16. The same. "Syphilis." Zum Gebrauch für Studierende und praktische Aerzte. Deutsche autorisierte Ausgabe, bearbeitet und durch Erläuterungen und Zusätze vermehrt von Arthur Kollmann. 12mo., Leipzig. Arnold, 1888.
 17. "The Life-Register" (being a scheme for recording the events of a lifetime of 71 years). 12mo., London, 1888.
 18. "On urinary calculi; the lessons which they teach and the problems they suggest." Being the essay appended to the tenth fasciculus of the New Sydenham Society's "Atlas of Pathology." 8vo., London. West, Newman & Co., 1888.
 19. "The leprosy problem." Reprinted from Friends' *Quarterly Examiner*, 1890. 8vo., London. West, Newman & Co., 1890.
 20. "A descriptive catalogue of the clinical museum and journal of proceedings." Part 1, 8vo., London, 1894.
 21. A smaller atlas of illustrations of clinical surgery. 8vo., London. West, Newman & Co., 1895.
 22. "Discussion on the affections of the nervous system in the early (Secondary) stages of syphilis." 8vo., London. Reprinted from *Proc. Roy. Med. Chir. Soc.*, 1895.
 23. "The Centuries." A chronological synopsis of history on the "Space-for-time" method. Second edition (the first privately printed). West, Newman & Co., London; The Educational Museum, Haslemere, 1897.
 24. "Syphilis." New and enlarged edition. 8vo., Cassell, 1909.
 25. New Sydenham Society—retrospective memoranda. 8vo. (portrait). London. H. K. Lewis, 1911.
 26. "On leprosy and fish-eating; a statement of facts and explanations." 8vo., London. Constable, 1906.
- Also Editor of :—
27. *Ophthalmic Hospital Reports and Journal of the Royal London Ophthalmic Hospital*. London, 1863-79.
 28. "Archives of Surgery." London, 1889-1900.
 29. "The Polyclinic." London, 1900-1901.

A REVIEW OF THE LITERATURE ON THE CRYSTALLINE LENS

BY

DOROTHY ROSE ADAMS

So many articles have already been written on the subject of the crystalline lens, that an attempt to add to their number seems to demand an apology. So far, however, ophthalmologists and chemists have carried on their investigations independently, and it is hoped that this article will serve to correlate what is known of the biochemistry of the lens with the changes observed in pathological, and more especially, in cataractous lenses. The first half of the paper is a summary of the facts which have been brought to light, merely by chemical analyses of normal and cataractous lenses. The latter half deals with the action of light on the lens, and enters more fully into a discussion of the probable causes of cataract.

A. Chemical Analyses of the Crystalline Lens

An analysis of the human lens was first made by Berzelius, who gave the name of krystallin to the lens protein. Further analyses of animal lenses were made by Laptschinsky, 1876, and Morner, 1894. The latter identified three proteins:

- (1) Albumoid, a proteinoid which is found especially in the nucleus of the lens, and which is insoluble in water and in acid.
- (2) Two water-soluble proteins, which like globulins, are completely precipitated by saturation with magnesium sulphate at 30°C. One, β -krystallin, is soluble in acetic acid solution.

The krystallins were found to preponderate in the cortex, α -krystallin in the outer, and β -krystallin in the inner layers. Coagulation temperatures on heating the proteins with 0.05—0.1 per cent. KOH, were for α -krystallin 72°, β -krystallin 63°, and for albumoid 50°. Morner also found slight traces of albumen, and identified the presence of cholesterol and lecithin. He estimated the nitrogen and sulphur contents of the proteins, and obtained figures which compared very favourably with those of Jess, who, at a later date, was able to use much better methods of purification and analysis:

TABLE I.

NITROGEN.		SULPHUR.	
(Morner, 1896)	(Jess, 1921)	(Morner, 1896)	(Jess, 1921)
16.62 per cent.	16.34 per cent.	Albumoid 0.70 per cent.	0.87 per cent.
16.68 per cent.	16.46 per cent.	α-Krystallin 0.56 per cent.	0.68 per cent.
17.04 per cent.	17.00 per cent.	β-Krystallin 1.27 per cent.	1.34 per cent.

The protein content of the lens was found to vary with age, a decrease of protein in old age being noted by Cahns, Michel, 1884, and Wagner, 1886. Wagner also observed that in a senile cataractous lens, no protein could be found in the nucleus of the lens, and only a trace of globulin in the cortex; whereas in other forms of cataract, *e.g.*, traumatic and lamellar, normal proteins were found. Morner had shown (1896), that the amount of insoluble protein increased in the senile lens, a process rather analogous to the formation of keratin in the skin. Jess (1920), proved that there was a simultaneous decrease in the amount of water-soluble proteins, especially of β -krystallin, and he suggested that this might lead to the hardening of the nucleus and the sclerosis which cause a loss of the power of accommodation in old age. By the use of Fischer's method for protein hydrolysis, and Abderhalden's method of amino-acid estimation, Jess was able to make a thorough analysis of a large number of ox lenses. His figures (1921 and 1922) show interesting differences in the amino-acid contents of the three proteins.

TABLE II.

In 100 gm. substance :—

	α -KRYSTALLIN	β -KRYSTALLIN	ALBUMOID
Glycocoll ...	0	0	0
Alanine ...	3.6	2.6	0.8
Valine ...	0.9	2.1	0.2
Leucine ...	5.7	2.8	5.3
Aspartic Acid ...	1.2	0.4	0.5
Glutamic Acid ...	3.6	2.7	4.6
Tyrosine ...	3.5	3.7	3.6
Proline ...	1.8	1.4	1.9
Phenyl Alanine ...	5.5	4.1	4.6
Serine ...	+	+	+
Tryptophane ...	+	+	+
SH. as Cystine ...	2.3 } (cystein & cystine)	4.9 } (cystein & cystine)	3.1 } (cystine only)
Melanin ...	1.1	0.1	0.6
Histidin ...	3.635	2.63	2.74
Arginin ...	7.85	7.5	10.26
Lysin ...	3.75	4.6	3.8
Ammonia ...	7.1	11.4	6.0

Tyrosine and tryptophane are present in each of the proteins, while glycocoll is absent from them all. β -krystallin gives a strong positive test for cystein, whereas α -krystallin contains only a little, and albumoid practically none. β -krystallin is peculiar in its large content of valine, alanine, ammonia and cystein, while it is comparatively poor in melanin and leucine. Albumoid is markedly poor in valine, but richer in arginin than the other proteins. Because of its low content of glycocoll and alanine, it cannot be classed as a skeleton protein. The proportions of diamino- to mon-amino-acids in the krystallins make them resemble albumens rather than globulins.

