ability of cortisone to inhibit neovascularisation might be connected with its inhibitory effect on endothelial proliferation, which had been noted by Newell and Dixon (1951) and confirmed by Ashton and Cook (1951a). He quoted three possible modes of action of cortisone suggested by Kinsell, viz:-

1. Acts by freeing lysins from eosinophils, large mononuclears and other cells.

2. Acts at the level of the cell membrane, placing a block between the toxin and the cell protoplasm.
3. Acts within the cell from some action on an enzyme system.

He concluded, however, that all that could be said with certainty was that the cortico- steroids act at the cell level through some as yet unknown action upon the mesenchymal tissue.

Steen (1951a) reported that when cortisone was added to tissue cultures there was no suppression of growth or inhibition of mitotic activity in either fibroblasts or epithelial cells, even when the concentration of cortisone was twenty-five times greater than usual therapeutic levels. Neither did the serum of patients receiving intensive systemic cortisone treatment have any inhibitory effect on growth in tissue cultures. He therefore concluded that the undoubted inhibitory effect of cortisone upon fibroblastic activity, which had been observed clincally and experimentally, (Duke Elder and Ashton 1951), must be explained by some mechanism acting at the cellular level in the living organism. He observed that, in the presence of living cells, cortisone acetate crystals combined with glucose to

form a new and soluble compound, which he called cortisone glucoside. He suggested that in this way insoluble cortisone acetate became available to inhibit fibroblastic activity.

Menkin (1940b) had found that the increased capillary permeability produced by an inflammatory exudate, or by leucotaxin, could be wholly or partly inhibited by an extract from the adrenal cortex. He had also noted that in the early stages of a tissue response to injury the P.H. of the inflammatory exudate was alkaline, and the cells present were mainly polymorphs, while in the later and more chronic stages of an inflammatory reaction the P.H. of the exudate gradually became acid, and polymorphs were replaced by macrophages. (Menkin 1940a). Continuing this work, he showed that cortisone acetate suspension could inhibit the increased capillary permeability and outpouring of cells induced by leucotaxin or alkaline exudates, while it did not appreciably inhibit increased capillary permeability and cellular exudate induced by acid exudates. (Menkin 1951a). He attributed the increase in capillary permeability which occurred in the presence of acid exudates, to

a substance which he isolated from the pseudo-globulin-albumin fraction of the exudate, and called exudin. (Menkin 1951b). It is of considerable interest that he found the effects of exudin, though uninhibited by cortisone, to be inhibited by adreno-corticotrophic hormone (A.C.T.H.) (Menkin 1951c).

There has been some variation of opinion concerning the actual effect of cortisone on capillary permeability. Duke Elder, (1951a), stated that capillary permeability in an inflammatory process was decreased by cortisone. Woods (1952a), felt that there was insufficient evidence that cortisone acted through depressing the local permeability of capillaries. Von Sallman and others(1952a) investigating the effect of cortisone on wound healing in rabbits, found the permeability of the blood aqueous barrier to fluoresceine only slightly less in cortisone treated rabbits than in untreated controls, while McDonald and others (1953) found that cortisone had no effect, in the normal eye, on the permeability of the blood aqueous barrier to fluoresceine. McDonald and others (1953) also found that the permeability of the inflamed eye to strepotmycin was not significantly reduced by cortisone. Menkin (1951a)

had reported that commercial cortisone acetate (Merck) in saline suspension and containing an aqueous vehicle and 1.5% Benzyl alcohol, actually increased capillary permeability in normal tissues; but he showed that this effect was caused by the aqueous vehicle of the preparation and occurred especially when small doses were employed. In greater concentrations, where less vehicle was required, the effect on capillary permeability was negligible. In addition - as already noted - he observed that cortisone acetate suspension did inhibit the increased capillary permeability induced by alkaline exudates or leucotaxin; whereas it did not appreciably affect increased capillary permeability induced by acid exudates. Duke Elder (1951c) found that capillary permeability was increased by leucotaxin and hyaluronidase, and that these substances were inhibited by cortisone. It would seem, therefore, that although cortisone has no direct action on capillary permeability in normal tissues, it can, in acutely inflamed tissues by virtue of its inhibitory effect on leucotaxin, prevent the increase of capillary permeability and cellular exudation, which would normally occur.

Discussion.

Inflammation is the basic local reaction of the body tissues to irritation and, in any given instance, its general features are modified only by the nature of the irritant factor inducing inflammation and the anatomical site of the inflammatory process. In the group of cases about to be considered the initial irritant factor is trauma - operative or otherwise - and since this is a temporary phenomenon, it may be expected in the absence of virulent infection or allergens, to invoke a temporary and limited tissue response. In the majority of ocular post-operative cases - where trauma has been elective - and in some post-traumatic cases, the tissue response to injury exhibits minimal inflammatory features, which can be regarded as being closely related to the processes of defence and repair. In a proportion of cases however, perhaps in response to co-incident or superimposed allergy, the exudative features become prolonged and over-exuberant, are harmful rather than reparative, and iridocyclitis supervenes. The anatomical site of this inflammatory

process is of peculiar importance. Visual function is dependent on transparency of the ocular media, and if function is to be preserved it is essential that the exudative features of an excessive inflammatory reaction be controlled. Consideration of the mode of action of cortisone suggests that by virtue of its ability to suppress acute inflammatory exudates, this drug should be a valuable therapeutic agent in the acute stages of post-operative and post-traumatic iridocyclitis.

PART II.

PRESENTATION OF CASES.

Part II.

Presentation of Cases.

The present survey was undertaken in order to make a personal assessment of the therapeutic value of cortisone acetate in the treatment of post-operative and post-traumatic iridocyclitis.

Section 1.

Route of Administration of Cortisone.

In 1951 and 1952, at the commencement of the investigation, cortisone was still in short supply in this country. The topical route of application offered an economical method of using the drug and there was consequently a strong inducement to ascertain what degree of control of ocular inflammation could be achieved by this method. In addition, it was obvious that if topical application should prove of sufficient value, the drug would have a potentially wider sphere of usefulness, since, the detailed clinical supervision necessarily attendant on systemic administration could be avoided. Opinion varied concerning the degree of intraocular penetration of cortisone which was attainable by

topical therapy, though, of the various methods of topical application, the subconjunctival route appeared to offer some advantages. Leopold and others (1951a) had shown that cortisone introduced by subconjunctival injection could penetrate the intraocular fluids in detectable quantities. They found that specimens of aqueous taken from rabbits fifteen minutes to six hours after cortisone treatment showed traces of cortisone following subconjunctival injection, but no traces after drops or retrobulbar injection. (Leopold and others 1951b). In addition, at any given time, the concentrations of cortisone remaining in the aqueous were higher after subconjunctival administration than after drops or retrobulbar injection. The use of a wetting agent, such as Zephiran 1/3,000, in place of saline as a diluent for drops, somewhat improved the concentrations achieved by this method (1951c).

Although Woods, in 1950, stated that cortisone, administered topically, had not been demonstrated to have any effect on exudates on the vitreous, some later workers were of the opinion that topical cortisone, and particularly subconjunctival cortisone, was effective in the posterior segment of the globe.

Gordon and others (1951) felt that topical cortisone encouraged the absorption of vitreous exudates, and McLean and others (1951), discussing the treatment of choroiditis and optic neuritis with subconjunctival cortisone, were of the opinion that enough absorption took place to affect the posterior portion of the globe. Agatson (1952) stated that in his experience with uveitis, cases which failed to respond to subconjunctival injection also failed to respond to intramuscular cortisone.

Leopold and Maylath (1952), working with rabbits, found that subconjunctival cortisone produced higher concentrations in the aqueous, and in the vitreous, than did drops, and that it did so more rapidly. Twenty-four hours after the administration of subconjunctival cortisone there had been a greater fall of concentration in the anterior chamber than in the posterior chamber, and after forty-eight hours there was still a concentration in the vitreous of thirty gamma per millilitre. In rabbits, the levels reached and maintained in both aqueous and vitreous, when subconjunctival injections were given once daily, were comparable with intramuscular administration of 100 mg. daily. Similar concentrations were obtained

whether 1.25 mg. or 12.5 mg. were given subconjunctivally, but disappearance was slower with injections of 12.5 mg. No advantage in the rate of disappearance was found with doses of 25 mg. These figures suggested that therapeutic effects comparable with those of systemic administration might possibly be achieved by the use of subconjunctival injection though, in the human eye, there would obviously be difficulty in continuing daily injections for a prolonged period.

From the literature reviewed it appeared that intraocular concentrations following subconjunctival injection were likely to be higher and more prolonged than those achieved by instillation of cortisone into the conjunctival sac. In addition, administration of cortisone by injection offered the opportunity of knowing exactly how much cortisone each patient received, an important point, since, for a considerable part of their treatment, cases were to be supervised as out-patients. Retrobulbar injection did not seem to offer any advantage in intraocular penetration, and was at any rate considered unsuitable for prolonged treatment. The subconjunctival route of administration was therefore chosen for the treatment of all cases in the series.

Section 2.

Selection of Cases and Method of Treatment.

Thirty-two cases are presented. They were first seen at the Glasgow Eye Infirmary between September, 1951 and November, 1953.

The cases selected were those in which iridocyclitis, having occurred for the first time within twelve weeks of intraocular operation or injury, appeared to bear a direct relationship to trauma. Four cases were however included in which it was thought that cortisone might be beneficial, although iridocyclitis had appeared after a longer interval. These were relapsed cases, in which the original attack of iridocyclitis had occurred in the immediate post-operative or post-traumatic period. Only severe and moderately severe cases of iridocyclitis were included. Each case, at the commencement of treatment, showed marked ciliary injection along with either aqueous flare or keratic precipitates. In addition, one or more of the following signs were present - dilated iris vessels, posterior synechiae, exudates in the anterior or the posterior chamber.

All cases were treated with subconjunctival injections of a saline suspension of cortisone acetate, 25 mg. to the cc. (Cortone Acetate, Merck & Co., U.S.A.). Injections were given with a number 20 gauge hypodermic needle, using a 1ml. all glass syringe. Satisfactory local anaesthesia was obtained by instilling one drop of a 5% solution of cocaine hydrochloride at minute intervals for five minutes preceding injection. A few patients complained of discomfort in the eye during the first hour after the injection, others experienced relief, and the majority noticed no change.

In each case, dosage, frequency of injection, and duration of treatment were controlled by clinical indications and did not therefore conform to a rigid plan. In general, patients received a first injection of 0.4 ml. (10 mg.) of cortisone and subsequent injections of 0.2 ml. (5 mg.). The more severe cases received two injections of 0.4 ml. before reduction to 0.2 ml. Treatment was divided into three phases as follows - a) Intensive - during which injections were given first every three days, and then every five days until the more acute exudative features had subsided. b) Weekly - during which injections were given every seven days

until all inflammatory signs had disappeared, or until there had been no improvement for several weeks.
c) Withdrawal - during which the interval between injections was gradually increased to ten, fourteen, twenty-one and twenty-eight days, and cortisone was slowly withdrawn. This rate of withdrawal may have been over cautious, more recent experience suggesting that it might, with safety, have been curtailed in some instances.

In each case a mydriatic was instilled three times daily initially, with gradual reduction to once daily as the interval between the cortisone injections was extended. Mydriasis was generally maintained for several weeks after cortisone had been withdrawn. The following mydriatics were employed: gutt. atropine sulphate 1%, gutt. hyoscine hydrobromide ¼%, and gutt. lachesine 1%. The variation in choice of mydriatic is discussed in a later section.

The following investigations were carried out in each case:- Wasserman reaction, Gonococcal fixation test, Mantoux skin test, and X-ray of chest, sinuses and teeth.

Antibiotics were administered locally and/or systemically where there seemed a possibility of

infection in the eye, or where there was an indication in the general condition.

Section 3.

Post-operative Cases.

This group consists of twenty-one cases which developed iridocyclitis after a variety of intraocular operations. Iridocyclitis appeared within four weeks of operation in twelve cases, within eight weeks of operation in one case, and within twelve weeks of operation in three cases. Four of the five remaining cases developed iridocyclitis between the sixth and the twelfth post-operative month. In the fifth case iridocyclitis did not occur until two and a half years after operation. The delay between the onset of iridocyclitis and the commencement of cortisone treatment was fourteen days or less in sixteen of the cases, and in eleven of these it was seven days or less. In five cases the delay was between fourteen and thirty-one days.

Sixteen cases occurred after cataract extraction, two after corneo-scleral trephine, one after iridectomy, one after iridotomy, and one after combined iridotomy and capsulotomy. The sixteen cases of cataract extraction included nine senile cataracts, five diabetic cataracts, one secondary and one congenital

cataract. (Table 1.) The ages of the patients varied from seven to seventy-eight years. Among the senile cataracts there were four patients in the eighth decade, two in the seventh decade and three in the sixth decade. In the diabetic group, one patient was in the eighth decade, two in the seventh, one in the fifth, and one in the second. The patient with secondary cataract was forty-two years of age and the case of congenital cataract seven years of age.

The Senile Cataracts: (Table 2.)

Five of the nine senile cataracts (cases 1,2,3, 4 and 5) showed a good response to cortisone and achieved clinical cure of iridocyclitis, but case 5 later developed low-grade iridocyclitis in the unoperated eye. Two cases showed a good initial response to cortisone, but of these, case 6 failed to continue treatment so that follow up was inadequate, and case 7 relapsed. Two cases responded poorly to cortisone.

Clinical cure of iridocyclitis was obtained in cases 1 - 5. Four of these were extra-capsular extractions and one was an intra-capsular extraction. Vitreous loss had occurred at operation in three of

TABLE 1.

POST-OPERATIVE CASES.

Type of Operation.		Number of Cases.	
Cataract Extractions	Senile	9	16
	Diabetic	5	
	Secondary	1	
	Congenital	1	
Trephine.			2
Iridectomy.			1
Iridotomy.			2
	Total		21

TABLE 2.

THE SENILE CATARACTS.

Case No.	Sex	Age (years)	Type of Extraction	Total Cortisone (mg.)	No. of Injections	Period of Treatment (weeks)	Result	Follow up (months)	Final V.A.
1	M	60	Extra	80	14	17	Cured	20	$\frac{6}{6}$
2	M	68	Extra	115	22	29	Cured	24	$\frac{6}{6}$
3	M	59	Extra	50	8	8	Cured	30	$\frac{6}{9}$
4	M	54	Intra	65	12	12	Cured	$8\frac{1}{2}$	$\frac{6}{24}$
5	F	77	Extra	110	21	22	Curedx	$29\frac{1}{2}$	$\frac{6}{18}$
6	F	71	Extra	45	8	8	Im-proved	-	P.of L.
7	F	78	Extra	195	35	41	Re-lapsed	$15\frac{1}{2}$	$\frac{6}{12}$
8	M	51	Extra	115	21	21	Unim-proved	30	$\frac{6}{18}$
9	M	76	Extra	130	23	40	Unim-proved	6/	P.of L.

Extra - Extracapsular.
Intra - Intracapsular.
x - Iridocyclitis occurred in the second eye.
/ - Patient died of intercurrent disease.
P.of L.- Perception of light.

the extra-capsular extractions and in the single intra-capsular case, which was a vectis extraction. At the commencement of treatment each case showed marked ciliary injection with heavy endothelial bedewing and aqueous flare. In cases 1,2, and 3 the presence of exudates in the anterior chamber, or the vitreous, precluded any appreciation of fundus detail, while in case 4, the position of the optic disc could just be made out through vitreous haze and floaters. Numerous fine K.P. and dilated iris vessels were present in the latter case, and K.P. were probably present in cases 1 and 3, though bedewing and striate keratitis prevented their detection till a later date. Cases 1 and 3 improved very rapidly, probably because their inflammatory signs were particularly marked in the anterior segment of the globe. In case 3, a dense gelatinous exudate in the anterior chamber disappeared in the first twenty-four hours of treatment. In both cases ciliary injection, keratitis, bedewing and flare, were greatly reduced within six days. Case 1 showed considerable separation of the lips of the section at the commencement of treatment, but the use of cortisone did not appear to interfere with the eventual closure

and healing of the wound. This finding is in agreement with the observations of Duke Elder (1951d) and of Ashton and Cook (1951b). The former noted that although in highly vascularised tissues cortisone delayed the healing process, this effect was less obvious in the avascular cornea. The latter were of the opinion that in the cornea any deleterious effect of cortisone on epithelial growth was not great. Case 4 showed gradual but very steady improvement throughout treatment, while case 2 made little or no progress for two weeks, and then improved rapidly. In all four cases, the main absorption of vitreous exudates began about the end of the fourth week of treatment, and thereafter proceeded steadily. The most marked improvements in visual acuity occurred after the fourth week. Final visual acuities were 6/6 partly in cases 1 and 2, 6/9 partly in case 3, and 6/24 in case 4, in which the operated eye was known to have been partially amblyopic.

Case 5, a woman of 77 years, achieved clinical cure of iridocyclitis and retained visual acuity of 6/18 in the operated eye, but later developed low-grade iridocyclitis in the unoperated eye. In this case, vitreous loss and rupture of the lens capsule had

occurred at an attempted intra-capsular extraction in the right eye. On the eighteenth post-operative day a moderate degree of iridocyclitis developed. Sixteen days later the inflammatory signs became more severe, there being marked ciliary injection, considerable endothelial bedewing, heavy aqueous flare, dilated iris vessels, and a few fine K.P. A hazy view of the optic disc and retinal vessels could be made out, though there were large vitreous exudates and the visual acuity was limited to appreciation of hand movements. Subconjunctival injections of cortisone were commenced, and were attended by rapid improvement in the first ten days. By the end of four months treatment, pigmented K.P. were the only remaining signs of iridocyclitis, and the visual acuity was 6/18. Cortisone was withdrawn two months later.

In the follow-up period both eyes were examined by slit-lamp microscopy at each visit. For ten months there was no evidence of activity, but at the end of this period (i.e. 16 months after operation) iridocyclitis developed in the left (unoperated) eye. Ciliary injection, endothelial bedewing, and many small and medium-sized grey K.P. were present. The vitreous was hazy, and corrected visual acuity had

fallen from 6/24 to 6/60. Subconjunctival injections of cortisone were started in this eye. Gradual improvement followed, and at the end of two months iridocyclitis was fairly well controlled, though faint endothelial bedewing persisted and there were many pigmented K.P. Cortisone was withdrawn two and a half months later. The condition remained unchanged for six months but at this point sub-acute secondary glaucoma developed. Neither miotics nor cortisone reduced the intra-ocular pressure and after a few days acute glaucoma suddenly supervened. A broad iridectomy was carried out, and subconjunctival cortisone was given for two weeks post-operatively, without recurrence of iridocyclitis or of glaucoma. Two months later lens opacities had increased and the visual acuity was reduced to counting fingers at 1 metre.

Throughout the whole of this period the condition of the right eye remained unaltered.

Case 6 showed a good initial response to cortisone but follow up was inadequate. Iridocyclitis occurred after an extracapsular extraction, at which there had been vitreous loss. The patient left hospital ten days after operation and failed to report to the out-patient dispensary until eight weeks had elapsed.

She was then found to have marked ciliary injection, superficial and deep vascularisation of the upper third of the cornea, diffuse endothelial bedewing, striate keratitis, a heavy aqueous flare and numerous medium-sized fresh K.P. The iris was drawn up and attached to a secondary pupillary membrane. Ophthalmoscopy revealed no red reflex, but projection of light was accurate. She was readmitted to hospital, and after four weeks' treatment with cortisone all the exudative features, with the exception of a faint aqueous flare and a few pigmented K.P., had disappeared. A gap had appeared in the pupillary membrane, and a small area of red reflex could be seen. At this stage the patient was allowed home and once more failed to return as an out-patient, despite repeated enquiries. The visual acuity on dismissal was limited to perception of light, but capsulotomy at a later date might have produced improvement.

Case 7, a woman of 78 years, relapsed after having shown a good response to cortisone. Iridocyclitis developed eleven months after an extracapsular extraction at which there had been vitreous loss. The condition failed to respond to routine methods of treatment and eleven days after

its commencement, marked ciliary injection, endothelial bedewing, heavy aqueous flare, fine grey K.P. and dense vitreous haze were present. Cortisone treatment was started and was followed by steady improvement. By the end of the fourth month iridocyclitis had been quiescent for several weeks. Only one or two pigmented K.P. remained and visual acuity had improved from counting fingers at one foot to 6/18. It was decided to extend the interval between injections from two weeks to three weeks. On the sixteenth day following, the patient complained that the eye was hazy and painful. Examination revealed marked ciliary injection, heavy aqueous flare, and hypopyon. The intraocular pressure was 45 mm. (Schiotz.) The patient was readmitted to hospital and cortisone injections were given at three day intervals, the first two injections being each of 10 mg. Apart from prompt disappearance of the hypopyon and a fall in intraocular pressure, the eye showed little or no improvement during the next two months. The visual acuity had fallen to 1/60. Cortisone was gradually withdrawn. At this point daily inunction, to the skin, of ung. hydrarg. ammon. dil. 4% was prescribed. The eye

steadily improved, and after four weeks the only remaining signs of iridocyclitis were faint ciliary injection, a trace of flare, and a few pigmented K.P. Corrected visual acuity was now 6/60. Six weeks later mercury inunction was gradually reduced, and after a further two months was stopped completely. In a follow-up of thirteen months there was no sign of active inflammation and the visual acuity had gradually improved to 6/18.

Two cases responded poorly to cortisone. Case 8 developed iridocyclitis nine months after a right extracapsular extraction. Needling had been performed three months after operation and was followed by corrected visual acuity of 6/12. Six months later the patient developed marked ciliary injection, endothelial bedewing, a heavy aqueous flare and a small number of grey K.P. The iris pillars were caught up in the depths of the section. After four weeks' treatment with local heat and mydriatics there was little change in the condition and cortisone injections were started. In the first two weeks the K.P. disappeared and ciliary injection, endothelial bedewing, and aqueous flare became less marked. During the third week of treatment however,

the eye suddenly became more irritable and photophobic. Ciliary injection and flare increased and the vitreous became very hazy. A large peridontal abcess was found to be present in relation to unerrupted upper central incisors. X-ray of the sinuses at this stage revealed fluid levels in both maxillary antra, though similar x-rays taken before the commencement of cortisone treatment, had shown only minimal mucosal thickening in the antra. The unerrupted teeth were removed under systemic penicillin cover and the abcess was drained. Subconjunctival cortisone was continued during the following two months, but there was never any real improvement, and the visual acuity, which had been 6/18 at the end of the first two weeks of treatment, fell to 6/24. Cortisone was gradually withdrawn. Subsequently two types of non-specific protein therapy were tried. First, a course of three intravenous injections of typhoid and paratyphoid A and B bacilli was administered, and was followed by some improvement, but it was ill-sustained. Next, a course of sub-cutaneous injections of antigonococcal vaccine was given. The injections were administered weekly, in increasing doses, and were attended by steady improvement in the condition of the eye. At the end

of ten weeks considerable vitreous haze remained, but apart from a few fine pigmented K.P. there were no other signs of activity, and the visual acuity was 6/36. Two months later an extracapsular extraction was performed on the left eye. Unguentum cortisone 1% was instilled in this eye three times daily for several weeks after the extraction. Needling was performed three and a half months after operation and a few days later slight aqueous flare and mild endothelial bedewing were present. These inflammatory signs subsided after subconjunctival injections of cortisone had been given at three and five day intervals for a few weeks. The visual acuity was 6/6. Meanwhile, in the right eye, iridocyclitis remained quiescent and, with a successful result achieved in the left eye, the visual acuity in the right suddenly improved to 6/18 partly. In a follow up of twenty-six months there was no recurrence of inflammatory signs in either eye, but the visual acuity in the rignt eye gradually deteriorated to 6/36. This seemed to be due partly to increase in density of the secondary cataract, and partly to "drawing up" of the iris pillars.

Case 9 also responded poorly to cortisone. This patient developed severe iridocyclitis fifty-three

days after an extracapsular extraction, and cortisone treatment was started sixteen weeks later. At the commencement of treatment ciliary injection and endothelial bedewing were present. Deep corneal vessels infiltrated the section and K.P. were numerous. The iris, which was extremely vascular, was adherent to a dense secondary membrane, and a faint red reflex could be seen in one small area only. Visual acuity was limited to appreciation of hand movements. During nine months of treatment, cortisone failed to gain complete control of the iridocyclitis, though ciliary injection and iris vascularity were considerably reduced during its administration. Transient improvements occurred from time to time, but whenever an attempt was made to extend the interval between cortisone injections, the inflammatory signs became worse. Finally, when cortisone was gradually withdrawn, the exudative features increased greatly. Shortly afterwards the patient, who was 78 years old, contracted pneumonia and died.

Summary of Senile Cataracts:

Clinical cure of iridocyclitis without relapse was obtained in five out of nine cases. Each of the cases which was cured developed iridocyclitis within twenty-eight days of operation, and the longest

interval between the appearance of iridocyclitis and the commencement of cortisone treatment was sixteen days. Two other cases showed a good initial response to cortisone but one failed to continue treatment and the other relapsed. These cases also had a short delay between the appearance of iridocyclitis and the commencement of cortisone treatment; but in the case which relapsed, iridocyclitis had not appeared till eleven months after operation. Two cases responded poorly to cortisone. They did not develop iridocyclitis till two, and nine months respectively after operation; and the delay before cortisone started was over three weeks in each case. Eight of the cases followed extracapsular extraction and one followed an intracapsular extraction. Vitreous loss had occurred at operation in five of the extracapsular extractions, and in the single intracapsular case. Three of these had a good result, one responded well initially but follow up was inadequate, one relapsed, and one had a poor result. Excluding the case which failed to continue treatment, the shortest follow up was six months, and the average follow up twenty-six and a half months.

The Diabetic Cataracts: (Table 3)

In the diabetic group, there were five cases. Two showed a good response, two a fair response, and one a poor response.

Complete clinical cure of iridocyclitis was achieved in cases 10 and 11. Case 10, a 15 year old girl who had had a linear extraction performed four and a half weeks after preliminary needling, developed iridocyclitis on the sixth post-operative day. Numerous fine grey K.P. could be seen, and there was marked ciliary injection, considerable endothelial bedewing, a faint aqueous flare, and dense vitreous haze. Treatment with cortisone began four days after the commencement of iridocyclitis, and was continued for just over four months. During this time the eye improved slowly but very steadily, and final visual acuity was 6/6 partly. Follow-up for two and a half years was uneventful. Case 11, a woman of 62 years, developed iridocyclitis nine days after an intracapsular extraction. The inflammatory signs were so severe that cortisone was started immediately. Marked ciliary injection, extensive striate keratitis, heavy endothelial bedewing, and a dense aqueous flare were present. Thick white exudate in the anterior

TABLE 3.

THE DIABETIC CATARACTS.

Case No.	Sex	Age (years)	Type of Extraction	Total Cortisone (mg.)	No. of Injections	Period of Treatment (weeks)	Result	Follow up. (months)	Final V.A.
10	F	15	Linear	90	17	17	Cured	30	6/6
11	F	62	Intra	95	17	18	Cured	19	6/9
12	M	77	Extra	70+	12+Gtt.	95	Improved	8x	3/60
13	F	49	Intra	80	15	9	Improved	30	6/36
14	M	65	Intra	110	20	16	Un-improved	11	C.F. 1 metre

Extra = Extracapsular.
Intra = Intracapsular.
x = Patient died of intercurrent disease.
C.F. = Counting fingers.

chamber obscured the iridectomy. The corneal signs, the aqueous flare, and the exudate responded rapidly to cortisone. By the fifth day, fine grey K.P. could be seen on the posterior surface of the cornea, and on the tenth day it was just possible to make out the optic disc and retinal vessels through the vitreous haze. Steady improvement followed during four months of treatment, and at the end of this time a few very fine pigmented K.P. were the only remaining signs of iridocyclitis. Final visual acuity was 6/9 partly, and there was no relapse during a follow-up of nineteen months.

Cases 12 and 13 showed only a fair response to cortisone. Case 12, a 78 year old male, had lost the sight of his left eye after an intracapsular extraction in August 1950. Seventeen days after the operation, he had developed low-grade iridocyclitis which remained active for several months. Ten months after operation corrected visual acuity was 6/60 - 1. Much vitreous opacity remained and there was considerable diabetic retinopathy which partially involved the macula. A few months later, a large vitreous haemorrhage occurred and failed to absorb. Thereafter, visual acuity was limited to perception of light with

poor projection. In July 1952, an extracapsular extraction was performed on the right eye. Fourteen days later corrected visual acuity was 6/18 partly, but twenty-eight days after operation iridocyclitis appeared. There was considerable ciliary injection, a heavy aqueous flare, and a large number of K.P. Numerous dilated vessels were visible on the iris and on the remains of the posterior capsule, while details of the fundus were obscured by dense vitreous haze and large floaters. Cortisone treatment began eight days after the appearance of iridocyclitis. After eight weeks' treatment the patient refused to have further sub-conjunctival injections. He was therefore instructed to instil guttae cortisone 1% into the right eye five times daily.

The cortisone drops were made up as follows:-
1 Volume of saline suspension of cortisone acetate (Merck) 25 mgms. per c.c. was diluted with 4 volumes of the following buffer solution:

Sodium acid phosphate with one molecule of water	4.6 gms.
Sodium phosphate anhydrous	4.7 gms.
Sodium chloride	4.8 gms.
Benzalkonium chloride	1:5,000 q.s.

(Quantity sufficient to make 1,000 c.c.s.)

Slow but steady improvement occurred during cortisone treatment. At the end of six months, ciliary injection had disappeared, the K.P. had become fine and pigmented, and there were no visible iris vessels. A faint aqueous flare remained and there was still some vascularisation of the capsule remnants, though this was much reduced. Minimal evidence of diabetic retinopathy could be made out through a small gap in the posterior capsule. The corrected visual acuity was, however, only 6/60, though from the appearance of the eye one would have expected it to have been better. It was ascertained that the patient smoked two ounces of heavy pipe tobacco weekly, and that for many years previously, he had smoked four to five ounces weekly. Bjerrum screen examination showed his discrimination between red and green targets to be very poor. No definite scotoma could be elicited, but his co-operation for the test was not good. He was advised to give up pipe-smoking. For three months he reduced his consumption to one ounce weekly, and then stopped smoking for a period of six months. During this period the inflammatory signs remained unaltered, and visual acuity improved to 6/36 - 1. Twelve months after the commencement of treatment one drop

of cortisone was being instilled every second day, and the patient was attending the out-patient dispensary monthly. At one of these routine visits he was found to have an allergic dermatitis of the lids, of two weeks' duration. He had ascribed this to the cortisone drops, and had discontinued them. The sensitivity was in fact to atropine, and an alternative mydriatic was provided. Meanwhile iridocyclitis had again become active, and heavy aqueous flare and fresh K.P. were in evidence. Instructions were given to revert to the use of cortisone drops three times daily. Gradual improvement followed, until the visual acuity once more became 6/60, and slight bedewing and faint flare were the only signs of active inflammation. Three months after the sensitivity episode an attempt was made to withdraw cortisone, but the inflammatory signs at once increased, and treatment had to be resumed. At intervals throughout the next year further attempts were made to discontinue cortisone, but on each occasion the condition relapsed, and throughout most of this period cortisone was continued in the form of drops, or ointment twice daily. Even so, there was considerable variation in both the

inflammatory condition and the visual acuity, and, from time to time, vitreous haze and aqueous flare became more dense, and iris vessels more numerous. The degree of retinopathy was variable, and this was probably the main factor in the fluctuation of the visual acuity between 6/36 and 6/60. In general, however, the tendency was towards thickening of the pupillary membrane, increasing retinopathy and decreasing visual acuity. Two years after the commencement of cortisone treatment the eye was white and there were no iris vessels, but fine pigmented K.P., endothelial bedewing, and aqueous flare remained. The visual acuity was 5/60. Troublesome superficial punctate keratitis had been present for some months and it was decided to withdraw cortisone. Four months later the number of pigmented K.P. seemed slightly increased, and some iris vessels had reappeared. Bedewing, flare, and vitreous haze seemed little changed, but visual acuity had fallen to 3/60. Superficial punctate keratitis was still present, and it was decided not to revert to cortisone treatment. No change occurred during follow-up of eight months, at the end of which period the patient contracted pneumonia and died.

Case 13, a woman of 49 years, had had her right eye enucleated in 1933, following repeated intraocular haemorrhage. In 1935 an iridectomy was performed in the left eye, preliminary to cataract extraction, but it was followed by iridocyclitis. In 1948 posterior synechiae were separated and an intracapsular extraction was carried out. Eighteen months later many large K.P., heavy aqueous flare, and dense vitreous haze appeared. Investigations at this time revealed a positive Mantoux test and calcified glands at the hilum of the right lung were found, and the patient was given a desensitising course of injections of old tuberculin. Gradual improvement followed until there was no sign of inflammatory activity, only a few pigmented K.P. remaining. The visual acuity was 6/36. One year later acute iridocyclitis recurred, with the presence of endothelial bedewing, heavy aqueous flare, numerous large grey K.P., and dense vitreous haze. Cortisone treatment was started ten days after the appearance of active iridocyclitis. Improvement, gradual at first, was most rapid between the seventeenth and the twenty-ninth day. After nine weeks' treatment, injections were being given every ten days. The visual acuity was once more 6/36, and although pigmented K.P. and a faint aqueous flare remained, there was no other sign of activity. At

this stage the patient failed to report for six weeks, and since at the end of this time there appeared to be no increase in inflammatory signs, cortisone injections were not resumed. The condition remained unchanged for twenty-five months, when the patient again complained of hazy vision. Moderate aqueous flare was present and there was thought to be some increase in vitreous haze, although the visual acuity was still 6/36. It was decided to give further subconjunctival injections of cortisone and during their administration the inflammatory signs gradually lessened. At the end of three months the vitreous was clearer, but considerable aqueous flare and large crenated K.P. remained. The visual acuity was still 6/36. Cortisone treatment was continued in the form of 1% drops.