The most interesting fact arising from Jess's analyses, is the variation in the cystein content of the proteins. As in other animal tissues, the presence of cystein (or of an SH-compound) in the lens, causes it to give a strong purple colouration with an alkaline solution of sodium nitroprusside (Arnold, 1910). The reaction is not diminished by drying the lens, nor by long storage of the lens in alcohol or formalin (Reis, 1912), and it is still given by the water-soluble proteins after precipitation. Albumoid has no nitroprusside reaction. Heffter stated that the reaction is negative in proteins which will not reduce sulphur to H_2S , such as fibrin, casein, and ovomucoid, *i.e.*, those which do not contain cystein or any S.H. compound. This fact is confirmed by Jess's observations that not only does albumoid lack cystein, but that in a senile

or cataractous lens from which the nitroprusside reaction is absent, or diminished, albumoid is present in increased amount. Jess thinks that this protein has actually replaced β -krystallin, to which the nitroprusside reaction of the normal lens is chiefly due. In criticism of this view, it is probable that soluble protein diffuses out from the lens into the aqueous in the early stages of cataract, and is destroyed by ferments.

Tests were made by Reis (1912), on the nitroprusside reaction of human cataractous lenses. The cortex and nucleus were separated and dried at 37° C., and then tested. Normally, the two parts of the lens give an equally intense reaction, but it can be seen that a pathological lens may lose the reaction from its cortex or its nucleus, or from both (see Table III).

TABLE III (REIS).

TYPE OF CATARACT.	NO. OF CASES.	NITROPRUSSIDE REACTION.	
		CORTEX.	NUCLEUS.
1. C. Hypermature	8	Negative	Negative
2. C. Mature	23	67 per cent. Neg.	98 per cent. Neg.
3. Unripe Cataract	20	15 per cent. Neg.	85 per cent. Neg.
		10 per cent. Pos.	15 per cent. Trace
		75 per cent. Trace	—
4. C. Tumescens	1	Positive.	Trace
5. C. Traumatica	1	Positive.	Positive.

In the case of other tissues, such as muscle, it was shown by Arnold (1912) that the presence of cystein is correlated with an active metabolism. It is highly probable from the work of Reis and Jess, that this is also true of the lens. The slightest interference with the circulation of the eye, leads to degenerative changes in the lens. These may be due to a lack of oxygen, yet very little is known as to how the lens utilizes its supply of oxygen. Further, the peculiar mode of nutrition of the lens, prevents any excessive use of oxygen, or rapid elimination of waste products. Yet in order to maintain its transparency under all conditions, it is probably necessary for the lens to keep up an active metabolism.

A consideration of the work of de Rey Pailhade, Thunberg, Heffter, etc., on autoxidation systems, led Goldschmidt (in 1917) to the idea that a similar balanced system—SH—SS—might exist in the lens, whereby the latter would be enabled to carry on a metabolism involving very little wear and tear. By using a modification of Heffter's method (based on the power of cystein-containing tissues to reduce sulphur to H S) Goldschmidt found that the cystein content of the ox lens decreased with increasing age. If cystein were used in the inner respiration processes,

cystine would be produced, and the latter might either be reconverted into cystein by some intracellular mechanism, or simply be broken down and removed as a waste product. An estimation of the sulphur content of lenses of different ages, showed that the sulphur did not disappear from the lens simultaneously with the loss of cystein, but remained practically constant throughout life. It appears then, that the—SH—SS—system in the lens is reversible. The nitroprusside reaction of the lens may be some indication of the degree of autoxidation remaining in the lens.

Further work on the autoxidation system of the lens, has been done in recent years (1922-24), probably as the result of the stimulating effect of the discovery of glutathione (Hopkins, 1921), and of the work which led up to that discovery.

Abderhalden and Wertheimer, in the course of some experiments on autoxidation (1922), observed :

(a) That the oxygen uptake of the lens is very small being $1/8-1/10$ that of muscle (*cf.* Ahlgren).

(b) That some of the SH-reacting compound of the lens is dialysable, *i.e.*, it is not all bound up with the protein.

(c) That the lens tissue will reduce m-dinitrobenzol (*cf.* Lipschitz). The lens becomes coloured gold in the process probably because cystine is formed.

(d) That alcohol accelerates the disappearance of cystein from the lens.

Gunnar Ahlgren (1923) and Goldschmidt (1924) have both made use of Thunberg's methylene blue technique to study the autoxidation of the lens. According to Ahlgren :

(1) The lens reduces methylene blue five times as rapidly as nerve, and half as rapidly as muscle.

(2) Cooling the tissue (*cf.* Thunberg's "cryolability of certain dehydrogenases"), and the presence of narcotics, hinder the reaction which occurs most rapidly at a certain optimum pH.

(3) Lens tissue will oxidize lactic, fumaric, malic and maleic acids, but not succinic acid.

Ahlgren suggests that the reduction power of the lens is due to an enzyme, and that possibly the lens contains a donator substance which acts as a substrate to the enzyme. The activity of the latter depends on the presence of a small amount of oxygen. He also recalls the fact that Lo Cascio showed the presence of oxidases and catalases in the lens (1922).

Goldschmidt's paper (1924) "Ueber die Autoxidation der normalen und pathologischen Linse," is worthy of a full summary :

(1) He recognizes the dialysable constituent of the lens, which gives a nitroprusside reaction (*cf.* Abderhalden and Wertheimer) as being glutathione.

(2) He finds that after exhaustive extraction of the lens with N/10 H_2SO_4 the residue still gives a strong NPR.

(3) By using the methylene blue technique, with proper precautions for buffering the lens tissue, and for obtaining the correct end-point, he finds that the unextracted tissue will decolourize the dye rapidly, whereas extracted tissue does so only after the addition of cystine (1 mgm. is sufficient).

From this experiment it is clear that the lens protein has the power to reduce cystine to cystein, and the latter is then able to reduce methylene blue in the usual way.

(4) After extraction of the lens with N/10 H_2SO_4 till the filtrate no longer gives a NPR, and then drying the residue with alcohol and *in vacuo* over H_2SO_4 .