Case 14 responded very poorly to cortisone. Severe iridocyclitis with hyphaema and secondary glaucoma occurred one year after an intracapsular extraction. Choroidal detachment had been present for two weeks after operation, but the visual acuity in the sixth post-operative week had been 6/9. Cortisone treatment began twenty-six days after the appearance of iridocyclitis. Eighteen days later the intraocular pressure remained high, the hyphaema was still present, and the inflammatory signs were little altered.

Cyclodialysis was carried out, and after this procedure the hyphaema cleared rapidly and the intraocular pressure remained normal; but ciliary injection, endothelial bedewing, moderate aqueous flare, numerous dilated iris vessels, and many grey K.P. remained. Cortisone was continued for three weeks with no appreciable improvement apart from very slight lessening of the aqueous flare and of the ciliary injection. Dense vitreous haze remained, and the visual acuity was only 2/60. Cortisone treatment was discontinued. In the following three months there was some increase in inflammatory signs. A fine exudative membrane appeared on the anterior vitreous face, and visual acuity fell to 1/60. A second course of subconjunctival cortisone, lasting for eight weeks, effected no improvement.

Summary of Diabetic Cataracts:

Of five cases, two were cured, two showed a fair response with a considerable degree of control of iridocyclitis, and one was unimproved.

The two cases with a good result developed iridocyclitis within nine days of operation and the interval between the appearance of iridocyclitis and the commencement of cortisone treatment was nine days

or less. The two cases showing a fair response developed iridocyclitis fifty-nine days and two and a half years respectively after operation, but in both cases the delay before cortisone treatment commenced was short being ten days or less. The case which had a poor result did not develop iridocyclitis until one year after operation, and the delay before cortisone treatment started was twenty-six days. There were two extracapsular and three intracapsular extractions; one extracapsular and one intracapsular case occurred in both the good and the fair results, and the case with the poor response had had an intracapsular extraction. The significance of post-operative complications was doubtful. One case with a fair response had had a post-operative hyphaema, and the case with a poor result had had choroidal detachment for two weeks after operation.

The single case of secondary cataract, case 15, (Table 4) occurred in a man aged forty-two years. Before operation both eyes showed extensive posterior cortical lens opacity, fine pigment dust on the posterior cornea and areas of iris atrophy. There were no active inflammatory signs, and the patient was unaware of any previous eye trouble. His general medical history was negative, and the investigations

TABLE 4.

THE SECONDARY CATARACT AND THE CONGENITAL CATARACT

Case No.	Sex	Age (years)	Type of Operation	Total Cortisone (mg.)	No. of Injections	Period of Treatment (weeks)	Result	Follow up. (months)	Final V.A.
15	M	42	Intra	100	19	24	Cured	28	6/18
16	F	7	Discission	75	14	17	Cured	20	H.M.

Intra = Intracapsular extraction.
H.M. = Hand movement.

carried out revealed no abnormalities. Vitreous loss occurred during an intracapsular extraction on the right eye, and the lens was removed with a vectis. Six days after operation, mild ciliary injection, faint aqueous flare, and a number of dilated iris vessels appeared. Four days later, the ciliary injection was more marked, the flare more dense and the iris more vascular. In addition there was vitreous haze with many floaters, the optic disc and retinal vessels being only just distinguishable. Cortisone treatment was started and, from the fifth day onwards, was attended by continuous improvement, which was most marked in the second and third weeks, and again in the fifth week. Corrected visual acuity after eight days was 6/60, after four weeks it was 6/18, and at the end of seven weeks of treatment, it was 6/6. Ciliary injection had disappeared, one fine iris vessel was still visible, a faint aqueous flare remained, and a number of K.P. were present but they were all pigmented. The vitreous still contained floaters, but the general haze had gone and a good view of a normal fundus could be obtained. In the following four months cortisone was very gradually withdrawn, and during this time the vitreous floaters became fewer, the single iris vessel was no longer

visible, and the aqueous flare disappeared.

Ten days after cortisone had been stopped, the patient developed an extensive shallow retinal detachment. A small retinal tear was discovered near the periphery in the ten o'clock meridian, and a dialysis was present in the eleven o'clock meridian. Surface and penetrating diathermy were applied. The retina remained in position for three months, the visual acuity being 6/9 but at the end of this time shallow retinal detachment developed in the lower periphery. No tear could be found. Transillumination was positive, and the question of scleral resection was raised, but the visual acuity was unaffected, and the patient was unwilling to consider further operative treatment. The detachment remained apparently unaltered during twenty-six months, but the visual acuity gradually fell to 6/18. There was no recurrence of iridocyclitis during follow-up of thirty-one months.

The case of congenital cataract, case 16, (Table 4) occurred in a child of seven years. There was a history of maternal rubella during pregnancy. The left eye, apart from the presence of hypermetropic astigmatism, was normal, and its corrected visual acuity was 6/9. Dense cataract was present in the

right eye, and discission was carried out for cosmetic reasons. Twenty-seven days after operation, the eye became injected, and fine endothelial bedewing and faint aqueous flare were present. Seven days later the bedewing and flare were more marked, and numerous large discreet grey K.P. had appeared. The vitreous was hazy, there were many floaters, and no fundus details could be made out. Cortisone treatment was started and was followed by rapid improvement, which was most marked between the fourth and the fifteenth day. On the fourth day, retinal vessels could be made out and the K.P. were fewer. After three weeks only a few K.P. remained, the vitreous was much clearer and a fairly good view of the fundus was obtainable. Five weeks after the commencement of cortisone treatment, lens matter was absorbing rapidly, and the only signs of abnormality were the presence of a slight ciliary flush and a few pigmented K.P. situated at the lower angle of the anterior chamber. Cortisone was withdrawn very gradually and during the next four and a half months the ciliary flush subsided, though the pigmented K.P. remained. The eye being amblyopic, visual acuity was limited to counting fingers at one foot. There was no

recurrence of iridocyclitis in a follow-up of twenty months.

Details of the remaining cases in the post-operative group are summarised in Table 5. Two cases developed iridocyclitis after corneo-scleral trephine. Both cases responded well to cortisone, but one subsequently relapsed. Case 17, a 64 year old male diabetic patient, developed dilated iris vessels and fine posterior synechiae five days after operation. On the sixth day, the iris vessels were more numerous, and in addition marked ciliary injection, striate keratitis, and endothelial bedewing had appeared. The anterior chamber was shallow, and no fundus details could be made out. Cortisone treatment was started, and was attended by rapid improvement of the keratitis, the bedewing, and the vascularity of the iris. On the third day of treatment the corrected visual acuity was 6/60 and by the fifth day it was 6/36. The anterior chamber had become less shallow, and aqueous flare was now evident. Some fundus detail could be made out, and a choroidal detachment was visible at the lower and temporal periphery. Dilated iris vessels were still present but were smaller and fewer. By the eighth day visual acuity had improved to 6/18.

TABLE 5.

THE GLAUCOMAS.

Case No.	Sex	Age (years)	Type of Operation	Total Cortisone (mg.)	No. of Injections	Period of Treatment (weeks)	Result	Follow up (months)	Final V.A.
17	M	64	Trephine	80	15	21	Cured	18	$\frac{6}{12}$
18	M	59	Trephine	125	23	20	Relapsed	$31\frac{1}{2}$	Nil. (Enuc.)
19	M	69	Iridectomy	115	22	27	Un-improved	29	Nil. (Enuc.)
20	F	73	Iridotomy	100	22	21	Un-improved	15	Nil. (Enuc.)
21	F	74	Iridotomy	45+Gtt.	7+Gtt.	20	Un-improved	19	P.of L.

Enuc. - Enucleation.
P.of L. - Perception of light.

Aqueous flare disappeared after two and a half weeks, and visible iris vessels after five weeks. Eight weeks after the commencement of treatment, the patient developed a skin sensitivity reaction to atropine sulphate. At the same time ciliary injection reappeared, and for the first time a few fine K.P. were seen. Visual acuity fell to 6/24. During the following two weeks the K.P. became pigmented, and severe superficial punctate keratitis developed - the keratitis is discussed more fully in a later section. Cortisone treatment was continued, and within a month ciliary injection had again disappeared, and visual acuity was 6/12 partly. Injections were gradually stopped during the following nine weeks, and no relapse occurred during a follow up of eighteen months.

Case 18, a male aged 59, developed heavy aqueous flare, dilated iris vessels, posterior synechiae and striate keratitis on the fifteenth day after a corneo-scleral trephine had been performed on the right eye. Seven days later the iris was more vascular, and, although the pupil was now well dilated, the iridocyclitis on the whole was markedly worse. In addition to the previous signs there was marked ciliary injection, heavy endothelial bedewing and a

considerable number of K.P., some of which were grey and some pigmented. The optic disc and retinal vessels could barely be made out, and corrected visual acuity, which had been 6/6 before operation had fallen to 6/36. Cortisone treatment was started. Three days later, apart from slight lessening of endothelial bedewing, there was no sign of improvement, and, indeed, the visual acuity had fallen to 6/60. On the seventh day of treatment however, photophobia, pain and blepharospasm disappeared dramatically, while the cornea became clearer and the iris vessels fewer. Aqueous flare was suddenly much less dense, but considerable ciliary injection remained and K.P. were still numerous, though many had become pigmented. A fairly good view of the fundus could be obtained and visual acuity was 6/24. By the fourteenth day, ciliary injection was slight and the cornea was clear. A few very fine pigmented K.P. remained, but there were no visible iris vessels, and the aqueous flare had disappeared. A clear view of the fundus could now be obtained, and the visual acuity had improved 6/18 + 1. At this stage the intraocular pressure, which had varied since operation from 10 to 12 mm. Schiotz, rose to 38 mm. Schiotz. For six weeks the

pressure remained between 38 and 40 mm. and the visual acuity fell to 6/24 partly. Apart from mild ciliary injection there was no evidence of iridocyclitis. A cyclodialysis was performed, and the pressure returned to normal. In the left eye the intraocular pressure had been varying between 34 and 37 mm. and a cornoscleral trephine was performed on this eye one week after the cyclodialysis on the right. Both eyes had topical cortisone cover, before, during, and after the operations. The left eye, during the first week after operation, showed pigment dust on the posterior corneal surface and a few fine posterior synechiae, but no further signs of iridocyclitis developed and the right eye remained quiescent. Two weeks after the trephine had been performed in the left eye cortisone was discontinued in both eyes. At the end of a further two weeks there was no sign of inflammatory activity in either eye; the intraocular pressures were normal and the visual acuity in each eye was 6/18. The situation remained unaltered for almost three months. At the end of this period a few new K.P. appeared in the right eye and its visual acuity was found to have fallen to 6/36. Fourteen days later acute glaucoma and severe iridocyclitis

recurred in this eye. A paracentesis was carried out, and two weeks later a second corneo-scleral trephine was performed; but the intraocular pressure remained high and the iridocyclitis active. A further eight week course of cortisone injections did little to relieve the situation. The patient was unwilling to have the eye removed, and, after a period of absolute glaucoma, phthisis bulbi ensued. Follow-up for thirty-one months showed the condition of the left eye to be unaltered.

The three remaining post-operative cases showed a poor response to cortisone.

Case 19 developed iridocyclitis in the left eye 7 months after a broad iridectomy had been performed to relieve an attack of acute glaucoma. Initially, only a few dilated iris vessels and a number of fine K.P. were present. A mature cataract was apparent, but perception of light was accurate. Gutt. atropine sulphate ½% was instilled t.i.d. For four weeks the intraocular pressure remained normal and during this period some of the K.P. became pigmented. At the end of this time, intense ciliary injection, heavy endothelial bedewing, and many large grey K.P. appeared. A number of posterior synechiae were present, and the

intraocular pressure was moderately raised (32 mm Schiotz). Gutt. atropine sulphate 1% was instilled t.i.d. and subconjunctival injection of cortisone was commenced. At the end of three weeks the intraocular pressure had become normal, and endothelial bedewing was slightly less marked, but otherwise there was no improvement. A further four weeks of therapy found the situation essentially unchanged and the interval between injections was increased to one week.

During the next four months the inflammatory signs decreased at times, but there was no sustained improvement. At the end of this period, a number of deep vessels had invaded the cornea from the lips of the keratome incision, ciliary injection was still marked, and K.P. were numerous. A few days later the patient developed kerato-conjunctivitis, and cortisone was discontinued. Subsequently, courses of intravenous protein shock therapy and intramuscular autohaemotherapy were instituted without improvement. Three months after cortisone had been withdrawn the inflammatory signs became more severe and absolute glaucoma supervened. Enucleation was advised and carried out.

Of the remaining two cases, one developed iridocyclitis after iridotomy and the other after combined iridotomy and capsulotomy. Both patients were diabetics and both showed a poor response to cortisone. Case 20, a 73 year old woman, had had an intracapsular extraction, with complete iridectomy, performed two years previously. Three days after the extraction excision of iris prolapse had been carried out, but one iris pillar remained drawn up to the section, and during the following two years the whole iris gradually became drawn up. At this stage an iridotomy was performed, and four weeks later the corrected visual acuity was 6/18. Eleven weeks after operation the eye became painful and developed an aqueous flare, ciliary injection, and vitreous haze with floaters. Gutt. atropine 1% was instilled twice daily, and local and systemic penicillin were administered. Four and a half weeks later, the condition was markedly worse. The vitreous haze was more dense, and fundus details were obscured; there was marked ciliary injection, considerable endothelial bedewing, and heavy aqueous flare. Numerous dilated iris vessels could be seen and the corrected visual acuity had fallen to 6/60 + 1.

Cortisone treatment was started. At times, during the first weeks of treatment, ciliary injection, or flare, or bedewing became less; at other times the vitreous haze cleared, and extensive diabetic retinopathy could be made out; but these remissions were only transitory. On one occasion, the visual acuity was 6/36 but it soon reverted to 6/60, and gradually, as the retinopathy involved the macula, this acuity could only be obtained fleetingly with peripheral vision. The iris vessels steadily increased in number, until pronounced rubeosis iridis was present. At the end of four months' treatment, there had been no real improvement, and during the following two and a half months, cortisone was gradually withdrawn. Six weeks later, severe secondary glaucoma developed. It proved intractable and the eye was enucleated.

Case 21, a 74 year old woman, had a history of extracapsular extraction with vitreous loss. Mild iridocyclitis had occurred three weeks after operation and had responded well to Gutt. atropine sulphate topically and sulphatriad systemically. Eighteen months after operation, the iris was drawn up and adherent to a dense secondary membrane. Visual acuity was reduced

to appreciation of hand movements, but perception of light was good. There were no visible iris vessels but the secondary membrane was vascularised, and fine pigmented K.P. were present. A combined iridotomy and capsulotomy was performed, but was followed by an exudative reaction in the iris and secondary membrane, and the gap closed within a few weeks. Four weeks later, the operation was repeated, and twenty days later severe acute iridocyclitis developed. Ciliary injection, bedewing, and aqueous flare were marked; there were a number of large, fresh K.P. and the iris and secondary membrane were heavily vascularised. Subconjunctival injections of cortisone were started, and in the first week there was considerable improvement. At the end of three weeks, the ciliary injection, bedewing, and flare had almost disappeared, and the K.P. had become crenated and pigmented. The gap in the secondary membrane, however, had again become closed by a fine fibrinous network, and there was some increase in the intraocular pressure. One week later, a further capsulotomy was carried out. This time subconjunctival cortisone was given, before and after the operation. On the eighth post-operative day, the patient was unwilling to have further injections

and treatment was continued with 1% cortisone drops, which were initially instilled every four hours. There was no recurrence of iridocyclitis, and the gap in the membrane remained open for four weeks, but during the next eight weeks it gradually became occluded, and the retina was again obscured. Cortisone was gradually discontinued over the next six weeks. During a follow-up of nineteen months, iridocyclitis remained quiscent, but the anterior chamber gradually became more shallow, till the iris and secondary membrane were in contact with the posterior surface of the cornea. The eye became soft and painless, and projection of light was inaccurate.

Summary and Discussion of the Post-Operative Cases:

Ten of the twenty-one cases in this group showed a good response to cortisone and achieved clinical cure of iridocyclitis. Three others responded well initially, but two of them relapsed, and in the third case follow-up was inadequate. Of the eight remaining cases two were improved and six unimproved. (Table 6). The final visual acuities are shown in Table 7. Of the ten cases which were cured, five retained visual acuity of 6/9 partly or more. In four cases final visual acuity was poorer, but there were extenuating

TABLE 6.

POST-OPERATIVE CASES.
RESPONSE TO CORTISONE.

Operation.	No. of Cases	Cured	Improved	Relapsed	Unimproved	Inadequate Follow up
Extraction Senile Cataract.	9	5	-	1	2	1 ✓
Extraction Diabetic Cataract.	5	2	2	-	1	-
Extraction Secondary Cataract.	1	1	-	-	-	-
Discission Congenital Cataract.	1	1	-	-	-	-
Trephine.	2	1	-	1	-	-
Iridectomy.	1	-	-	-	1	-
Iridotomy.	2	-	-	-	2	-
Totals.	21	10	2	2	6	1 ✓

✓ Good response during period of observation.

TABLE 7.

POST-OPERATIVE CASES.
FINAL VISUAL ACUITY.

Clinical Result	No. of Cases	6/6 – 6/9	6/12 – 6/24	6/36 – 6/60	H.M. or P.of L.	No V.A. (Enucleation)
Cured	10	5	4	-	1	-
Improved	2	-	-	2	-	-
Relapsed	2	-	1	-	-	1
Unimproved	6	-	1	-	3	2
Inadequate Follow up	1	-	-	-	1	-
Totals	21	5	6	2	5	3

H.M. - Hand movements.
P.of L. - Perception of light.
V.A. - Visual acuity.

factors. Case 17, which achieved visual acuity of 6/12 partly, suffered from chronic glaucoma and a visual field charted before operation, using a 3 mm. white target at a distance of one metre, showed general contraction to 10°. Case 15 retained visual acuity of 6/9 for some time after cortisone had been withdrawn, but later developed a retinal detachment, and the visual acuity after operation was 6/18. Case 4, in which final visual acuity was 6/24, had a history of strabismus in childhood, and the operated eye was known to have been partially amblyopic. In case 16 a discission had been performed, for cosmetic reasons, on a unilateral congenital cataract, and the visual acuity after operation was limited to appreciation of hand movements. The tenth case retained visual acuity of 6/18 but developed low-grade iridocyclitis in the unoperated eye ten months after the withdrawal of cortisone. A somewhat similar case occurred in the post-traumatic group and the importance of these two cases, with regard to the possible aetiology of the iridocyclitis in the second eye, is discussed in a later section.

Two cases relapsed after an initial good response. When cortisone was finally withdrawn, one retained visual acuity of 1/60 and the other the ability to

count fingers at 15 cms. Subsequent improvement to 6/12 in the first case was probably due to other methods of treatment. The second case eventually developed absolute glaucoma and progressed to phthisis bulbi, the eye being later enucleated.

One other case showed good initial response, but failed to continue treatment. When last seen, iridocyclitis was well controlled, but the iris was adherent to a dense secondary cataract, and vision was limited to perception of light with accurate projection.

Two cases showed a fair response to cortisone and were improved by treatment. In the first, iridocyclitis was controlled, but vitreous haze remained, and the final visual acuity was 6/36. In the second, iridocyclitis was partially controlled, but the inflammatory signs were never entirely suppressed. Each attempt to withdraw cortisone resulted in a relapse, and on each occasion subsequent control of the iridocyclitis by cortisone was a little less adequate. When cortisone was finally withdrawn, the visual acuity fell from 6/60 to 3/60.

The six cases which were unimproved, initially showed a certain - but quite inadequate - response to cortisone. At the end of treatment the visual

acuity in one case had fallen from 6/18 to 6/24 two cases could count fingers at 1 metre, and three cases retained only perception of light. Two eyes were subsequently enucleated. It will be seen that of the twenty-one cases thirteen retained useful visual acuity and eight did not.

The shortest follow-up in the post-operative cases, after cortisone had been withdrawn, was six months, the longest follow-up was two years seven and a half months, and the average follow-up twenty months. These figures exclude case 6, in which follow-up was inadequate, and case 13 which relapsed and was still receiving cortisone treatment at the time of writing. The latter case was under observation for 3 years and 2 months.

In the whole group, there were eleven extracapsular and five intracapsular cataract extractions. Of the extracapsulars, six were cured, three improved, and two unimproved. Among the intracapsulars three were cured, one improved and one unimproved. (Table 8). There was therefore no clear indication that the type of extraction which had been performed in these cases influenced the end results of treatment.

TABLE 8.

COMPARISON OF RESULTS IN EXTRACAPSULAR AND INTRACAPSULAR CATARACT EXTRACTIONS.

Type of Cataract Extraction	No. of Cases.	Result		
		Cured	Improved	Unimproved
Extracapsular	11	6	3	2
Intracapsular	5	3	1	1

Vitreous loss had occurred at four of the extractions. Of these two were cured and two improved. Choroidal detachment followed operation in two of the diabetic cases. One of these was cured and one was unimproved. Hyphaema occurred in one diabetic case which was improved. The direct complications of operation which were encountered, although they may have been factors precipitating iridocyclitis, did not appear greatly to influence the results of its treatment.

Eight of the twenty-one cases in this group suffered from diabetes. The success rate in these cases was 37½%, in comparison with 58% in the non-diabetic cases. Both groups showed 25% fair results.

In the ten cases which were cured, iridocyclitis appeared within twenty-eight days of operation (average 10.5 days) and the longest delay before commencement of cortisone treatment was ten days (average 2.9 days). The two cases which initially responded well but later relapsed, developed iridocyclitis eleven months and fifteen days, respectively, after operation, and in each case the delay before cortisone commenced was short, being eleven and seven days respectively.

Similarly in the three cases which were improved but not cured, the intervals between operation and iridocyclitis were long - being sixty days, fifty-nine days, and two and a half years respectively - while the intervals before cortisone commenced were short - being three, eight, and ten days, respectively. In four of the six unimproved cases, iridocyclitis did not appear until three months or more, after operation; and in the two others it occurred seven, and fifty-three days respectively, after operation (average five and a half months). Among the unimproved cases the average delay between the appearance of iridocyclitis and the commencement of cortisone treatment was forty-five and a half days. These findings are summarised in Table 9. The figures suggest that the best results with subconjunctival cortisone are likely to be achieved in cases which develop iridocyclitis in the immediate post-operative period, and in which the interval between the appearance of iridocyclitis and the commencement of cortisone treatment is short. In the present group, no case which developed iridocyclitis more than twenty-eight days after operation, had a completely successful result; and among the successful cases, the average

TABLE 9.

POST-OPERATIVE CASES.

Intervals between Operation & Iridocyclitis & between Iridocyclitis & Cortisone Treatment.

Case No.	Interval between Operation and Iridocyclitis (Days)	Average (Days)	Interval between Iridocyclitis and Cortisone Treatment (Days)	Average (Days)	Result
1	23	10.5	0	2.9	Cured
2	8		0		
3	6		1		
4	10		10		
5	6		1		
10	6		4		
11	9		0		
15	6		4		
16	27		7		
17	4		2		
7	308	210	11	7.8	Relapsed
18	15		7		
6	60		3		Improved
12	59		8		
13	912		10		
8	266	162	28	45.5.	Un-improved
9	53		112		
14	365		28		
19	196		28		
20	84		28		
21	7		49		

time before iridocyclitis appeared was only ten and a half days. In addition, of twelve cases which did develop iridocyclitis within twenty-eight days of operation, only was was unimproved. The maximum interval, between the appearance of iridocyclitis and the commencement of cortisone treatment, which was followed by a good result was ten days, and the average interval among the cured cases was only 2.9 days. Of fourteen cases which commenced cortisone treatment within ten days of the appearance of iridocyclitis, none was unimproved. In comparison, the six unimproved cases did not develop iridocyclitis until an average of one hundred and sixty-two days after operation, and the delay before cortisone treatment commenced averaged forty-five and a half days. The figures for the relapsed and improved cases lay between these extremes. With one exception, they showed a long interval between operation and the appearance of iridocyclitis, (average two hundred and ten days), but a short delay before cortisone treatment was commenced (average 7.8 days).

The case of choice would appear to be that in which iridocyclitis occurs within twenty-eight days of operation, and in which cortisone treatment is

commenced not more than fourteen days later, and ideally not more than seven days later. In cases in which iridocyclitis has reached a subacute or chronic stage, one would expect, in the light of Menkin's work (1951 a,b,c) to which reference has already been made, that results with cortisone would be less dramatic. In such cases it would seem more reasonable to employ systemic A.C.T.H.

Section 4.

Post-Traumatic Cases.

This group consists of eleven cases which developed iridocyclitis after penetrating injury of the eyeball.

The age group included a boy of four years, a girl of eight and a half years, a sixteen year-old youth and eight adult males, of whom there were three in the third decade, two in the fourth decade, and three in the fifth decade. The two children were injured while playing with broken glass, and among the others there were five industrial and four domestic injuries. Nine of the cases were seen by an ophthalmic surgeon within eight hours of injury, and the two remaining cases were seen fourteen hours and four days respectively, after injury. In six cases the entry wound was confined to the cornea, in three it was mainly corneal but extended also over the area of the ciliary body, in the remaining two cases the wound was scleral, and in one of these the ciliary body was involved. Traumatic cataract was noted at the first examination in five cases, and may have been present in one other case in which the lens was initially obscured by hyphaema and exudate,

and was later found to be cataractous. Magnetic intraocular foreign bodies were present in five cases and were removed by a Mellinger's ring magnet, four by the anterior route, and one by the posterior route.

In seven cases, iridocyclitis appeared between the seventh and fourteenth day following injury. Three cases developed iridocyclitis on the fifteenth, eighteenth, and nineteenth day respectively, after injury, and in the remaining case iridocyclitis appeared sixty-three days after injury. The longest delay between the appearance of iridocyclitis and the commencement of cortisone treatment was fourteen days, the average delay being only 3.4 days.

Six cases achieved clinical cure of iridocyclitis in the injured eye, but one of these later developed low-grade iridocyclitis in the uninjured eye. Two cases initially responded well but later relapsed, and the remaining three cases were unimproved.

The response of the post-traumatic cases to cortisone is summarised in Table 10.

Cases 22, 23, 24 and 25 achieved clinical cure of iridocyclitis and retained good vision. Three of these were industrial injuries and one was a domestic injury.

TABLE 10.

POST-TRAUMATIC CASES.

Case No.	Sex	Age (years)	Interval between Trauma & Iridocyclitis (days)	Total Cortisone (mg.)	No. of Injections	Period of Treatment (weeks)	Result	Follow up (months)	Final V.A.
22	M	30	7	85	16	35	Cured	21	$\frac{6}{5}$
23	M	28	8	80	14	17	Cured	18	$\frac{6}{6}$
24	M	26	19	90	17	26	Cured	6	$\frac{6}{6}$
25	M	47	10	90	17	16	Cured	$18\frac{1}{2}$	$\frac{6}{9}$
26	M	16	10	105	20	38	Cured	$26\frac{1}{2}$	P.of L.
27	M	44	63	90	17	26	Curedx	16	$\frac{6}{60}$
28	F	$8\frac{1}{2}$	13	65	12	14	Relapsed	19	Nil. (Enuc.)
29	M	32	9	95	17	15	Relapsed	12	Nil. (Enuc.)
30	M	43	18	55	10	4	Un-improved	6	Nil. (Enuc.)
31	M	4	15	20	3	1	Un-improved	32	Nil. (Enuc.)
32	M	25	8	26	5	2	Un-improved	8	Nil. (Enuc.)

x - Iridocyclitis occurred in the second eye.
V.A. - Visual acuity.
P.of L. - Perception of light.
Enuc. - Enucleation.

Case 22, a male aged 30, sustained a penetrating tri-radiate corneal wound when a glass reflector broke as he was fitting an electric bulb. He was not seen by an ophthalmic surgeon until four days after the injury. There was neither lens damage nor intraocular foreign body and, apart from some ciliary injection, there were no inflammatory signs. Topical application of a mydriatic and an antibiotic was prescribed. Four days later a few fine K.P. and a faint aqueous flare appeared. The following day the eye became painful and watery. On the eleventh day after injury there was considerable photophobia and marked ciliary injection. The K.P. had increased in number, and fibrinous exudate extended in strands from the corneal wound into the anterior chamber. The pupil was fairly well dilated but one or two fine posterior synechiae were present and a number of dilated iris vessels could be seen. Only a hazy view of the retina was obtainable. The visual acuity was 6/30. Subjunctival cortisone was begun. Three days after the first injection, the iris vessels, the strands of fibrinous exudate and all the K.P. except one, had disappeared. The visual acuity was now 6/36 + 1 and six days later it was 6/24. At this stage only

faint bedewing, marked ciliary injection, and one fine K.P. remained. The ciliary injection disappeared after four weeks of cortisone treatment, by which time the visual acuity was 6/6 partly. Gradual withdrawal of cortisone was uneventful apart from transient appearance of faint aqueous flare at times. The final corrected visual acuity was 6/5 partly, and follow-up of twenty-one months was without incident.

Case 23, a male aged 28 years, sustained an irregular penetrating corneal wound while using a steel hammer and chisel. He was seen by an ophthalmic surgeon about eight hours after injury. The lens was cataractous and a small piece of steel was extracted with a magnet, by the anterior route. Iridocyclitis appeared eight days after injury and one week later, in spite of intensive topical treatment with mydriatics and antibiotics, the condition of the eye had deteriorated. Ciliary injection, endothelial bedewing, large fresh K.P., aqueous flare, dilated iris vessels, and posterior synechiae were present. Cortisone treatment was commenced. Rapid improvement occurred during the first week of treatment and was maintained during the second and third weeks. At the end of the third week, neither bedewing nor iris vessels were present, but

a few fresh K.P. appeared. In the succeeding weeks, ciliary injection and aqueous flare gradually diminished, but small numbers of fresh K.P. continued to appear and disappear until three months after the commencement of treatment. The K.P. then gradually disappeared or became pigmented, and cortisone was slowly withdrawn. Lens matter had absorbed and corrected visual acuity was 6/6 partly. There was no relapse during follow-up of eighteen months.

Case 24, a 26 year old labourer, was struck with a spanner, and sustained a right-angled penetrating wound in the upper temporal quadrant of the right cornea. He was seen by an ophthalmic surgeon a few hours after injury. The lens capsule was found to be ruptured, and a localised area of lens opacity was present. Lens matter and exudate straddled the pupil margin in the ten o'clock meridian, and in this area there were a number of dilated iris vessels. X-ray of the right orbit was negative.

The patient's spectacles had been shattered by the blow and two tiny particles of glass could be seen in the corneal wound. A small clear glistening spot which was detected on the iris in the ten o'clock

meridian, was thought to be a third particle of glass, but the presence of lens matter and exudate made the appearances equivocal, and after a few days the glistening spot could no longer be seen. Fifteen days later, however, a spicule of glass was found to be protruding from the limbus in the 6 o'clock meridian. When removed, it measured 3 x 1 mm.

Eight days after injury, although lens matter and organised exudate remained in the anterior chamber and a few dilated iris vessels could be seen, the eye appeared relatively quiet, and the patient was dismissed from hospital. Four days later aqueous flare appeared. In the next seven days further signs of iridocyclitis developed, and the patient was readmitted to hospital. Subconjunctival injections of penicillin, and intravenous protein shock therapy (25,000,000 organisms of phenolized T.A.B. vaccine Parke Davis & Co.) were administered, but twelve days after admission, ciliary injection, aqueous flare, and endothelial bedewing had increased, and a considerable number of fresh K.P. had appeared. The ring of exudate on the iris and lens was heavily vascularised, and the greater part of the lens had become opaque, reducing the visual acuity to 1/60. Treatment with

subconjunctival cortisone was commenced and rapid improvement ensued. Bedewing and flare disappeared within a few days, and ciliary injection within fourteen days. Seven weeks after the commencement of cortisone treatment, there remained only one visible iris vessel in the 11 o'clock meridian, and a few tiny grey K.P. on the lower nasal quadrant of the cornea. The ring of exudate on the iris and lens was no longer vascularised and had shrunk to half its original size. In the next few months, a number of fine grey K.P. were present for transient periods, and ciliary flush appeared from time to time, but five and a half months after the commencement of treatment there remained only one or two fine old K.P., which had not altered in appearance for a number of weeks. There had been no ciliary injection for five weeks, though an occasional iris vessel could still be seen at times in the 11 o'clock meridian. Two months later, the lens matter was absorbing rapidly. Fine grey particulate matter floated in the anterior chamber and adhered to the posterior cornea, but there were no inflammatory signs.

By the end of the fourth month, the interval between injections had been increased to two weeks,

and during the succeeding three and a half months cortisone was gradually withdrawn. Much of the lens matter gradually absorbed, and thirteen and a half months after the commencement of treatment, the lower half of the retina and part of the optic disc and macula could be made out. The vitreous appeared clear, and so far as could be seen the retina was normal. Corrected visual acuity was 6/6 partly, and follow-up of six months was uneventful.

Case 25, a male estate worker aged 47, sustained injury to his right eye by a piece of steel, which penetrated the sclera, nasal to the cornea and beyond the ciliary body. He was seen two hours after injury. The entry wound was clearly visible, and ophthalmoscopic examination revealed considerable vitreous haemorrhage. A piece of steel, 8 x 6 x ½ millimetres, was extracted through the entry wound, using a Mellinger's ring magnet. Some vitreous loss occurred. During the following ten days intensive topical application of mydriatics and antibiotics was carried out. In addition, the patient was given a course of systemic penicillin, and protein shock therapy, which was administered intravenously using a phenolised T.A.B. Vaccine (Parke

Davis and Co.) Eight days elapsed between the first injection of 25,000,000 organisms, and the second of 40,000,000 organisms. Each produced a maximum temperature of 101.4° Fahrenheit.