(a) The power of the residue to reduce cystine remains unchanged, and it is not destroyed by heat nor by exposure to a stream of air.

In these respects and in its insolubility in water, the residue entirely resembles the thermostable reducing system found by Hopkins in the muscle of the rat.

(b) The system can be absolutely destroyed by treatment with 0.5 per cent. hydrogen peroxide, and subsequent washing will not restore the reduction power. In comparison, a whole encapsulated lens offers some resistance to the action of H_2O_2 , and after treatment retains some power of reduction, though the reduction time is much prolonged. Probably the lens capsule hinders diffusion into the lens. Also the H_2O_2 may attack the glutathione first and be able to oxidize only some of the cystein (or SH) of the thermostable system.

(5) By following Thunberg's data, Goldschmidt estimates that a whole ox lens can reduce 76.56 c.mm. of oxygen. He states, however, that this does not necessarily give accurate information as to the normal oxidation activity of the lens.

(6) At the end of a primary reduction experiment, *i.e.*, reduction due simply to the glutathione, the blue colour of the methylene blue could be restored by re-admitting air to the tube. The tissue was able to reduce the dye again, for as many as six times, in approximately the same lengths of time, *e.g.*, reduction times for :

(a) Quarter of a fresh ox lens—20, 34, 27, 32, 47 mins.

(b) Dried ox lens—21, 49, 48, 48, 45, 59 mins.

This experiment also supports the idea that the oxidation reduction system of the lens is reversible.

(7) Experiments on human lenses showed that the reduction time increased with increasing ages, and was much accelerated by the addition of cystine. Immediately reduction had ceased, the NPR was found to have vanished. This was not the case in the ox lens. The pathological human lens clearly contained a

thermostable reduction system, but it was not so easily isolated as from an ox lens. Also, in a pathological lens the reduction time seemed to depend on the state of maturity of the cataract. Lenses which had entirely lost their primary reduction power, regained it in the presence of cystine.

(8) The effect of change in hydrogen-ion concentration. For an ox lens the reduction power is at an optimum at pH. 8.3, and it ceases at pH. 6.0. The human lens is more sensitive to a change in pH., and it ceases to reduce if the medium is more acid than pH. 7.0.

In the discussion of his experiments, Goldschmidt remarks that it is still unknown how the lens activates the oxygen with which it is supplied. In the autoxidation system, glutathione most probably acts as a hydrogen donator, and is thus able to reduce such hydrogen acceptors as methylene blue (*in vitro*), or oxygen (*in vivo*). The thermostable system serves to reduce the glutathione after the latter has been oxidized. This explanation is a more probable one than that offered by Ahlgren. The power of the lens to oxidize certain fatty acids, is however, most likely enzymatic in character.

Some recent experiments by Adams (1924) on fresh animal lenses, confirm Goldschmidt's observations as to the presence of an autoxidation system in the lens. The oxygen uptake of the lens tissue was measured directly in a Barcroft microrespirometer, and parallel results were obtained by using Thunberg's methylene blue technique. The results may be summarized as follows:

(1) A whole ox lens was found to have a gradual oxygen uptake, e.g., in two hours an ox lens of 2 gm.wt. consumes 125-130 c.mm. of oxygen. The uptake is accelerated and increased in the presence of glutathione, and markedly increased if both linseed oil and glutathione be present.

(2) The power of the lens to utilize oxygen is considerably decreased by drying the lens, and is entirely absent after dialysis of the lens. But addition of a few mgm. of glutathione to a suspension of dried or dialysed lens restores the oxidation power to normal.

(3) A thermostable residue can be prepared from the lens which has no oxygen uptake of its own, but with glutathione, it gives a typical oxygen uptake curve. It reacts also with linseed oil and glutathione together, and develops a large and rapid oxygen uptake.

(4) One of the three proteins of the lens, viz., β -krystallin, functions pre-eminently as a thermostable residue.

(5) The average glutathione content of an ox lens, as estimated by Tunnicliffe's method is 0.305 gm. per cent.—a high value in comparison with other tissues. A decrease in the amount of

glutathione was observed after the lens had been exposed to heat rays. The decrease was more marked after exposure to ultra-violet light.

Experiments on the degenerated lens prove that it is poor either in cystein or in glutathione or in both. That it suffers especially from a lack of glutathione, is shown by the fact that the cortex of a lens may have lost its reduction power, but will still give a NPR, *i.e.*, it still contains some bound cystein. Morgagnian cataract and *c. traumatica*, are forms of cataract in which both the primary (glutathione) system, and the thermostable reduction system are absent. In *c. brunescens*, however, only the primary system is lost.

Goldschmidt suggests that the most probable cause of all cataract which is not definitely traumatic in origin, is a gradual rise in the hydrogen-ion concentration in the lens. The—SH—SS—equilibrium is known to be very sensitive to such a change, and its upset would involve a decrease in oxidation. This added to the condition of increased acidity, might probably lead to precipitation of the lens proteins. Further, whereas normally the oxygen brought to the lens may be supposed to be used at once by the glutathione, in a disordered state of metabolism the oxygen might cause the oxidation of the cystein in the thermostable system. In criticism of Goldschmidt's view, it must be remembered that Burdon-Cooper has stated that in all cases of cataract which he examined clinically the aqueous humour was alkaline. It is difficult to believe that the lens would be acid if the aqueous were alkaline. Adams' observations suggest another way in which the autoxidation system of the lens may become disordered, *viz.* : That since ultra-violet and heat rays are both present in ordinary sunlight they may cause an appreciable destruction of the glutathione in the lens. This could occur in an alkaline aqueous humour.

Other theories as to the possible causes of cataract will be discussed more fully in the section of the paper which deals with the action of light on the lens. A review of the analytical work which has been done on the lens, would not be complete without a short summary of the facts known concerning its content of lipoids. Apart from the proteins these seem to be the only remaining constituents of any importance in the lens. Jacobsen, Kuhn, Cahns, and others noted that the lipoids seemed to increase in the senile lens. Leber (1905), suggested that they might play some part in the onset of cataract by providing a solvent for such harmful substances as acetone and butyric acid. The micro-chemical and pathological tests made by Toufesco (1906), also bore witness to an increase of lipoids in the senile lens.

Valentin (1919), identified glycerin ester, cholesterin ester, free

cholesterol, and a cholin-containing phosphatid, in the normal lens. He found from his experiments that some or all of these lipid substances, which normally are in solution, might become deposited in crystalline or amorphous particles, which varied in composition and amount in different forms of cataract.

Goldschmidt (1922), made an analysis of human lenses of known ages, and found an interesting variation of the lipoids with age, *e.g.* :

(a) Cholesterin : Was at a maximum in the first year; at a minimum in the years 10-20; and rose again in the years 70-80.

(b) Phosphatid : Was very low (only 0.4 per cent.) in the first year; at a maximum (4.8 per cent.) in years 10-20; then underwent a fall 60-70; and finally rose.

(c) An acetone-soluble substance : Was at a maximum of 1.0-2.0 per cent. in the years 10-20, and fell steadily to 0.6 per cent. at 80.

(d) A benzol-soluble substance : Was at a maximum of 0.4 per cent. in the years 1-10, then fell to a steady level of 0.1 per cent.

Goldschmidt notes that in senile cataract, cholesterin crystals are often macroscopically evident in the lens. He suggests that the lipoids may act as oxygen fixators in the process of respiration. Further work is undoubtedly needed to elucidate the part which lipoids play in the normal lens metabolism, especially in view of the results recently obtained by Meyerhof (1924) and others, showing the remarkable acceleration of oxidation which occurs after the additions of lecithin to a balanced SH—SS—system.

Note on the Organ-Specificity of Lens Proteins

Uhlenhuth and others discovered that lenses of different species gave the same immune reactions, as proved by precipitin, anaphylaxis, and complement-fixation tests. Thus the specificity of the reaction is determined not by the species, as in immunity towards serum proteins, blood, bacteria, etc., but by the organ from which the antigen is derived. This organ-specificity of the lens is so pronounced that a lens anti-serum reacts with a lens of the same species, even of the animal which provided the serum.

It has been discussed whether this property is relative or absolute (Römer, and Gebb, and von Szily). Krusius suggested that the nucleus of the lens is responsible for organ-specificity, while the cortex proteins retain a certain degree of species-specificity. Hektoen (1923), failed to find any species-specific antigens in the lens.

The experiments of Schoeppe, and of Guyer and Smith, suggest that injection of lens protein into an animal may cause the

appearance in the blood of ferments which have a specific power of destroying all other lens proteins, *e.g.*, in the lens of the foetus. The evidence for and against this is, however, very conflicting.

For the purpose of this present article the importance of this immunological work on the lens is that it seems to denote a similarity in the chemical constitution of the proteins, and possibly therefore, a similarity in the metabolic processes which occur in the lenses of different vertebrates.

The Action of Light on the Crystalline Lens

In dealing with the chemistry of the lens, we have regarded it merely as an object for analysis, but in considering the effect of light upon it, it is a significant fact that we are dealing with an actively living tissue. From an early date the injurious effects of light, and especially of the invisible rays, have been known, and it has become impossible to regard the normal passage of light through the lens as an uneventful process. Instead, it is possible that light plays an important part in the chemical processes of the lens.

Quite early in the history of biology, it was discovered that ultra-violet light, in comparison with infra-red and visible rays, has a unique power of influencing living matter. It was not surprising therefore that in the early years of investigation on the effect of light on the lens, ultra-violet was considered the most likely cause of cataract.

It was shown by various workers, Brucke (1845), Donders (1853), de Chardonnet (1883), and Helmholtz (1896), that the media of an ox eye, *viz.*, the aqueous and vitreous humours, the cornea and especially the lens, are able to absorb ultra-violet light. de Chardonnet also noted that the degree of absorption seemed to vary with the age of the lens. Although the methods used in these experiments were rather primitive, for they consisted usually in allowing ultra-violet light to pass through the eye medium on to a fluorescent screen, and the only measure of the power of absorption was the decrease in fluorescence, yet the results have been fully confirmed by later experimenters, *e.g.*, Widmark, Mascart, who worked on human as well as on animal lenses. Hertel in 1903, was able to show that the lens of a live rabbit absorbs ultra-violet light.

The work of Schulek, and Birch-Hirschfeld showed the significance of this function of the lens, *viz.*, that by absorbing ultra-violet light, the lens protects the retina from injury. Merely half an hour's exposure to ultra-violet rays, *in vivo*, of a rabbit's eye, from which the lens had been removed, caused vacuoles to

appear in the nerve cells of the retina, and a disappearance of chromatin from the inner granular layer. No such changes were found in the retina of the normal eye, which was exposed in the same way, and its lens remained transparent. Further, in order to injure the retina of a normal eye at all, such a powerful source of ultra-violet light had to be used that the anterior structures were injured.

The following classification given by Schanz and Stockhausen (1909), and confirmed later (1912) by E. K. Martin, shows to what degree the various rays of the spectrum are able to pass through the media of the human eye:

(a) Rays $\lambda 760-400\mu\mu$ are visible rays, and pass to the retina unchanged.

(b) Rays $\lambda 400-350\mu\mu$ produce fluorescence in the lens. They pass to the retina and become visible if the lens is removed.

(c) Rays $\lambda 350-300\mu\mu$ penetrate the eye, but are absorbed by the lens.

(d) Rays $\lambda 300-0\mu\mu$ do not penetrate the eye, but are absorbed by the cornea.

Record has often been made by de Chardonnet, Schulek, Widmark, Birch-Hirschfeld and others, that after removal of the lens for cataract, the eye has increased visibility in the ultra-violet end of the spectrum, and is superior to the normal eye in this respect.

It was suggested by Schulek, that the continual passage of light, and especially of ultra-violet rays, through the lens during life, must have some effect on that organ, especially if it absorbed them. It was only reasonable to suppose that it might lead to degenerative changes in which the lens became clouded, and which often seemed to terminate in cataract. This theory was supported by Handmann (1909), who noted that senile cataract began in the inner lower quadrant of the lens, *i.e.*, in the area most exposed to direct sunlight; and further, that in cases of cataract occurring in one eye only, it could be generally associated with the habitual position of the patient during work, whereby the affected eye was exposed to stronger light than its fellow. Also Chalupecky, who exposed lenses to the light of a quartz mercury vapour lamp, stated that he was able to produce in them changes similar to those which occurred in a senile lens. He differed from the popular theory, by denying that ordinary daylight was sufficiently strong in ultra-violet radiations, to be able to cause cataract in a lens. The theory was, however, further supported by the observations of von Hirschberg, and of Grosz. The former noted that cases of cataract were extremely numerous in hot climates, where the sunlight is very rich in ultra-violet light. Grosz reported that in Hungary, cataract occurred frequently among agricultural labourers, who worked all day exposed to the sun.