On the tenth day following injury, the eye was still irritable and photophobic and intense ciliary injection was present. There was heavy endothelial bedewing and a very dense aqueous flare. Posterior synechiae were present, and dilated iris vessels visible. Gross vitreous haemorrhage obscured the details of the fundus, though a faint red reflex was obtainable. Visual acuity was limited to the appreciation of hand movements. At this stage, treatment with subconjunctival cortisone was started. During the first week there was little apparent change, but in the following two weeks improvement was rapid, and at the end of the third week, though ciliary injection, faint flare, and a few K.P. remained, there was no endothelial bedewing and the iris vessels had disappeared. There were still many large vitreous floaters and a dense area of organised exudate could be seen in the lower vitreous, but the disc and greater part of the retina could be made out in some detail.

Visual acuity had improved to 6/18 - 2. K.P. and flare gradually disappeared, ciliary injection became minimal, the vitreous opacities cleared considerably and the area of white exudate in the lower vitreous became smaller. A tiny posterior cortical lens opacity appeared but did not increase, and the visual acuity ten weeks after the commencement of cortisone treatment was 6/12 - 1. In the following five weeks cortisone was gradually withdrawn. There was no relapse, and during a follow-up of eighteen and a half months the visual acuity further improved to 6/9 - 2.

Case 26 achieved clinical cure of iridocyclitis, but the visual acuity remained poor. The patient - a sixteen year old youth - was trying to free a blocked mains water pipe, when the water escaped under pressure, and a piece of metal flew into his eye. He was seen by an ophthalmic surgeon a few hours after the injury, and was found to have a large irregular, penetrating, corneal wound. Traumatic cataract was present, and rupture of the iris had occurred at its pupillary margin. A piece of metal was extracted by the anterior route, using a Mellinger's magnet. Ten days later marked ciliary injection and aqueous flare were present,

and a filmy grey exudate extended from the corneal wound into the anterior chamber. The lens opacity had remained localised and a faint red reflex was obtainable, though dense greyish white exudate was present in the anterior vitreous. Visual acuity was limited to perception of light. Two days later the exudative features were more pronounced, and dilated iris vessels, endothelial bedewing, and marked striate keratitis were present. Subconjunctival injections of cortisone were commenced and were attended by steady improvement, which was most marked in the second and third weeks of treatment. Striate keratitis and exudate in the anterior chamber disappeared by the fifth day, and iris vessels by the eleventh day. On the seventeenth day ciliary injection and bedewing had almost gone. The aqueous flare, in this case, was slow to disappear and was still present after three and a half months of cortisone treatment - i.e. long after the eye was white and other signs of inflammatory activity had gone. The membrane in the anterior vitreous gradually thinned until the disc and some retinal vessels could be made out, but visual acuity never improved beyond counting fingers at two feet.

In the period from the beginning of the third to the end of the seventh month of treatment, cortisone was gradually and uneventfully withdrawn. Seven months after injury the lens had become completely opaque and the eye was divergent. During twenty-six and a half months follow-up there was no recurrence of iridocyclitis, but perception of light became limited to the upper temporal part of the field, and the presence of retinal detachment was suspected.

Case 27, a male aged 44 years, achieved clinical cure of iridocyclitis in the injured eye but retained final visual acuity of only 6/60 and later developed low-grade iridocyclitis in the uninjured eye. This patient had been struck on the left eye by a splinter of wood, while chopping sticks. He was seen by an ophthalmic surgeon about three hours after injury. A penetrating, linear, corneal wound extended horizontally across two thirds of the diameter of the cornea. Aqueous humour had escaped, the lens capsule was ruptured, and lens matter lay in contact with the posterior surface of the cornea. X-ray of the left orbit was negative. The corneal wound was closed with interrupted silk sutures. Mydriatics and antibiotics

were given topically and systemically. One week later the eye was photophobic and irritable, showing marked ciliary injection and striate keratitis. The iris was adherent in several places to lens matter, which still protruded into the reformed anterior chamber, but was no longer in contact with the posterior surface of the cornea. Pain was present at times, and the intraocular pressure was found to be slightly raised. A discission was performed, and linear extraction was carried out seven days later. During the extraction the partially healed corneal wound ruptured, and lens matter escaped through it. In the immediate post-operative period, photophobia, ciliary injection, and striate keratitis were present. Nine weeks after injury numerous large, fluffy, confluent K.P. appeared on the lower posterior corneal surface, and many fine grey K.P. could be seen scattered over the remainder of the posterior cornea. Aqueous flare was present, and ciliary injection had increased. A faint red reflex was obtainable, but there was no view of fundus detail, and visual acuity was limited to appreciation of hand movements. Subconjunctival injections of cortisone were commenced. In the first four days very little

change was observed, but seven days later aqueous flare had disappeared, and although a few fine K.P. remained round the area of the corneal scar, the large confluent K.P. had shrunk to a few clumps at the lower angle of the anterior chamber. Five weeks later, apart from a mild ciliary flush, there was no evidence of iridocyclitis. The disc, vessels, and macula, could be made out fairly clearly, and corrected visual acuity was 6/12 partly. During the next five months the interval between injections was gradually increased. From time to time slight ciliary injection was present for a few days, and an occasional K.P. appeared, became pigmented, and disappeared; but when cortisone was finally withdrawn six and a half months after the commencement of treatment, there were no inflammatory signs.

During the first six months of the follow-up period, corrected visual acuity, in the left eye, gradually decreased to 6/60. There was no evidence of inflammatory activity, and the vitreous seemed clear, but striae had developed on the anterior vitreous face, and only a very distorted view of the fundus was obtainable. The condition of the vitreous face

probably accounted for the fall in visual acuity. Throughout the follow-up period both eyes were examined by slit-lamp microscopy at each visit. For nine months there was no evidence of activity, but at the end of this period, (i.e. seventeen and a half months after injury), numerous fine K.P. and some endothelial bedewing appeared in the right (uninjured) eye. There were no other inflammatory signs, the vitreous was clear, and the visual acuity in this eye was 6/6 partly. The patient had experienced no discomfort and was unaware of any alteration in his visual acuity.

He was admitted to hospital. Mydriatics were instilled, and intravenous protein shock therapy was instituted. Three injections of a phenolized T.A.B. vaccine (Parke Davis & Co.) were given within two weeks. The endothelial bedewing disappeared, the K.P. became pigmented, and the visual acuity remained unaltered. A further follow-up of six and a half months was uneventful. Throughout the whole of this period the condition of the left (injured) eye remained unchanged, the only sign of past iridocyclitis being the presence of some fine pigment dust on the posterior surface of the cornea.

During this second period in hospital, general investigations were repeated. The only positive finding occurred in the X-ray of sinuses, which revealed some opacity in the right antrum, and showed the nasal septum to be deflected to the right side. Similar appearances had been recorded in the initial investigations. In the opinion of the consultant otorhinolaryngologist to the hospital the condition was slight and did not require treatment.

Cases 28 and 29 initially responded well to cortisone, but later relapsed, case 28 fifteen months after cortisone had been withdrawn, and case 29 during the course of cortisone treatment. In both patients, the penetrating wound involved the ciliary body as well as the cornea.

Case 28 - an 8 year old girl - sustained injury while playing with a piece of broken glass. She was seen by an ophthalmic surgeon two hours after injury, and was found to have a penetrating wound, 12 mm. long and forked at both ends, involving cornea, limbus, sclera and ciliary body. Considerable vitreous loss had occurred. X-ray of the orbit revealed a foreign body - probably glass - which was situated posteriorly in the

orbit and was extraglobular. The foreign body was left in situ, and the wound was closed with OO white silk sutures. Thirteen days after injury, endothelial bedewing, aqueous flare, and a number of fine grey K.P. appeared. By the eighteenth day there was in addition, considerable ciliary injection and the eye was photophobic and watery. Subconjunctival injections of cortisone were started. Rapid response in the first week of treatment was followed by steady gradual improvement. At the end of six weeks there were no signs of activity, and the visual acuity was 6/36. The interval between injections was gradually increased, cortisone being finally withdrawn two months later. During this period there was no sign of iridocyclitis, but six weeks before cortisone was stopped a shallow detachment appeared in the lower temporal quadrant of the retina. No tear or dialysis could be found, and in the ensuing weeks, the detachment became more extensive. During eleven months' follow-up there were no inflammatory signs, but towards the end of this period the lens gradually became opaque. From the eleventh to the fifteenth month of follow-up the patient failed to report despite repeated enquiries. She then attended

complaining of photophobia and irritation of one week's duration. The eye was watery and injected. A faint ciliary flush and numerous fine dilated iris vessels were present. In view of the severity of the original injury, the presence of cataract and detachment, and the consequently poor visual prognosis, it was considered inadvisable to retain the injured eye, and enucleation was carried out. The second eye remained normal during a further follow-up of nineteen months.

Case 29, a male aged 32, worked as a wire drawer. He stated that a length of wire had snapped, and a piece about 20 cm. long had stuck into his left eye. He added that he had pulled the wire out of his eye. He was seen by an ophthalmic surgeon a few hours after injury. A deep, shelving, penetrating, wound, five or six mm. long stretched nasally from the limbus at the 4 o'clock meridian. Hyphaema, endothelial bedewing, folds in Descemet's membrane, and subconjunctival haemorrhage were present. X-ray of the orbit revealed an intraocular foreign body. Paracentesis was carried out, and a piece of wire, 10 mm. long, was extracted by the anterior route, using a Mellinger's ring magnet. Three days after operation,

marked ciliary injection and dense endothelial bedewing were present. Hyphaema half filled the anterior chamber, and a gelatinous looking exudate occluded the pupil. Subconjunctival injections of cortisone were started. During the first week, the gelatinous exudate became much less, and the endothelial bedewing slightly less, so that many fine K.P. and numerous iris vessels could be seen. At the end of ten days, ciliary injection, flare, and endothelial bedewing remained marked. Eighteen days after the commencement of cortisone treatment, there was still considerable ciliary injection and fine striate keratitis; deep vessels invaded the cornea, and K.P. and dilated iris vessels remained, but the endothelial bedewing had disappeared and flare was minimal. The lens was cataractous, only a rim of red reflex being visible in the upper part of the pupil. Projection of light was good. In the following two months there was steady improvement; ciliary injection, flare, and iris vessels disappeared; deep corneal vessels became few and fine, and though a number of K.P. remained, they were smaller, fewer, and not fresh. Organised exudate persisted on the iris and lens in the eight o'clock

meridian, but had shrunk to small proportions and was no longer vascularised. This was the position eleven weeks after the start of cortisone treatment. Two weeks later, faint ciliary flush reappeared and the eye became slightly watery. During the following week, a considerable number of large fresh K.P. were seen, and aqueous flare and a number of dilated iris vessels were once more present. This relapse occurred when cortisone injections were still being given at weekly intervals. It was considered inadvisable to retain the eye and it was enucleated fourteen weeks after the commencement of cortisone treatment. During one year of follow-up the right eye remained normal.

Cases 30, 31 and 32 showed a limited response to cortisone treatment, but improvement was not sufficient to justify retention of the severely injured eyes.

Case 30, a man of 43 years, injured his right eye while removing tacks from furniture. He was not seen by an ophthalmic surgeon until fourteen hours after injury, when he was found to have a tri-radiate penetrating corneal wound, a small irregular pupil, and an opaque lens. X-ray of the orbit was negative

Topical and systemic penicillin, and a mydriatic were prescribed. A few days later, there was considerable swelling of the lens and anterior synechiae of iris to the corneal wound. The eye remained irritable, with marked ciliary injection, photophobia, and lacrimation, and twelve days after injury the intraocular pressure was 40 mm. (Schiotz). A linear extraction with complete iridectomy was carried out. Some vitreous loss occurred and the nasal pillar of the iris remained slightly drawn up to the wound. One week after operation the eye became photophobic, irritable, and painful. Ciliary injection was marked, and there was considerable endothelial bedewing and striate keratitis along with a moderate aqueous flare. Some lens matter remained in the pupil area and protruded into the anterior chamber. There were synechiae of lens matter to the corneal wound and of iris to lens matter. A faint red reflex was present, but no fundus details could be made out, and projection of light was poor in the upper nasal quadrant of the visual field. Treatment with subconjunctival cortisone was started. In the first three days, there was considerable lessening of pain, ciliary injection, and bedewing;

but photophobia and lacrimation were still troublesome and aqueous flare remained. Nine days after the commencement of cortisone treatment the bedewing, keratitis, and flare had gone, but photophobia and ciliary injection were still prominent. A few days later flare reappeared, and in another week fine K.P. were to be seen. In the succeeding week, the K.P. became larger and more numerous, endothelial bedewing reappeared, ciliary injection increased and a small nasal iris prolapse appeared under the conjunctiva. The intraocular pressure again rose to 40 mm. (Schiotz), and projection of light was now accurate only in the temporal half of the visual field. At the same time the left eye became watery, photophobic and slightly injected, and although there was no other inflammatory sign in this eye it was considered unwise to retain the injured eye, since cortisone was not adequately controlling the exudative reaction. Enucleation was advised and was carried out four and a half weeks after injury. The left eye remained normal during a follow-up of six months.

Case 31, a 4 year old child, had his right eye injured while playing with broken glass. He was

examined by an ophthalmic surgeon six hours after injury and found to have a prolapse of iris and a penetrating linear corneal wound extending from the ten o'clock to the two o'clock meridian. The iris prolapse was excised and the corneal wound, which was in good apposition, was covered with a conjunctival flap. The eye remained fairly quiet until fourteen days after the injury, when ciliary injection, endothelial bedewing and aqueous flare became evident, and numerous iris vessels appeared. Subconjunctival injections of cortisone were commenced. There was some lessening of ciliary injection, bedewing, and flare, but the iris vessels increased in number and the iris was seen to be incarcerated in the depths of the corneal wound. Twelve days after cortisone treatment had commenced, the eye was still very irritable. A number of large K.P. had appeared and the iris remained extremely vascular. It was decided to enucleate the eye. The left eye remained normal during a follow-up of two years and eight months.

Case 32, a 25 year old fitter, sustained a penetrating injury to his left eye, while hammering steel. The wound was scleral and situated just

beyond the limbus in the nine o'clock meridian. The iris was drawn towards the wound, but there was no actual iris prolapse. A localised opacity could be seen in the upper nasal quadrant of the lens, and a small hyphaema was present. X-ray of orbit confirmed the presence of an intraocular foreign body, and a piece of steel was extracted through the entry wound, using a Mellinger's ring magnet. Mydriatics, topical and systemic antibiotics, and protein shock therapy, were all employed in the immediate post-traumatic period. One week after the injury the eye remained watery and photophobic, with considerable endothelial bedewing, a heavy aqueous flare, and numerous tiny K.P. In the upper nasal quadrant, there was a patch of vascularised exudate on the anterior surface of the lens, and a number of posterior synechiae and dilated iris vessels were present in this area. No red reflex could be made out and focal illumination revealed the presence of a dense membrane in the anterior vitreous. Perception of light was present, but projection was inaccurate.

Subconjunctival injections of cortisone were started, and after seven days' treatment the exudate on the anterior surface of the lens had disappeared;

watering and photophobia were less, but the endothelial bedewing and the aqueous flare were more marked. By the end of the second week there had been no further improvement, and at this point a large hyphaema appeared and the eye became painful. Six days later iridocyclitis had become more active, watering and photophobia had recurred, and the hyphaema was still present. It was felt that it would be unwise to retain the eye longer, and it was enucleated. The right eye remained normal during a follow-up of eight months.

Discussion of Post-Traumatic Cases.

Of the eleven cases in this group, six showed a good response to cortisone, two responded well but later relapsed, and three showed a poor response to cortisone.

Clinical cure of iridocyclitis occurred in six cases and four of these achieved final visual acuity of 6/9 partly or more. A fifth case retained only appreciation of hand movements, and unabsorbed lens matter, poor projection of light and suspected retinal detachment, made further improvement in this case unlikely. The sixth case retained visual acuity of 6/60, but developed low-grade iridocyclitis in the

uninjured eye nine months after cortisone had been withdrawn. The question arises of the exact nature and aetiology of the iridocyclitis in the "sympathising" eye in this patient (case 27) and in the somewhat parallel case (case 5) which occurred in the post-operative group. The differential diagnosis would appear to be between sympathetic ophthalmitis, endophthalmitis phaco-anaphylactica (lens induced uveitis), and coincidental uveitis. It seems unlikely that the cases were examples of sympathetic ophthalmitis, since the inflammatory signs were not fulminating and were strictly unilateral. The clinical details of case 5 agree, in the following points, with the description of lens induced uveitis given by Kronenberg (1955) :-

1) Capsule rupture occurred at operation.
2) Iridocyclitis appeared in the unoperated eye many months later.
3) The operated eye suffered no inflammatory change or diminution in visual acuity during the active iridocyclitis in the unoperated eye.
4) Iridocyclitis in the unoperated eye was characterised by marked ciliary injection and by numerous K.P., many of which were fairly large.

These findings, together with the fact that general investigations revealed no aetiological pointer to coincidental uveitis, suggest that the case was one of lens induced uveitis. The eventual progress of the case did not however corroborate Kronenberg's categorical statements that 1) cases of lens induced uveitis show a complete lack of response to usual methods of treatment, such as mydriatics, foreign protein or cortisone, and 2) failing prompt removal of the lens in the unoperated eye, complete destruction of intraocular tissues and total loss of vision, including light perception, occurrs. In the present instance, iridocyclitis was largely controlled by the use of cortisone and mydriatics, and it was possible to discontinue cortisone after two and a half months. Eighteen months after the commencement of iridocyclitis, visual acuity had become limited to counting fingers at one metre, but the main factor responsible for the poor vision appeared to be increasing lens opacity. The patient declined to have lens extraction carried out in this second eye. Case 27, though in many respects very similar in clinical detail to case 5, may not have been one of anaphylaxis, since the iridocyclitis was less severe, the K.P. were small,

and a possible cause of coincidental uveitis was presented by the infected right antrum. The response to protein shock therapy was good.

Kronenberg mentions that three of the four cases of lens induced uveitis in his personal series were known to have previously developed allergic dermatitis. Both of the cases at present under consideration had developed skin sensitivity reactions to atropine sulphate, prior to the appearance of iridocyclitis in the "sympathising" eye. Case 25 was also sensitive to scopolomine hydrochloride and to lachesine. A known tendency to allergic dermatitis, in cases of suspected lens induced uveitis, would presumably however be regarded as corroborative evidence of very minor importance.

Of the five remaining cases in the post-traumatic group, two responded well initially, but later relapsed, and three were unimproved. All five eyes were enucleated. It will be seen that of the eleven cases in this group five retained useful visual acuity and six did not.

The shortest follow-up on the cases, after cortisone had been withdrawn, was six months. The longest follow up was thirty-two months and the average

follow-up 16.6 months.

In six cases, the entry wound was limited to the cornea. Five of the six clinical cures occurred in this group. The entry wound in the sixth cured case involved the sclera only. In four cases the entry wound involved the ciliary body, and all four eyes had to be enucleated. In the fifth eye which was enucleated, the entry wound involved the cornea only. (Table 11). The figures suggest that the use of subconjunctival cortisone, after iridocyclitis has developed, does not alter the usually poor prognosis of penetrating injuries which involve the ciliary body.

In five cases an intraocular foreign body was present and was removed by magnet extraction. In three cases the foreign body was removed within eight hours of injury. These cases were among the cures, and two of the three retained good vision. In the two remaining cases, more than twenty-four hours elapsed between the entry of the foreign body and its extraction. Both eyes were enucleated. It would appear that the presence of an intraocular foreign body, provided it can be promptly removed, need not adversely affect the end results of cortisone treatment.

In the present group of cases, lens damage, which

TABLE 11.

POST-TRAUMATIC CASES.

Relationship between Site of Penetrating Wound and Result.

Site of Penetrating Wound	No. of Cases	Result	
		Cure	Enucleation
Cornea	6	5	1
Sclera	1	1	-
Ciliary body	4	-	4

occurred in five of the six cured cases, did not militate against a good result.

Iridocyclitis appeared ten days or less after injury, (average 8.6 days) in six cases. This group included four of the six cures and three of the five cases which retained useful visual acuity. The remaining five cases developed iridocyclitis more than ten days after injury, (average 25.6 days). They included one case which achieved clinical cure of iridocyclitis and retained good vision, one case which developed low-grade iridocyclitis in the uninjured eye, and three of the five enucleations.

The interval which elapsed between the onset of iridocyclitis and the commencement of cortisone treatment was not found to influence the end results, but it was relatively short in all cases, the maximum delay being fourteen days, and the average delay only 3.4 days.

As with the post-operative group, it would appear that the cases which develop iridocyclitis in the immediate post-traumatic period have a greater chance of success. The case of choice is probably that in which iridocyclitis appears within about ten days of a penetrating injury, in which the entry wound has not involved the ciliary body. The disturbing

appearance of iridocyclitis in the uninjured eye of case 27, after nine months of uneventful follow-up, and the relapses which occurred in cases 28 and 29, suggest that unless the above criteria are satisfied, and unless it appears likely that good visual acuity will be achieved, it is probably not justifiable to administer cortisone in attempts to retain injured eyes which have developed iridocyclitis.

Appendix 1.

The Enucleations.

In the series as a whole, eight eyes were enucleated. Histological sections from these eyes were examined by the late Dr. J.D. Fraser (Pathologist, Glasgow Eye Infirmary). He was of the opinion that the use of cortisone had not resulted in any significant variation from the histological appearances usually found in eyes enucleated because of post-operative or post-traumatic iridocyclitis. This finding is scarcely surprising since, in each of the cases in question, cortisone had failed to control the iridocyclitis which was present.

Appendix 2.

Mydriasis and Sensitivity Reaction.

Mydriasis was achieved with gutt. atropine sulphate 1% in all except five patients who were known to have been previously allergic to this drug. In four of these, (cases 2, 8, 11, and 27), gutt. hyoscine hydrobromide ¼% was used. The fifth patient (case 4), who was known to be sensitive to both atropine and hyoscine, was given gutt. lachesine 1%.

Ten patients in the present series developed skin sensitivity reactions to drugs while being treated with topical cortisone. Nine of these occurred during the course of subconjunctival injections, and one, (case 12), developed sensitivity to atropine sulphate while being treated with cortisone drops. In the first group, seven patients (cases 3, 5, 7, 9, 17, 24, and 32) became sensitive to atropine sulphate, and mydriasis was continued with gutt. hyoscine hydrobromide ¼%. Case 9 had previously been known to be albucid sensitive, and case 32 had become sensitive to ung. penicillin at an earlier stage in cortisone treatment. Two patients, (cases 2 and 27), known before treatment commenced to be atropine

sensitive, became sensitive to hyoscine while receiving cortisone, and mydriasis was continued with gutt. lachesine 1%. It is apparent that cortisone, administered by the subconjunctival route, will not prevent the occurrence of skin sensitivity reactions in a proportion of cases. This finding is in agreement with the experience of Duke Elder and others (1951).

Appendix 3.

Investigations.

The following investigations were carried out in each case - X-rays of chest, sinuses, and teeth or gums; Wassermann reaction; Gonococcal complement fixation test; Mantoux skin test.

The Wassermann reaction and the Gonococcal complement fixation test were negative in all cases. Eight of the thirty-two cases showed negative results to all the investigations. A further twelve cases had positive findings which were restricted to evidence of musosal thickening in one or more sinuses, and/or a positive Mantoux reaction. Of the remaining twelve patients, six had positive findings in the chest and six showed evidence of infection in one or more sinuses. Among the positive chest X-rays, with one exception, the reports were of chronic bronchitis with emphysema or fibrosis. One case had a pleural transudate, associated with congestive cardiac failure.

Of the cases with completely negative investigations, 50% were cured. The rate of cure among cases with positive findings in the investigations was also 50%; but in this group it is interesting to note that those

with definite evidence of chronic infection in the chest and sinuses showed a rate of cure of 70%, while those with findings of apparantly lesser importance - such as mucosal thickering of sinuses, or a positive Mantoux reaction - showed a rate of cure of only 30%. The presence of chronic inflammatory change in the chest or sinuses did not therefore appear to weigh against a successful response to topical cortisone. It is surprising however that these cases showed no particular tendency to relapse on withdrawal of cortisone although, in practically all of them, the condition of the chest or sinuses remained unimproved throughout both treatment and follow-up. This finding suggests that the changes in the chest and sinuses were not of immediate aetiological significance in the occurrence of iridocyclitis.

PART III.

A COMPARATIVE STUDY OF THE THERAPEUTIC VALUE OF TOPICAL CORTISONE.

Section 1. Published Reports.

Section 2. Comparable Cases not Treated by Cortisone.

PART III

A Comparative Study of the Therapeutic Value of Topical Cortisone.

Section 1.

Published Reports.

Hobbs (1951) stated that cortisone appeared to have a field of usefulness in post-operative iridocyclitis, but that further trial was needed to determine the precise indications for its use.

Duke Elder, (1951e), reported that 25% of cases of post-operative and post-traumatic iridocyclitis, which were treated with cortisone, showed little or no improvement. This figure included cases from the literature as well as a personal series, and about three-quarters of the total cases had been treated with topical cortisone. In his personal series, thirty-two cases were treated with drops or subconjunctival cortisone or both. Of these, twenty-six were cases of post-operative iridocyclitis. Eight were cured, ten improved, and eight unimproved.

One "cured" case subsequently relapsed. The six remaining cases occurred after penetrating injuries. Of these three were cured, and three improved, (Duke Elder 1951f). Purnell and Leopold (1952) gave details of thirty cases of post-operative iridocyclitis, twenty-one of which were treated with frequent subconjunctival injections of cortisone (doses of 1.25 mg. or 2.5mg. t.i.d.), and nine of which were given cortisone drops diluted one in four with either normal saline or Zephiran solution. Twenty-three cases improved, two relapsed, and five were unimproved. Hobbs (1951) treated thirteen cases of post-operative uveitis with topical cortisone and concluded that in only five of them was "improvement such as to suggest that cortisone had been of certain help." Fine and Goodwin (1952) reported the effects of topical cortisone in nine cases of post-operative and thirteen cases of post-traumatic iridocyclitis. In the post-operative group, six cases showed a definite therapeutic effect, one showed doubtful benefit, and in two there was no therapeutic effect. Among the thirteen post-traumatic cases, a definite therapeutic effect was obtained in only one case, while in twelve there was no effect. These

traumatic cases had occurred under conditions of active military service and, on the average, treatment did not commence until between ten and twenty days after injury. In four of the cases a retained foreign body was present. Most of the group were treated by subconjunctival injection, but a few cases were treated with drops.

Woods (1951) reported the effect of topical application of cortisone in eight cases of post-operative uveitis. Good results were obtained in six cases, but there were two subsequent relapses and the remaining two cases showed no improvement. Leopold and others, (1951c), used subconjunctival cortisone in six cases of post-operative uveitis, of which four improved and two relapsed. Two cases of phaco-anaphylaxis were given subconjunctival cortisone with improvement in one case, and no improvement in the other. Fitzgerald and others (1951) reported four cases of post-operative uveitis. Two were treated with cortisone drops (one in one dilution) and two received subconjunctival injections combined with drops (one in four dilution). All four cases improved and in the two latter cases it was thought that the eyes would

probably have been lost without the use of cortisone. Agatson (1951) treated four cases of post-operative uveitis with topical cortisone. Two cases had drops and subconjunctival cortisone, one had subconjunctival cortisone alone, and one had drops alone. All four cases were reported cured. The duration of follow-up was not mentioned. Three cases of post-operative iridocyclitis were reported by Lavery and others (1951). One received subconjunctival cortisone and had a good result with rapid clearing of vitreous opacities. The two others showed good results after only two weeks' treatment with cortisone drops, but one of them relapsed three months later. Scheie and others (1951) treated three cases of post-operative iridocyclitis with cortisone drops. One case improved and two had remissions. Taylor (1952) used cortisone drops, with success, in two cases of post-operative iridocyclitis.

Gordon and others (1951) obtained a good result in one case of post-traumatic iridocyclitis treated topically, and Little (1951) reported a successful result in one post-traumatic case treated with cortisone drops. Olsen and others (1951), Steffensen and others (1951), Thorpe (1951), and Trope (1951), each reported

one case of post-operative iridocyclitis, treated with cortisone drops with good effect. The case of Steffensen and others was still having treatment at the time of reporting.

Hull (1953) stated that he had found topical cortisone of little help in ocular injuries and felt that it did not influence the course of post-operative iridocyclitis. No details were given of clinical histories, doses employed, or duration of treatment. Hobbs (1951) was of the opinion that the effects of cortisone in post-operative uveitis showed wider variations than in other groups of uveitis, and that they were far less easy to assess.

SUMMARY.

Reports of 135 cases of post-operative and post-traumatic iridocyclitis treated with topical cortisone have been collected from the literature. 114 cases occurred after operation. Of these, 25 were reported cured, 57 improved, 24 unimproved and 8 relapsed. 38 cases had been treated by subconjunctival injection, 2 had received subconjunctival injection along with some other form of topical cortisone, and 49 cases were treated with cortisone drops only.

In 49 cases the authors did not state which form or forms of topical therapy had been employed.

In the post-traumatic group there were 21 cases, of which 5 were cured, 4 were improved, and 12 were unimproved. 10 cases had been treated by subconjunctival injection, and 4 by drops. In 7 cases it was not stated which form of topical therapy had been employed.

It was not possible to assess separately the response of cases which had received cortisone by the subconjunctival route only, since most authors reported the results of all forms of topical therapy collectively.

Section 2.

Comparable Cases not Treated with Cortisone.

When the present investigation was planned it was intended that a series of control cases, treated by standard methods and not receiving cortisone, would be observed. Unfortunately such a policy was quickly found to be impracticable. By September 1951 there was a wide-spread belief among opthalmologists that cortisone was of value in many forms of iridocyclitis. Consequently, surgeons referring cases for inclusion in this series were understandably unwilling that, in the process of random sampling, cortisone be witheld from a proportion of their cases, irrespective of severity. Indeed, it already seemed doubtful if it would be ethical to adhere to such a rigid policy. Moreover, it had become obvious that any attempt to persist in having a control series would merely result in the comparison of a group of severe cases receiving cortisone with a group of mild cases not receiving cortisone. The ideal of concurrent control cases was therefore abandoned and, as an alternative, a

search was made in hospital records, prior to 1950, for comparable cases. The criteria of selection were the same as had been applied to the personally observed cortisone treated cases and considerable care was taken to ensure that the collected cases were as nearly as possible comparable in all respects.

Twenty-one cases of post-operative iridocyclitis and fifteen cases of post-traumatic iridocyclitis were collected. The interval between operation or trauma and the appearance of iridocyclitis was twelve weeks or less in all except three cases, in which iridocyclitis appeared after a longer interval. There was practically no delay in these collected cases between the appearance of iridocyclitis and the commencement of the chosen treatment. A mydriatic had been administered in all cases, and in some instances additional therapy such as diathermy, subconjunctival or retrobulbar injection of antibiotics, systemic administration of antibiotics, oral salicyclates, or mercury inunction, had been employed.

With the exception of one post-operative and two post-traumatic cases, the periods of follow-up in the collected cases were similar to those obtaining in the

cortisone treated series. In one post-operative case, only one month's follow-up was available, so that the recorded result of "cured"may have been unduly favourable. In two of the post-traumatic cases only one month's follow-up was obtained, but in each case the injured eye had been enucleated before the end of this period.

There were only two diabetic patients among the collected cases in comparison with seven in the cortisone treated series, a factor which should if anything have favoured the former group.

A comparison of the end results obtained in personally observed cases treated with subconjunctival cortisone, in published cases treated with a variety of topical cortisone, and in collected cases which had not received cortisone, is shown in Tables 12 and 13.

Table 12 indicates that in the post-operative group a higher rate of cure and improvement was achieved in cases which received cortisone. In addition the rate of cure, as distinct from improvement, appeared to be greater when cortisone was administered by subconjunctival injection than when a variety of topical therapy was employed. This superiority of

TABLE 12.

POST-OPERATIVE IRIDOCYCLITIS
Comparison of Response in Cortisone Treated and Non-Cortisone Treated Cases.

Result	21 Personal Cases. (Sub-conj. cortisone)	114 Published Cases. (Topical cortisone)	21 Collected Cases. 1946-1950 (no cortisone)
Cured	42.9%	21.9%	28.6%
Improved	14.3%	50%	14.3%
Unimproved	28.6%	21.1%	47.5%
Relapsed	9.5%	7%	-
Cyclitis other eye.	4.7%	-	4.8%
Sympathetic	-	-	4.8%

TABLE 13.

POST-TRAUMATIC IRIDOCYCLITIS.
Comparison of Response in Cortisone Treated and Non-Cortisone Treated Cases.

Result	11 Personal Cases. (Sub-conj. cortisone)	21 Published Cases (Topical cortisone)	15 Collected Cases. 1946-1950 (no cortisone)
Cured	45.5%	23.8%	6.7%
Improved	-	19%	6.7%
Unimproved	27.3%	57.2%	80%
Relapsed	18.2%	-	-
Cyclitis other eye.	9%	-	-
Sympathetic	-	-	6.7%

the subconjunctival route of administration was again apparent in the figures for post-traumatic cases. (Table 13). Several factors may have contributed to the higher rate of cure achieved in the personally observed cases. Firstly, the exclusive use of subconjunctival injection in the present series ensured that the patient always received the treatment prescribed. Secondly, intraocular concentrations achieved by subconjunctival injection may have been higher and more prolonged than those achieved by other forms of topical therapy. Thirdly, cortisone treatment was continued until the maximum improvement in inflammatory signs had been achieved - even when this necessitated prolonged therapy - and withdrawal of cortisone, when commenced, was extremely gradual and cautious.