From 1907 onward, special study was made of the peculiar type of cataract which occurs among glassworkers, and in addition to an improvement in our knowledge of the action of ultra-violet light, we learned that infra-red rays were almost certainly a co-factor in the production of cataract. Indeed, some observers, *e.g.*, Meyhofer and Birch-Hirschfeld, considered that the cataract in glassworkers was entirely due to heat. Their theory was supported by Crookes, who in the course of investigations made for the Royal Society Committee in 1913, found that the light which came from the tanks of molten glass abounded in infra-red rays.

In criticism of the view that cataract could be due to the direct action of heat on the lens, Hess pointed out that the lens first became clouded in its hinder pole, whereas heat would exert its maximum effect on its anterior surface. Also, Vogt maintained that only a white heat would produce an infra-red radiation sufficiently penetrating to cause a harmful effect in the lens. Further, it would be difficult to explain the localization of the cataract in the centre of the lens, in view of the fact that the iris is a good conductor of heat.

Other investigators, *e.g.*, Leber, Hartridge and Hill, favour the view that heat might bring about cataract indirectly, by affecting the secretion of aqueous humour, or by causing the latter to become concentrated. The experiments of Hartridge and Hill (1915), and of Luckeish (1915), on the power of the eye media to absorb infra-red rays, showed that each separate medium, cornea, aqueous humour, lens or vitreous humour, gave absorption bands in the infra-red which closely resembled those given by equal thicknesses of water. Further, Hartridge and Hill demonstrated that heat radiations between λ 11,900 $\mu\mu$ and 7,000 $\mu\mu$ pass into the eye unchecked, and a great deal reaches the retina. The power of the iris to absorb heat is very marked, and is four times that of the lens, which absorbs only 12 per cent. of the light which reaches it through the pupil. They suggested that although the continual small absorption of heat might lead to a coagulation of lens proteins, yet this effect was more likely to be due to some interference with the nutrition of the lens. In support of a suggestion made by Parsons, *viz.*, that the heat absorbed by the iris may affect the secretion of aqueous humour by the ciliary body, and hence may also disturb the nutrition of the lens, are the facts that :

(1) The greater part of the heat is absorbed by the posterior pigmentary layer of the iris, *i.e.*, the part which is in close contact with the ciliary processes, and with the posterior chamber of the eye. Any rise in temperature of the pigmentary layer, following

the absorption of infra-red rays, might be expected to affect the neighbouring ciliary processes and their glandular elements.

(2) A close relationship exists between the arterial supplies of the iris and of the ciliary body. It is possible therefore that both structures are supplied by intimately related lymphatic vessels, and vasomotor nerves. The latter may send some glandulo-motor nerves to the ciliary processes.

(3) In glassworkers' cataract especially, the slow development of the pathological condition cannot be due to any process of inflammation, particularly as other structures in the eye remain unaffected.

Hartridge and Hill suggest the possible hypothesis, that secretion of aqueous humour is stimulated when heat rays fall on the iris. Since the stimulus occurs regularly and for long periods, the process of secretion may come to depend more and more on the external stimulus, and itself may become periodic. As a result of its interrupted nutrition, the lens may develop cataract, especially in its least well nourished part, *i.e.*, its hinder pole.

E. K. Martin (1912) observed some interesting physiological effects following the exposure of rabbits' eyes, *in vivo*, to ultra-violet light, *viz.* :

(a) After moderate exposure, the central cells of the anterior capsule of the lens became swollen and were obviously stimulated to active proliferation. It is possible that such a change precedes the formation of an anterior capsular cataract in the human eye.

(b) More severe exposure produced opacity in the cornea, while the capsule and lens remained undamaged.

(c) In rabbits previously sensitized to washed cats' corpuscles, the specific haemolysins could only be detected in the aqueous humour after the eye had been exposed to ultra-violet light, and not before. According to Römer's theory, the transmission of haemolysins from blood to aqueous humour only occurs after a simple paracentesis or following an inflammatory lesion of the iris or ciliary body. The latter condition may have been caused in these experiments by the exposure to ultra-violet light.

Although it is highly probable that cataract is a secondary heat effect, it cannot be denied that ultra-violet light is absorbed by the lens, and it probably assists in the precipitation of the lens proteins. The power of the human lens to absorb light of short wave-length, is known to increase steadily during the life of the individual, until at the age of 50 years, it absorbs the whole of the ultra-violet rays, the violet, and part of the blue rays. Yoshiharu (1922) has recently shown that absorption seems to vary with the protein content of the lens, a fact which leads one to speculate as to whether the increased absorption in old age, is due to the loss of soluble protein, and to the apparent replacement of it by

insoluble albumoid. Soret (1883) was able to show that yolk and serum proteins, as well as lens proteins, were precipitated as the result of the absorption of ultra-violet light. Dreyer and Hanssen (1907), stated that such precipitation involved a change from soluble, into insoluble protein.

Schanz (1916) made some interesting observations on the precipitation of yolk protein by ultra-violet light. He found that :

(1) Whereas a visible precipitate was formed in an acid protein solution, an alkaline solution merely developed a gold colouration. Addition of ammonium sulphate to the alkaline solution would bring down a precipitate, but the latter decreased with increased time of exposure.

It appears that ultra-violet light had a more drastic effect on the alkaline solution, and caused actual destruction of the protein. The gold colour may have been due to cystine.

(2) That a temperature of 45° C. had the same effect as light on alkaline and acid protein solutions. This was confirmed by Young (1921).

Schanz considered that the precipitation was a reversible flocculation, and not denaturation.

(3) Addition of alkali to a solution of dialysed protein, rendered its absorption power superior to that of a neutral or acid protein solution.

Experiments made by Burge (1915) at about this time, may be compared with those of Schanz. In contradiction to the latter worker, Burge found that whereas light from a quartz mercury vapour lamp would coagulate solutions of egg-albumen, globulin, and vitellin, it would not coagulate in the same length of time, the protein of a normal lens, neither was the latter coagulated after 100 hours exposure. If, however, N/100 solutions of CaCl₂, MgCl₂, magnesium silicate, or of dextrose, were added to the lens, it rapidly became opaque when exposed to light from the same source. In a further study of the importance of salts to the metabolism of the lens, Burge made some remarkable discoveries :

(1) That sodium and potassium salts, acting alone on the lens, can cause nuclear opacity.

(2) That calcium, magnesium, and silicates, occur in increased amounts in senile cataractous lenses, *e.g.*, calcium in a normal lens is less than 0.08 per cent., but in a cataractous lens may be 15 per cent. Cataractous lenses from India showed an enormous increase in their content of sodium and silicates as compared with the normal, *e.g.* :

	SODIUM PER CENT.	SILICATES PER CENT.
Normal Lens	?	0
Cataractous Lens	25.06	3.63

(3) Salts and substances, such as dextrose, which aid the action of ultra-violet light, also decrease the fluorescence of the lens (*cf.* Schanz showed that in the human lens, its power to fluorescence is decreased in old age, while its absorption of ultra-violet light increases).

(4) By exposing the eye of a living fish to ultra-violet radiation, Burge was unable to cause any opacity in the lens, when the fish had been previously kept in tap water. In fish which had lived for ten days in water containing 0.1 per cent. sodium silicate, 0.1 per cent. dextrose, 0.8 per cent. calcium nitrate, and 0.8 per cent. calcium chloride, he obtained a distinct opacity of the cornea after an exposure of six hours, and an opacity in the lens after a second exposure. Similar results were obtained from experiments on frogs.

As a result of his experiments, Burge considers that the lens normally has the power of converting the light of short-wave length which it absorbs into light of long-wave length, which it passes on to the retina. Thus, it disposes of the surplus energy which might otherwise disturb its chemical system, and cause precipitation of its proteins. Salts destroy this power if they are present in hypernormal concentration, and they modify the proteins so as to render them more easily precipitable by light.

This theory raises the question again, as to whether an increase of salts in the aqueous humour of the eye, might not be another important factor in the origin of such a condition as glassworkers' cataract (as Leber suggested), or of the cataract which occurs in tetany (Stoeltzner). Nelson (1923) has shown, however, by experiments on the surviving lens, that a solution of a calcium salt will not produce any appreciable clouding in the lens, unless it exceeds a concentration of 2.25 per cent. It is very improbable that the calcium in the aqueous humour would reach such a concentration in any pathological condition.

Somewhat in advance of the theory held by Burge is that of Neuberg (1917), viz.: That without the accompanying presence of salts, the lens proteins would be unable to absorb any light at all. He further maintains that no pure organic compound has the power of light absorption. His theory received some support in the observations of Bovie (1913), and Young (1921), that denaturation of a protein can only occur if electrolytes are present, but it is contradicted by Schanz. The latter worker found:

(1) That protein which has been dialysed till it is chloride-free, still gives an absorption spectrum.

(2) That after the addition of salts to a solution of pure protein, the latter shows an increase in its power of absorption of light, which cannot be attributed to the mere presence of such salts.

It is probable that both proteins and salts are photosensitive; in any case, perfectly pure proteins are not found under natural conditions.

(3) That chemically pure organic substances such as acetone, most certainly are sensitive to light. Acetone and dextrose, in particular, increase the effect of sunlight on solutions of lens proteins.

From this last observation, and from a study of the Hallwachs, or photo-electric effect of organic substances, Schanz believes that a process of photosensitization may be continually taking place in the lens. Thus, it is probable that the protein molecules are continually absorbing electrons which are thrown off by some organic sensitizer in the lens. Precipitation of the proteins might be the reasonable outcome of such absorption. In support of his theory, Schanz found that the addition of a protein to a solution of an organic dye, caused an actual diminution in the photo-electric effect of the dye. It is interesting to compare this hypothesis with an observation made by Schulek, as early as 1896: "*Alles was das freie Ausschwingen der Elementarteile behindert, kann früher oder später zu Aenderungen des Aufbaues führen.*"

In conclusion, in spite of the numerous theories which have been brought forward, it is impossible to say that any one of them is an adequate explanation of the cause of cataract; each is probably a part of the truth. It certainly reveals how little is known of the chemical processes which constitute the normal metabolism of the lens, and how they are deranged in the onset of cataract. The phenomenon of the precipitation of the lens proteins has been studied too far apart from other chemical changes in the lens. Goldschmidt, and Jess and Koschella, have recently made an advance in the right direction in an attempt to explain the remarkable disappearance of the nitroprusside reaction from the cataractous lens. Jess and Koschella in 1923, repeated Chalupecky's experiments on whole lenses, but could find no diminution in the nitroprusside reaction of the lens, even after 36 hours exposure to the light of a quartz mercury vapour lamp. Removal of the capsule of the lens before exposure, or suspension of the lens in Ringer, made no difference in the result. They also repeated Burge's experiments and found that ultra-violet light acting on a lens suspended in 0.02 per cent. CaCO_3 solution, did not produce any trace of cloudiness. Adams (1924) observed a decrease in the glutathione content of the lens after exposure to ultra-violet light.

It must be remembered that Goldschmidt has given definite evidence that though the cataractous lens is often poor in glutathione the SH— of its protein may still remain. In lenses where there

is no trace of a nitroprusside reaction, and the autoxidation system is completely absent, there is a possibility that the loss of β -krystallin is the cause of both defects. Again, the observation of Abderhalden and Wertheimer, that ultra-violet light does not accelerate the oxidation of cystein, raises the question as to whether the loss of soluble SH— (chiefly glutathione), is a cause or result of cataract.

It is almost certain that some degree of hydrolysis of the lens protein occurs in cataract. The process of denaturation is according to the latest views, a first stage in hydrolysis (*cf.* the work of Harris (1923) on precipitation of egg albumen). Burdon-Cooper also states that he has constantly found deposits of tyrosine in cataractous lenses, and in the aqueous humour after the operation of needling. This suggests that hydrolysis may occur to a considerable extent.

The most suitable ending to a review on the crystalline lens is, not a summary of our imperfect knowledge of the subject, but a reiteration of the need for further investigation, especially from the biochemical standpoint.