In the post-traumatic group the rate of cure and improvement in cases which did not receive cortisone was strikingly low.- a finding which is probably related to a general tendency in the pre-cortisone era for any injured eye which developed severe iridocyclitis to be enucleated without resort to further therapy. The inclusion in the personally observed series of cases of severe iridocyclitis occurring in grossly

injured eyes probably accounts for the high relapse rate in this group.

Table 14 shows that in the post-operative group the proportion of cases which retained useful final visual acuity was higher in the personally observed cortisone treated cases than in the collected cases which had not received cortisone. In the post-traumatic group (Table 15) retention of useful visual acuity was proportionately even more frequent among the cortisone treated cases. This finding can be related to the fact that enucleation was carried out in 93.3% of post-traumatic cases which had not received cortisone, whereas in the personally observed cortisone treated series enucleation was necessary in only 45.5% of post-traumatic cases.

These results indicate that in post-operative and post-traumatic iridocyclitis treatment with topical cortisone acetate, in association with mydriatics, offers distinct advantage over previous standard methods of therapy, in that a higher proportion of cases achieve cure and improvement, with retention of useful visual acuity. The subconjunctival route of administration would appear to be superior to other methods of topical therapy.

TABLE 14.

POST-OPERATIVE IRIDOCYCLITIS
Comparison of Final Visual Acuity in Cortisone Treated and Non-Cortisone Treated Cases.

Final Visual Acuity	21 Personal Cases. (Sub-conj. cortisone)	21 Collected Cases. 1946-1950 (no cortisone)
More than $\frac{4}{60}$	61.8%	47.6%
Less than $\frac{4}{60}$	38.2%	52.4%

TABLE 15.

POST-TRAUMATIC IRIDOCYCLITIS.
Comparison of Final Visual Acuity in Cortisone Treated and Non-Cortisone Treated Cases.

Final Visual Acuity	11 Personal Cases. (Sub-conj. cortisone)	15 Collected Cases. (no cortisone)
More than $\frac{4}{60}$	45.5%	6.7%
Less than $\frac{4}{60}$	54.5%	93.3%

PART IV

OCCURRENCE OF KERATO-CONJUNCTIVITIS IN CASES TREATED WITH TOPICAL CORTISONE.

INTRODUCTION.

Section 1. Review of Literature.

Section 2. Presentation of Cases.

Discussion.

PART IV

Occurrence of Kerato-Conjunctivitis In Cases Treated With Topical Cortisone.

INTRODUCTION.

In the course of this investigation it was noticed that six of the twenty-one post-operative cases developed catarrhal conjunctivitis and punctate keratitis, in the treated eye, while receiving cortisone. Cultures from the conjunctival sacs of these cases yielded no growth, and microscopic examination of conjunctival smears showed a lymphocytic exudate - findings which suggested the possibility of virus infection. In each of the cases under discussion, ung. chloromycetin 1% was instilled q.i.d. in the affected eye while the results of culture were awaited. This treatment appeared to have no effect on the progress of the keratitis.

In four cases keratitis cleared up after cortisone had been withdrawn, and in the remaining two cases keratitis disappeared after four or five weeks, while the patients were still receiving cortisone treatment. In one of the latter cases the condition reappeared at

a later date during a second course of cortisone treatment.

This occurrence of punctate keratitis in six of twenty-one cases being treated with long-term topical cortisone raised the question of the nature and aetiology of the keratitis.

Section 1.

Review of Literature.

The nomenclature and description of punctate keratitis in the literature is confusing. The clinical condition which Fuchs described in 1889, and termed superficial punctate keratitis, had been thought in more recent years to include a number of clinical conditions of varied aetiology. The term has certainly been used from time to time to describe cases which differed in clinical detail from Fuchs' original picture.

Duke Elder (1938a) considered that the term superficial punctate keratitis referred to a condition, commonly occurring after upper respiratory infection, in which catarrhal conjunctivitis was followed, after three or four days, by the appearance of grey spots in the deeper layers of the corneal epithelium and in the superficial layers of the substantia propria. The spots varied from minute dots to large areas with vignetted edges. Staining with fluoresceine was variable, and corneal sensation was usually initially impaired. The condition lasted for a period varying from several weeks to several years, and was said not

to recur. The aetiology was stated to be uncertain, having been variously ascribed to virus infection, bacterial infection, neurotrophic factors, and nutritional factors. Gifford (1947) considered that the condition described by Fuchs included various forms of keratitis in which small infiltrates, either staining or not, occurred in the superficial corneal layers. He was of the opinion that keratitis usually persisted for from three weeks to three months, and considered that recurrences were not uncommon. He attributed the condition to infection with a virus, possibly allied to, but not identical with, that of herpes simplex. Duke Elder (1938b), discussing varieties of superficial keratitis, mentioned the occurrence of an epidemic form of kerato-conjunctivitis, and the term epidemic kerato-conjunctivitis is commonly found in the literature from 1938 onwards. The clinical descriptions which appear under this heading vary a little in detail, but sizeable epidemics in which the clinical findings are fairly constant have been reported from many parts of the world in recent years..

Hogan and Crawford (1942) reviewed the literature on epidemic kerato-conjunctivitis and produced a

detailed report of 125 cases. They considered the term to include Fuchs' superficial punctate keratitis, Adler's keratitis maculosa, and Stellwag and Dimmer's keratitis nummularis. In their personal series, patients first complained of a sandy or gritty sensation in the eye. This symptom was found to be accompanied by oedema of the caruncle or plica semilunaris, and was closely followed by oedema of the lower bulbar conjunctiva. Approximately twenty-four hours after the commencement of irritation, oedema of the lids developed and was often accompanied by pseudo-ptosis. After between thirty-six and forth-eight hours intense conjunctival hyperaemia was apparent, though there was little discharge and only moderate discomfort. In three-quarters of the cases the preauricular, submaxillary, or cervical glands were enlarged. Keratitis appeared between the second and the eighth day and took the form of punctate epithelial erosions which stained with fluoresceine. As the conjunctivitis regressed the epithelial erosions healed and, about the eighth day, were replaced by macular infiltrates of 1 - 1½ m.m. diameter. For the most part these were either non-staining and situated in the superficial

layers of the substantia propria, or (less frequently) faintly staining and situated in the deeper layers of the epithelium; but considerable variation in depth of infiltrates was to be found. In 13.6% of cases they occurred in the middle layers of the substantia propria, while in 6% of cases they were placed still more deeply, and were accompanied by keratic precipitates, wrinkling of Descemet's membrane, and aqueous flare. Corneal sensation remained normal in most of the cases. Twenty-five per cent of cases became bilateral. Young adults between 18 and 40 years of age were most frequently affected, and males out-numbered females by two or three to one. Children under 12 years of age were rarely affected. The incubation period varied between five and twelve days, but was most commonly eight days. Keratitis remained active for any period from two months to two years. The criteria for early diagnosis were, 1) early oedema of the plica and caruncle, 2) severe conjunctival injection without discharge, 3) the presence of enlarged glands, 4) the absence of bacteria in smears and cultures, 5) the presence of petechial haemorrhages in mucous membranes.

The picture presented by Hogan and Crawford is

clear cut and from 1949 onwards a considerable measure of agreement exists among writers on the subject, though nomenclature is at times still confusing, since some workers consider epidemic kerato-conjunctivitis and superficial punctate keratitis to be separate conditions, while others regard the terms as synonymous. Clinical observations vary in detail. The incubation period of epidemic kerato-conjunctivitis is said by Correard and Plessier (1949) to be 5 - 10 days, by Pelliteri and Fried (1950) to be 3 - 19 days, by Cockburn and Danielson (1955) to be 10 - 16 days, by Ryan and others (1955) to be 5 - 10 days, by Schneider and others (1956) to be 6 - 9 days, and by Winning (1956) to be 10 - 12 days. Correard and Plessier (1949), Berliner (1951) and Sezer (1953) state that the condition commences with an acute follicular conjunctivitis and glandular enlargement, while Braley and Alexander (1953) report that the condition is accompanied by little conjunctival reaction. Thygeson (1949), Correard and Plessier (1949), Fine and Goodwin (1952) and Sezer (1953) are of the opinion that the corneal infiltrates in epidemic kerato-conjunctivitis are typically subepithelial. Thygeson (1950) and Braley and Alexander (1953) mention superficial punctate

keratitis separately and state that the corneal infiltrates may be epithelial or subepithelial, while Fine and Goodwin (1952), in a review of corneal conditions, consider superficial punctate keratitis and epidemic kerato-conjunctivitis together, and state that the opacities are epithelial. Braley and Alexander (1953) note that in epidemic kerato-conjunctivitis the corneal infiltrates may or may not stain with fluoresceine, and Thygeson (1950) mentions that in superficial punctate keratitis the centres of the infiltrates stain irregularly. Berliner (1952), considering epidemic kerato-conjunctivitis and superficial punctate keratitis together, states that the infiltrates stain poorly. Schneider and others (1956) report that the conjunctival phase of the infection lasts for between two and three weeks, and that most corneal lesions clear between the fourth and the eighth week, though many are still present after twelve months. Winning (1956) noted that in his series attacks lasted between two and six weeks.

Early opinion on the aetiology of epidemic kerato-conjunctivitis was confined to statements of the unconfirmed theories to which reference has already been

made. (Duke Elder 1938a and Gifford 1947). In recent years a considerable volume of evidence has been built up in support of the theory that epidemic kerato-conjunctivitis is caused by infection with a virus. Sanders (1942), working with Braley, cultivated a virus from cases of epidemic kerato-conjunctivitis, by passage of conjunctival scrapings in mouse brain followed by growth in tissue culture. This virus produced the characteristic course of epidemic kerato-conjunctivitis in a human volunteer. Lépine and others (1949), were unable to transmit the virus of epidemic kerato-conjunctivitis to rabbits or dogs, but successfully transmitted it to mice to produce typical cerebral lesions. Although the virus could not be isolated it could be cultivated in Maitland's medium. Sezer (1953) was able to produce typical pathologic changes of epidemic kerato-conjunctivitis on chorio-allantoic membrane of fertile egg, and a virus which differed from that of herpes simplex, and which could be maintained indefinitely on chorio-allantoic membrane, was isolated. Sezer concluded that Koch's postulates appeared to be fulfilled by this work. Braley (1953) stated that the causative agent of epidemic kerato-conjunctivitis

was probably an intranuclear epithelial trophic virus, closely related to the viruses that cause encephalitis. Cockburn and others (1953) could however find no neutralising antibodies in sera from convalescent patients, against the Sanders-Braley epidemic kerato-conjunctivitis virus, and Cockburn (1954) concluded that, at that date, no virus was available which could be regarded with confidence as the aetiologic agent of epidemic kerato-conjunctivitis. Ormsby and Fowle (1954) found that the sera of sixty-one patients recovering from epidemic kerato-conjunctivitis failed to show neutralising antibodies to the Sanders-Braley strain of virus; but they isolated, from patients suffering from epidemic kerato-conjunctivitis, five strains of virus which proved to be mouse encephalitis virus, related to Theiler T.O strain. In later work Cheever (1957) studied two strains of virus, which were obtained from Braley and were believed to have originated from a pool made by Sanders during the 1942 outbreak of epidemic kerato-conjunctivitis. The two strains, which appeared to be identical, were found to be closely related to the St. Louis encephalitis virus. Antibody studies with convalescent serum, from recent

cases of epidemic kerato-conjunctivitis in the United States and Canada, yielded no evidence to suggest that the Sanders-Braley virus was the aetiologic agent in these recent outbreaks. Sanders (1957) agreed that the virus isolated by himself and Braley in 1942, had not, since that date, been unequivocally obtained. He felt that it was not clear whether the 1942 virus was related to the St. Louis encephalitis virus, but he remained convinced that it had been either the causative agent of the 1942 outbreak of epidemic kerato-conjunctivitis, or had at least been in some fashion closely related to it.

In 1953 Rowe and others published a report on the biological properties of a new group of viruses - the adenoidal - pharyngeal-conjunctival (A.P.C.) group. Six immunologically distinct types were described, and it was stated that type 3, obtained from nasopharyngeal secretions, probably caused acute febrile pharyngitis with conjunctivitis. Ryan and others (1955) stated that eight viruses in the A.P.C. group could be identified by immunological methods, and that of these, type 3 was often found in conjunctival infections. Fowle and others (1955) isolated three viruses of

type 3 A.P.C. group from cases of kerato-conjunctivitis. One of the strains could be adapted to cause irregular lesions on chorio-allantoic membrane of chick embryo, and also caused transient illness in the first and second mouse passages. Jawetz and others (1956a) stated that cases from which type 3 A.P.C. virus was isolated presented acute follicular conjunctivitis with regional adenitis and only mild systemic upset. Type 8 A.P.C. virus was isolated from a sporadic case of epidemic kerato-conjunctivitis without fever or systemic illness. Further work by this group on neutralizing antibodies, suggested that type 8 A.P.C. virus may play a role in the aetiology of epidemic kerato-conjunctivitis. (Jawetz and others 1956b). Winning (1956), in a preliminary report on an outbreak of epidemic kerato-conjunctivitis in Glasgow, stated that a virus belonging to the A.P.C. group was cultured from cases in his series. Ormsby and others (1956) discussed ten cases of epidemic kerato-conjunctivitis which they had observed since 1955. In four cases an A.P.C. virus was isolated in tissue cultures, and three of these were identified by Huebner as type 3 A.P.C. virus. One of the ten cases showed neutralising antibodies to the "Trim" virus of Jawetz.

These writers stated that convalescent serum from cases of epidemic kerato-conjunctivitis in Ontario in 1951 neutralised "Trim" virus, and they were of the opinion that, in Ontario, there were two immunologically distinct viruses of the A.P.C. group which caused kerato-conjunctivitis, one being the "Trim" virus of Jawetz and the other type 3 of the A.P.C. group. Ormsby (1956) reported that nine human types of A.P.C. virus had been described. Type 3 A.P.C. had been isolated from two epidemics in Canada, in which the presenting signs were fever, malaise, and cough, in children, and conjunctivitis in adults.

Fowle and others (1957) mentioned a case in which type 3 A.P.C. virus was isolated, and in which corneal opacities, which could not be distinguished from those of epidemic kerato-conjunctivitis, persisted for six months. Heubner and Rowe (1957), Bietti and Bruna (1957), and Mitsui and others (1957) all formed the opinion that type 8 A.P.C. virus was probably the specific aetiologic agent in epidemic kerato-conjunctivitis The workers in the latter group had been able to carry out experiments in which human volunteers inoculated with type 8 A.P.C. virus had developed lesions typical

of epidemic kerato-conjunctivitis. Huebner and Rowe felt that conjunctival irritation appeared to play a role in the establishment of infection, while Bietti and Bruna were of the opinion that a break in the corneal epithelium was of significance. Mitsui and Jawetz (1957) reported a case of epidemic kerato-conjunctivitis from which they isolated type 8 A.P.C. virus, and in which a greater than fourfold rise in neutralising antibody titer to type 8 A.P.C. supported the impression of active infection by this agent. Nevertheless, Jawetz and others (1957) were of the opinion that the evidence for the constant association of type 8 A.P.C. virus with epidemic kerato-conjunctivitis, though convincing, was incomplete, and that at the time of writing there was still no virus available which could be regarded with confidence as the aetiologic agent of epidemic kerato-conjunctivitis. Finally, Cockburn (1957) put forward the following theory on the epidemiology of epidemic kerato-conjunctivitis:- The causal agent is a virus of the adeno-virus (A.V.) group whose normal habitat is the naso-pharynx, but which is capable of causing pathology in the conjunctiva and to a lesser extent in the cornea. Usually it produces relatively

mild inflammation in an infected eye, but should conditions exist for the rapid passage of the pathogen from the infected eye to a series of susceptible eyes, then a strain of virus is produced that is much more specifically adapted to the superficial tissues of the eye. Infection with this virus strain produces the lesions of classical epidemic kerato-conjunctivitis.

Satisfactory specific treatment for types of keratitis thought to be of virus origin has not yet been found. The response to antibiotics has been poor and unconvincing. Considerable experimental and clinical work has been carried out to assess the effect of cortisone on virus infections in general. Kilbourne and Horsfall (1951) while culturing viruses on eggs, reported an increased growth of virus on those injected with cortisone. Leopold and others (1951d) treated experimental herpes simplex keratitis with topical cortisone and found the treated eyes more severely involved than the controls. Thygeson and others (1951), in similar experiments, in which three different strains of virus were used, observed improvement in only one of seven cases treated with subconjunctival cortisone, and in the six others infection in the treated eyes was of

identical or greater intensity than that in the controls. Thygeson (1951) was of the opinion that in experimental vaccinia and herpes simplex keratitis, cortisone increased the severity of the keratitis and greatly increased the incidence of encephalitis. Ormsby and others (1951 and 1952) formed the opinion that cortisone, applied intramuscularly, subconjunctivally, or in the form of drops or ointment, caused some arrest of conjunctival and corneal vascularisation but failed to shorten the course of experimental herpetic keratitis in rabbits. If however large intramuscular doses of cortisone were administered, the acute phase of herpetic infection was prolonged, and the onset of healing was delayed. These writers were uncertain whether the effects produced by cortisone resulted from interference with the natural mechanism of healing, or from enhancement of the growth of the virus. Hallett and others (1951a) used cortisone in the form of drops or ointment, in experimental virus keratitis in rabbits, and reported that in half the cases the treated eyes were worse than the controls and in the other half there was no improvement. When cortisone was administered systemically however, keratitis was retarded up to the

fifth day. Leopold and others (1951e) carried out similar experiments and stated that cortisone drops had no significant influence on the keratitis, but, during the first few days of keratitis, subconjunctival cortisone increased the severity of the lesion, while systemic administration reduced its severity. In the later stages there was no difference between treated and control eyes, irrespective of the route of administration of cortisone. Latte (1953) recorded that topical cortisone had an unfavourable effect on herpetic keratitis in rabbits, retarding healing for 8 - 10 days. Franceschetti and others (1952) and Boles and Cima (1953) found that topical cortisone had no curative effect on experimental herpetic infection of rabbit cornea, and Boles was of the opinion that its use facilitated the spread of infection to the central nervous system. Bruna and Salvi (1952) grew strain H.F. of herpes virus on the brains of mice and on chorio-allantoic membrane of chick embryo. The virus proliferated rapidly in the presence of cortisone, and the death rate of the treated animals was higher than that of the controls. Ormsby and Fowle (1954) while attempting to show neutralising antibodies to

the Sanders-Braley strain of virus, isolated five strains of mouse encephalitis virus. They found that cortisone increased paralysis and death in mice inoculated from both test and control cultures. Kimura and Okinmoto (1957) stated that experimental herpes simplex infection of the eye could be made worse by the cortico-steroid hormones, and that, in treated animals, the high incidence of death due to encephalitis suggested an enhancement of the generalised spread of the virus by the cortico-steroids, and/or increased multiplication of the virus.

It is apparent that the results of cortisone treatment in experimental virus keratitis - particularly herpetic keratitis - have been almost uniformly poor. In comparison, clinical trials of cortisone in types of keratitis thought to be of virus origin, have produced less clear-cut results.

Hogan and others (1951) were of the opinion that cortisone was ineffective and possibly deleterious in ocular virus disease. Gordon and others (1953) and Offret and Lombard (1953) found it often ineffective with only occasional good results. François and others (1952), reported good results with cortisone in old

keratitis of virus origin, while Marin Amat (1953) formed the opinion that topical cortisone was contraindicated in ocular virus disease.

Where writers mention specific virus conditions reports are more definite. Gordon and others (1951) stated that despite the fact that cortisone was said to have a deleterious effect on virus diseases, two cases of herpes zoster ophthalmicus responded well to topical cortisone, though a third failed to benefit. Duke Elder (1951g) reported 25% failures and 25% recurrences in eight cases of herpes zoster treated with topical cortisone.

In herpes simplex keratitis the greater weight of opinion suggests that cortisone is ineffective and sometimes harmful, though a number of writers report improvements after treatment with cortisone. Duke Elder (1951f) noted fifteen cases from the literature, in which 60% good results were claimed; but in a personal series of 7 cases only one case responded well, with relief of symptons, and the other six were unaffected. Trope (1951) reported one case of dendritic keratitis sucessfully treated with cortisone, and Lerner (1951) one case of dendritic keratitis with

iritis which responded favourably to subconjunctival cortisone. Barrios and Barrière (1951) felt that cortisone was effective in herpetic keratitis, while Offret (1951) was of the opinion that in two cases of herpetic keratitis cortisone had helped the healing of opacities. Von Sallman and others (1951) found seven cases of herpetic keratitis improved by topical cortisone. Soliman (1952) found the course of herpetic corneal affections shortened by the application of a combination of topical cortisone and aureomycin.

Rapisarda (1952), Melodia (1952), Latte (1953) and Hogan and others (1955) were all of the opinion that topical cortisone was totally ineffective in herpetic keratitis, while Offret and Lombard (1953) found its effect inconstant. Arruga (1952), Moser (1952), Thygeson (1953a) recorded the occurrence of corneal ulceration, hypopyon, and perforation, following the use of topical cortisone in dendritic keratitis. Thygeson (1951) had noted a general failure of cortisone to produce improvement in ocular infections of viral origin. In 1952 he stated that cortisone was of no value in herpes simplex of the cornea, and that in some clinical cases it had

proved harmful. One year later (1953b) he was of the opinion that the use of cortisone in the early stages of virus keratitis was absolutely contraindicated. Heath (1954) reported a case of recurrent attacks of simple keratitis associated with uveitis, which, on the twelfth day following the commencement of treatment with ½% cortisone drops, developed meningitis which was confirmed by C.S.F. examination. He suggested that the meningitis was of viral origin, and that cortisone had reduced local resistance to virus infection. Ormsby (1957) was of the opinion that hormonal therapy has a deleterious effect on superficial herpes simplex lesions.

In superficial punctate keratitis and epidemic kerato-conjunctivitis the reported results of treatment with cortisone are more favourable than in other forms of virus keratitis, but once more there are variations of opinion, with more failures and adverse effects reported in recent years.

Agatson (1951,) Leopold and others (1951a), McLean and others (1951), Von Sallman and others (1951), Schie and others (1951), Melodia (1952), Rapisarda (1952), and Hogan and others (1955) all report good results in

the treatment of superficial punctate keratitis with cortisone, though Schie and Hogan found that some relapses occurred. Duke Elder (1951f) collected reports of 12 cases of superficial punctate keratitis treated with topical cortisone, of which eight were said to have responded well, three to have relapsed, and one to have improved. In three cases which he observed personally, there was no dramatic response to cortisone. Purnell and Leopold (1952) treated nine cases of superficial keratitis with topical cortisone and reported eight improved and one relapsed. Fine and Goodwin (1952) found topical cortisone of doubtful therapeutic effect in three cases of superficial punctate keratitis. Two cases of epidemic kerato-conjunctivitis were similarly treated and one responded well, but the therapeutic effect in the other was doubtful. Braley and Alexander (1953) reported one case of superficial punctate keratitis improved with topical cortisone, but two others showed a pronounced increase in corneal opacities. Cockburn and Danielson (1955) discuss a case in which the onset of epidemic kerato-conjunctivitis was apparently related to the introduction of ½% cortisone drops in the treatment of

mild conjunctivitis of four weeks standing. Thygeson and others (1956) reported that of two hundred cases of herpetic keratitis and kerato-conjunctivitis, seven followed the use of topical cortisone.

The inferences to be drawn from the literature appear to be, 1) in corneal affections with herpes simplex virus, both experimental and clinical cases fail to respond to cortisone and may be aggravated by its use, 2) clinical cases of superficial punctate keratitis and of epidemic kerato-conjunctivitis sometimes respond to cortisone.

Section 2.

Presentation of Cases.

In the present series, six cases (numbers 5, 11, 12, 17, 19 and 20) developed kerato-conjunctivitis during the course of treatment with topical cortisone. The interval between the commencement of cortisone treatment and the appearance of keratitis varied from one and a half months to nine months, and the amount of cortisone administered before keratitis appeared, from 55 mg. to 111 mg. At the onset of keratitis cortisone injections were being administered in these cases at intervals which varied from one week to four weeks. The presence of kerato-conjunctivitis was discovered at routine visits. Two of the patients were attending at weekly intervals, and four of them at intervals of two weeks or more when keratitis occurred, so that in each case, discomfort had been present for several days before the keratitis was first observed. The patients had no serious complaint to make, but each had been aware of some general irritation in the form of photophobia, lacrymation and grittiness. On first consideration it seemed surprising that the patients, having been aware of some

ocular discomfort, had not sought immediate advice; but when it is remembered that each of them had recently suffered from severe iridocyclitis, with its attendant discomforts and fluctuations in well-being, and that they had become used to the occasional occurrence of some conjunctival irritation in the days following subconjunctival injections, it is perhaps less surprising that the relatively mild discomfort experienced in this instance, did not induce them to add to an already large number of out-patient attendances.

Examination of the cases showed that the bulbar and palpebral conjunctivae were injected, the palpebral conjunctiva had a velvety appearance, and in three cases follicles were present. A thin watery discharge was to be seen. The corneae were peppered with fine epithelial infiltrates which stained faintly with fluoresceine. Corneal sensation was initially absent or considerably dimished, in every case. Pre-auricular glands were enlarged on the affected side in two cases. The conjunctival signs disappeared within one or two weeks, but the keratitis remained active for periods varying from two weeks to ten months. A few subepithelial non-staining infiltrates were present in two of the cases initially, and infiltrates of this

type were to be seen in each of the cases from time to time during the period of active keratitis, but for the most part the infiltrates were situated in the superficial layers of the epithelium. In cases 20 and 11 keratitis lasted for six and eighteen weeks respectively, and healed fairly rapidly in two and seven weeks respectively, when cortisone was discontinued. Cases 19 and 17 remained active during eleven and thirty-three weeks of treatment respectively, and keratitis healed gradually but steadily during two and five months respectively, after the withdrawal of cortisone. In cases 5 and 12 keratitis disappeared after four and five weeks respectively, while the patients were still receiving cortisone treatment, but in case 12 the condition recurred at a later date during a second course of cortisone treatment. On the second occasion keratitis persisted through seven months of therapy, and was still present three months after cortisone had been withdrawn. This case, which exhibited much the most persistant keratitis of the group, had, at an earlier stage in treatment, declined to have further sub-conjunctival injections, and during both periods in which keratitis occurred, was being treated with cortisone in the form of drops.

One case developed kerato-conjunctivitis in the untreated eye. This case was the only one in which tonometer readings were being taken at each visit.

There seemed little indication of infective spread between patients, since keratitis appeared in single cases at fairly widely scattered intervals. On only one occasion were more than one of these cases examined on a single day. This occurred on 9/2/53 when cases 11, 17 and 20 attended, and case 20 was discovered to have kerato-conjunctivitis. Case 11 developed kerato-conjunctivitis on 16/3/53 and case 17 on 13/4/53, intervals of thirty-five and sixty-three days respectively. The incubation period of epidemic kerato-conjunctivitis has been estimated by a number of writers, (see page 135) and none of them suggest that it exceeds 19 days. In the hospital as a whole there was no evidence of epidemics of kerato-conjunctivitis coincident with these single cases.

DISCUSSION.

The picture presented is that of a mild form of kerato-conjunctivitis, similar in clinical detail to the description of epidemic kerato-conjunctivitis but not progressing to the most severe stages, in which the appearance of macular subepithelial infiltrates is accompanied by considerable diminution in visual acuity. Recent personal experience of the fairly large outbreak of epidemic kerato-conjunctivitis in Glasgow in 1955 and 1956 suggests that it is not uncommon to see less severe cases in which keratitis remains confined to the superficial epithelium.

Histories of injury, or of upper respiratory infection, occurring shortly before kerato-conjunctivitis, which are so commonly found in the epidemic form of the disease, were not clearly in evidence in the six cases under discussion. Each had certainly suffered operative trauma at an earlier date, but the shortest interval between operation and the appearance of kerato-conjunctivitis was seven weeks, and in five of the cases the period was one of several months. Only one case volunteered a history of upper respiratory infection two weeks before the onset of keratitis. Rather vague histories of "slight head cold" one week before keratitis

were elicited from two others, and the remaining three cases gave no history of respiratory infection. All six cases of epidemic kerato-conjunctivitis occurred in the post-operative group. A satisfactory explanation for the occurrence of cases only in this group and not in the post-traumatic group was not found.

It was noted that, with one exception, the six patients who developed kerato-conjunctivitis also appeared in the drug sensitivity group, and the question arose whether the superficial keratitis might not be merely a response of the cornea to irritation, following prolonged use of cortisone or mydriatics. But the fact that in cases 5 and 12 keratitis cleared while the patients were still receiving cortisone suggests that the cortisone was not itself a source of irritation. Similarly there was no clear indication that the mydriatics used could be implicated, since cases 5, 11, and 20 were still receiving atropine when keratitis cleared, and in case 12 atropine had been discontinued five weeks before keratitis occurred. In addition, it would be difficult on this basis to account for the occurrence of follicular conjunctivitis, dimished corneal sensation, and enlarged pre-auricular glands, coincident

with the keratitis. There did not appear to be any consistent relationship between the time of appearance of drug sensitivity and of kerato-conjunctivitis. In three cases the drug sensitivity preceded the keratitis and in two cases the keratitis preceded the drug sensitivity.

The persistence of kerato-conjunctivitis in four out of six cases throughout long periods of cortisone treatment (average four months), its rapid or steady disappearance in four out of six cases after withdrawal of cortisone, together with its recurrence in one case during a second course of cortisone treatment, suggests that the onset of kerato-conjunctivitis in these cases may have been related to the use of cortisone. The experimental work reviewed shows that in the presence of cortisone the growth and virulence of many viruses is increased, while the application of cortisone to clinical cases of virus keratitis frequently leads to an increase in the severity of the condition. Theodore (1955) suggests that cortisone used in virus infections releases the virus from its cell nucleus, and results in a rapid and extensive spread of infection. It seems possible that in the cases which occurred in the present

series prolonged use of topical cortisone created cconditions favourable to the occurrence of virus infection and to its persistance, so that, even in the absence of a generalised epidemic or of the common predisposing factors, an increased number of sporadic cases of epidemic kerato-conjunctivitis occurred.

SUMMARY.

Thirty-two cases of post-operative and post-traumatic iridocyclitis, treated with topical cortisone acetate, are presented. The series was undertaken on the hypothesis that cases of this type provided an example of non-granulomatous iridocyclitis, of known aetiology and often of limited duration, in which cortisone might be expected to be of particular therapeutic value.

The mode of action of cortisone is discussed, and the problem of tissue response to injury is considered, with special reference to the possible modifications of this response in the presence of cortisone.

Personal observations of thirty-two cases of post-operative and post-traumatic iridocyclitis, treated with sub-conjunctival injections of cortisone acetate, are recorded.

Sixteen cases achieved clinical cure of iridocyclitis, but two of these later developed low-grade iridocyclitis in the second eye. Two cases were improved by cortisone, a considerable degree of control of iridocyclitis being obtained. Of the remaining fourteen cases, four relapsed, nine were unimproved, and one responded well initially, but follow-up was inadequate.

Seventeen cases retained visual acuity of 6/60 or more, and of these, nine retained visual acuity of 6/9 or more. Fourteen cases achieved clinical cure of iridocyclitis and retained useful visual acuity. Fifteen cases failed to retain useful vision, and among these there were eight enucleations.

The average period of treatment was five months, and the average follow-up after cortisone had been withdrawn, was nineteen and a half months - these figures exclude one case in which follow-up was inadequate.

Ten patients developed skin sensitivity reactions to a variety of drugs while being treated with topical cortisone.

Six patients developed kerato-conjunctivitis in the treated eye while receiving topical cortisone.

Published reports of the effect of topical cortisone in post-operative and post-traumatic iridocyclitis are reviewed. Comparable cases from hospital records, prior to the use of cortisone, are discussed, and a comparison is made of results of treatment.

CONCLUSIONS.

1. Topical cortisone acetate, administered by sub-conjunctival injection is of value in the control of iridocyclitis occurring in post-operative and post-traumatic cases. Clinical cure of iridocyclitis, with retention of useful visual acuity, can be achieved in a number of cases in which the prognosis would otherwise be poor.
2. Optimum results, with regard to control of iridocyclitis and to final visual acuity achieved, are likely to be obtained when the intervals which elapse between the occurrence of trauma and the onset of iridocyclitis, and between the onset of iridocyclitis and the commencement of cortisone treatment, are short. In the post-operative group the case of choice appears to be that in which iridocyclitis occurs within twenty-eight days of operation, and in which cortisone treatment is commenced not more than fourteen days later, and ideally not more than seven days later. In the post-traumatic group the case of choice appears to be that in which iridocyclitis develops within ten days of the occurrence of a penetrating wound which has not involved the ciliary body.

3. Treatment with subconjunctival cortisone must be maintained during the whole of the natural period of activity of the iridocyclitis. Withdrawal of cortisone should be accomplished gradually over a period of months.

4. In view of the occurrence of late relapses, follow-up must be prolonged and meticulous. Cortisone treatment should therefore be reserved for cases which fall into the categories in which good results can be anticipated.

5. Administration of subconjunctival cortisone does not prevent the occurrence, in a proportion of cases, of drug sensitivity reactions.

6. It is suggested that prolonged use of topical cortisone may lower the resistance of the conjunctiva and cornea to virus infection and create conditions favourable to the occurrence and persistence of kerato-conjunctivitis.

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