REFERATA

- Abderhalden.—*Arch. Néel. d. Physiol.*, Bd. 7, S. 234, 1922.
 Abderhalden u. Weil.—*Zeitschr. f. Physiol. Chemie.*, Bd. 74, S. 7, 445, 1911; Bd. 77, S. 59, 1912.
 Abderhalden und Wertheimer.—*Arch. f. d. ges. Physiol.*, Bd. 197, S. 191, 1922.
 *Adams.—*Proc. Roy. Soc. B.*, 1925.
 Ahlgren.—*Skand. Arch. f. Physiol.*, Bd. 44, Nr. 5/6, 1923.
 Arlt.—*Augenkrank.*, Prague, Bd. 2, S. 235, 1853.
 Arnold.—*Zeitschr. f. Physiol. Chemie.*, Bd. 70, S. 300-314, 1910.
 Aschkinass.—*Wied. Annalen*, Bd. 55, S. 401, 1895.
 Balling.—*Zeitschr. f. Physiol. Chemie.*, Bd. 108, S. 186, 1920.
 Birch-Hirschfeld.—*Arch. f. Ophthal.*, Bd. 58, S. 469, 1904.
 Bovie.—*Science*, Vol. XXXVII, pp. 24 and 373, 1917.
 Brucke.—*Arch. f. Anat. u. Physiol.*, S. 262, 1845.
 Burdon-Cooper.—*Ophthal. Rev.*, Vol. XXXIII, No. 391, 1914.
 Idem.—*Brit. Jl. of Ophthal.*, Vol. VI, p. 386, 1922.
 Burge.—*Arch. of Ophthal.*, Vol. XLVI, p. 12; Vol. XXXVIII, p. 47, 1909; Vol. XLIV, No. 5, 1915.
 Idem.—*Amer. Jl. of Physiol.*, Vol. XXXVI p. 21, 1914; Vol. XXXIX, p. 335, 1916; Vol. XLIII, p. 429, 1917.
 Chalupceky.—*Wien. med. Wochenschr.*, Nr. 31, S. 1901; Vol. XXXII, S. 1986, 1913.
 Idem.—*Wien. klin. Wochenschr.*, Nr. 27, S. 1513, 1914.
 Idem.—*Strahlentherapie*, Bd. 8, Heft. 1.
 de Chardonnet.—*Comptes Rendus*, 1883.
 Idem.—*Séance de l'Académie des Sciences*, Vol. XCVI, p. 441, 1883.
 Ciaccio.—*Bioch. Zeitschr.*, Bd. LXIX, S. 313, 1915.
 Cramer.—*Klin. Monatsbt. f. Augenheilk.*, Bd. 45, (1) 47, 1907.
 Crookes.—*Philos. Trans. Roy. Soc.*, p. 1, 1913.
 Dreyer und Hanssen.—*Comptes Rendus*, Vol. CXLV, p. 234, 1907.
 Donders.—*Arch. f. Anat. u. Physiol.*, (1845), p. 459, 1853.
 Fischer.—*Zeitschr. f. Physiol. Chemie.*, Vol. XXXIII, p. 151, 1901.
 Gola.—*Malpigia*, Vol. XVI, 1913.

*To be published.

- Goldschmidt, M.—*Münch. med. Wochenschr.*, Nr. 12, S. 657, 1914.
 Idem.—*Arch. f. Ophthalm.*, Bd. 88, S. 405, 1914; Bd. 93, S. 447, 1917; Bd. 113, S. 160, 1924.
 Idem.—*Wien. Ophthalm. Gesellsch.*, 1921.
 Idem.—*Bioch. Zeitschr.*, Bd. 127, S. 210, 1922.
 Grosz.—*Arch. f. Augenheilk.*, Bd. 57, S. 40, 1907.
 Guyer and Smith.—*Jl. Exper. Zool.*, Vol. XXVI, p. 65, 1918; Vol. XXXI, p. 171, 1921.
 Handmann.—*Klin. Monatsbl. f. Augenheilk.*, Bd. 8, p. 962, 1909.
 Harris.—*Proc. Roy. Soc. B.*, Vol. XCIV, p. 426, 1922.
 Hartridge and Hill.—*Proc. Roy. Soc. B.*, Vol. LXXXIX, p. 58, 1915.
 Hayana.—*Tokyo Igak. Zasshi*, 31, No. 21, 1917.
 Idem.—*Jap. med. Lit.*, Vol. III, p. 60, 1918.
 Heffter.—*Beitr. z. chem. Physiol. u. Pathol.*, Nr. 5, S. 213, 1904.
 Idem.—*Med. Naturwiss Arch.*, Nr. 1, S. 81, 1908.
 Hektoen.—*Jl. Amer. Med. Assoc.*, Vol. LXXVII, p. 32, 1921.
 Hertel.—*Berichte d. Ophthalm. Gesellsch.*, Heidelberg, 1903.
 Hess.—*Graefe-Saemisch Handbuch, d. ges. Augenheilk.*, 3 Aufl., 2 T., Kap. 9, S. 249.
 Idem.—*Arch. f. Augenheilk.*, Bd. 57, S. 185, 1907.
 von Hirschberg.—*Berl. klin. Wochenschr.*, Bd. 35, Nr. 6, S. 113, 1898.
 Hiroishi.—*Arch. f. Ophthalm.*, Bd. 113, 3/4, p. 381, 1924.
 Hopkins.—*Bioch. Jl.*, Vol. XV, p. 286, 1921.
 Idem.—*Jl. Biol. Chem.*, Vol. LIV, p. 527, 1922.
 Jess.—*Zeitschr. f. Biol.*, Bd. 61, S. 93, 1913.
 Idem.—*Habilitationschr. München*, 1913.
 Idem.—*Arch. f. Augenheilk.*, Vol. LXXI, p. 266, 1911.
 Idem.—*Zeitschr. f. Physiol. Chemie*, Bd. 110, S. 1920.
 Idem.—*Arch. f. Ophthalm.*, Bd. 105, S. 428, 1921; Bd. 109, S. 463, 1922.
 Jess und Koschella.—*Arch. f. Ophthalm.*, Bd. 111, S. 370, 1923.
 Krusius.—*Zeitschr. f. Immunitätsforschung*, Vol. V., p. 669, 1910.
 Leber.—*Arch. f. Ophthalm.*, Bd. 62, S. 85, 1905.
 Legge.—*Report of the Medical Inspector in Factories and Workshops: Annual Report*, 1907.
 Lipschitz.—*Zeitschr. f. Physiol. Chemie.*, Bd. 109, S. 189, 1920.
 Lipschitz u. Gottschalk.—*Pflüger's Arch. f. d. ges. Physiol.*, Bd. 191, S. 1, 1921.
 Loeb Cascio.—*Ann. di Ottal. e. clin. Oculist.*, 1922.
 Luckiesh.—*Electric World*, Vol. LXII, p. 884, 1913; Vol. LXVI, p. 576, 1915.
 Idem.—*Report of Nela Laboratory*, Vol. I, No. 2, 1917.
 Martin, E. K.—*Proc. Roy. Soc. B.*, Vol. LXXXV, p. 319, 1912.
 Maseart.—*Comptes Rendus*, Vol. LXVIII, p. 402, 1869.
 Matthews and Walker.—*Jl. Biol. Chem.*, Vol. VI, p. 21, 1909.
 Meyerhof.—*Arch. f. d. ges. Physiol.* (Pflüger), Vol. CXCIX, 1923.
 Meyhofer.—*Klin. Monatsbl. f. Augenheilk.*, Bd. 24, S. 49, 1886.
 Meyhofer und Michel.—*Berichte d. Ophthalm. Gesellsch.*, Heidelberg, 1900.
 Michel.—*Cong. Intern. d. Scien. Med.*, Copenhagen, 1885.
 Michel und Wagner.—*Arch. f. Ophthalm.*, Bd. 32, S. 155, 1886.
 Morner.—*Zeitschr. f. Physiol. Chemie*, Bd. 18, S. 213, 1894; Bd. 93, S. 175, 1915.
 Nelson.—*Klin. Monatsbl. f. Augenheilk.*, Bd. 70, 1923.
 Neuberg.—*Berl. klin. Wochenschr.*, Nr. 4, 1917.
 Reis.—*Arch. f. Augenheilk.*, Bd. 72, S. 156, 1912.
 Idem.—*Arch. f. Ophthalm.*, Bd. 80, S. 558, 1912.
 de Rey Pailhade.—*Comptes Rendus (Académie d. Science)*, Vol. CVI, p. 1683, 1888; Vol. CVII, p. 43.
 Römer.—*Arch. f. Ophthalm.*, Bd. 60, S. 159, 1905.
 Idem.—*Arch. f. Augenheilk.*, Bd. 76/77, S. 120, 1914.
 Römer und Gebb.—*Arch. f. Augenheilk.*, Bd. 56 (Egb.), 1906; Bd. 78, S. 51, 1915.
 Idem.—*Arch. f. Ophthalm.*, Bd. 83, S. 504, 1912; Bd. 84, S. 186, 1913.
 Schanz.—*Arch. f. d. ges. Physiol.* (Pflüger), Bd. 161, S. 384, 1915; Bd. 164, S. 445, 1916; Bd. 169, S. 82, 1917; Bd. 170, S. 646, 1918.

- Schanz.—*Deutsch. Optische Wochenschr.*, Nr. 297, 1917.
 Idem.—*Münchener med. Wochenschr.*, Nr. 19, 29, 30, 1915; Nr. 68, S. 19, 1921.
 Idem.—*Bioch. Zeitschr.*, Bd. 71, S. 406, 1915.
 Idem.—*Arch. f. Ophthal.*, Bd. 86, S. 549 and 568, 1913; Bd. 88, S. 437, 1915; Bd. 89, S. 556, 1916; Bd. 91, S. 238, 1916; Bd. 96, S. 172, 1918; Bd. 106, S. 171, 1921; Bd. 107, S. 190, 1922.
 Schanz und Stockhausen.—*Arch. f. Ophthal.*, Bd. 65, S. 49 and 152, 1908; Bd. 73, S. 184 and 553, 1909.
 Schulek.—*Ungar. Beitr. z. Augenheilk.*, Bd. 1, S. 106, 1895.
 Setschenow.—*Arch. f. Ophthal.*, Bd. 5, S. 205, 1859.
 Soret.—*Comptes Rendus*, Vol. XCVII, pp. 314, 572, 642, 1883.
 von Szily.—*Klin. Monatsbl. f. Augenheilk.*, Bd. 49, S. 150, 1911; Bd. 51, S. 164, 1913.
 von Szily und Arisawa.—*Berichte d. Ophthal. Gesellsch.*, Heidelberg, S. 253, 1912.
 Thunberg.—*Ergeb. d. Physiol.*, Bd. 11, S. 328, 1911.
 Idem.—*Skand. Arch. f. Physiol.*, Bd. 35, S. 163, 1918; Bd. 40, S. 1, 1920.
 Tiffany.—*Indian med. Gaz.*, Vol. XLIX, p. 326, 1914.
 Toufesco.—*Annal. d'Ocul.*, T. 136, p. 1, 1906.
 Uhlenhuth.—*Deutsch. med. Wochenschr.*, 1906.
 Uhlenhuth und Händel.—*Zeitschr. f. Immunitätsforschung*, Bd. 4, H. 6, 1910.
 Valentin.—*Zeitschr. f. Physiol. Chemie*, Bd. 105, S. 33, 1919.
 Wick.—*Arch. f. Ophthal.*, Bd. 109, S. 224, 1922.
 Widmark.—*Skand. Arch. f. Physiol.*, Bd. 1, S. 264, 1889; Bd. 4, S. 288, 1892.
 Wieland.—*Berl. f. d. chem. Gesellsch.*, Bd. 45, 46, 47, and 54, 1921.
 Idem.—*Ergebn. d. Physiol.*, Bd. 20, S. 481, 1922.
 Yoshiharu.—*Mit. a. d. med. fak. d. kais. Univ.*, Bd. 29, H. 1, 1922.
 Young.—*Proc. Roy. Soc. B*, Vol. XCIV, p. 235, 1922.

HAEMATOMA OF THE CORNEA. A CLINICAL NOTE

BY

GEORGE YOUNG and ARTHUR W. D'OMBRAIN

COLCHESTER

WHILE preparing to perform a double sclerectomy on a female patient, aged 72 years, we observed a strange phenomenon which neither of us had ever seen before. The patient had absolute glaucoma in the right eye and a far advanced glaucoma in the left, the tension being nearly 90 and over 90 Schiötz in the two eyes respectively. We saw on the cornea of the right eye (absolute glaucoma) a couple of streaks of blood, about 1.5 mm. long, just below the upper part of the limbus. They seemed to be on the surface, but would neither flush nor brush away and did not stain the swab. As we watched, new streaks appeared on either side, spreading laterally further and further, and finally appearing as small bleb-like haematomata, protruding above the corneal level and occupying about $\frac{2}{5}$ ths of the circumference of the cornea. They exactly corresponded to the position of the most intense