IRITIS OF ALLERGIC ORIGIN*

VERA B. WALKER, M.Sc. (N.Z.), PH.D. (LOND.), M.R.C.S., L.R.C.P.

Oxford, England

In England the study of allergy in ophthalmology has been developing for the last 25 years, but it was not until 1947 that the results were sufficiently well established to justify a general discussion at the Royal Society of Medicine. At that meeting Mr. Gayer Morgan[1] (senior ophthalmic surgeon at Guy's Hospital) reminded us that almost every disease of the eye had been reported as allergic in origin in some particular patient. Since then the literature on the subject has been copious, but vague, and can be more easily understood if the word 'disease' is deleted and replaced by 'condition'.

To me[2] an allergic condition is acute in onset and, if recognized and treated at once, will clear up quickly, often within a few minutes or hours, leaving no permanent damage to the tissues involved; but it must be recognized that once a tissue has remained in an abnormal physiological condition for a longer time, as in recurrent keratitis or iridocyclitis, there may be secondary changes, due perhaps to pressure of oedema, perhaps to inflammation, perhaps to secondary infection, which must be healed by routine treatment and may leave permanent scarring.

ALLERGY IN GENERAL

The term 'allergy' is not in the English dictionary. It was first used by a Frenchman to describe an 'altered reaction', not just hypersensitivity to some drug or food but a changed type of reaction; thus, if one gets a dizzy headache after 1/10 gr. of quinine instead of after 25 gr. then one is *hypersensitive* to quinine, but if after the 1/10 gr. one gets not a headache but a spasm in the chest, an attack of gout, or a painful iritis, then one is *allergic* to quinine.

Many workers have considered an allergic reaction as a pathological state similar to the abnormal antibody-antigen relationship of bacterial immunology, but this cannot explain the simplest allergic response or immediate reaction as seen in hay-fever, urticaria, or a bee-sting; in these states a slight biochemical variation, possibly congential, in the serum alters its ability to permeate the walls of the capillaries allowing them to 'leak' and so produce the watery secretion of hay-fever or the fluid of oedema in enclosed spaces.

These reactions are *extracellular*, in contrast to the delayed or *intracellular* reactions of contact dermatitis, of asthma, or of rosacea keratitis. In extracellular allergy sensitivity can be transferred passively by plasma; in the delayed or intracellular type whole cells or their contents are required.

By using the fluid from an allergic oedematous swelling of one patient for an intradermal test on another known allergic patient, it is possible to satisfy oneself that free-histamine has been assembled in the fluid in this one organ; that is to say, the metabolism or distribution of histamine throughout the body has been upset and it has been collected in the 'shock tissue' of the moment, be it skin, lung, bladder or iris. From an attempt to show that histamine was still the offending substance in the more delayed type of allergic reaction a method of using a dose of free histamine for the diagnosis of the intracellular allergies due usually to some chronic bacterial or virus infection in a distant organ has been developed and was published in the *Acta allergologica* for 1954.[3]

To explain why one organ, be it eye, ear, chest or stomach, is selected as the 'shock tissue' to carry the full responsibility of an allergic attack takes us into the realm of metaphysics; but as it need not be the eye as a whole, but rather the conjunctiva, cornea, lens or iris alone, which may be concerned in any one patient, the simplest belief is that some localizing previous injury, either developmental or traumatic, is necessary. This idea would certainly help to explain a unilateral allergic condition in one of two symmetrical organs, and one-sided headaches after a motor-cycle crash.

ALLERGIC IRITIS

What part do these ideas play in helping in the investigation and treatment of iritis? If one remembers that the iris is a 'diaphragm of blood vessels and unstriped muscle fibres held together by a very loose spongy stroma' (Parsons and Duke-Elder), one cannot fail to recognize an almost ideal setting for an acute anaphylactoid reaction. That this reaction can be of either the immediate extracellular type or of the delayed intracellular type is illustrated in the 6 case-histories summarized below. They also serve to support the suggestion of Professor Pickering[4] that in the 'immediate response' group, histamine or some histamine-like substance is released and the effect can be neutralized by anti-histamines but not by cortisone, as happens in hay-fever or in angio-neurotic oedema; while in the delayed group, as in bacterial allergy in other tissues, there is an intracellular reaction which can be overcome by cortisone but not by antihistamine. *Cortisone does not cure: it only suppresses the mechanism of reaction.*

One practical point to remember is that when antihistamines are used in the treatment of iritis they must be supplied to the body by mouth or by injection, for no amount of antistin-privine slopped on to the conjunctiva will reach the iris in sufficient concentration to do any good. All patients with recurrent attacks of acute iritis should have a full range of allergy tests as part of the routine hospital investigations, for 20% of all iritis is due to allergy, the offending allergens being foods, inhalants, drugs, or toxins (including tuberculin).

Case 1. G.L., male (60). 1942-1950—14 attacks iritis. 1950—All investigations negative except allergy tests: horsehair +++, dog hair ++. Avoidance and antisin given and attack cleared in 8 days; desensitized by injection. 1955—Reported no iritis since 1950.

* A paper presented at the South African Medical Congress, Pretoria, October 1955.

Case 2. V.B., female (46). Recurrent iritis with urticaria. 1949—Meibomian swab, chest and sinus X-ray, teeth, urine, Mantoux test, blood count, ESR and WR all N.A.D.; allergy tests: house dust ++, grass pollen +++; desensitized by injection and remained symptom-free until: 1954—Iritis but no urticaria; re-test: house dust ++, grass pollen, ++; desensitized again. September 1955—Still symptom-free.

Case 3. B.S., female (33). 1950—First attack iritis, cleared up after 8 weeks with hot bathing and rest. 1951—Iritis cleared up in 5 weeks with cortisone, bathing and rest. 1952—Referred to Allergy Clinic: beef +++; healed in 1 week with antistin and avoiding beef. 1953—Ate beef in error: acute iritis, healed in 3 days with antistin tablets. 1955—Symptom-free for 2 years; still avoiding beef.

Case 4. R.N., male (51). Recurrent iritis since 1947. 1941—Tuberculous glands removed from neck. 1947—First attack iritis; all usual investigations negative. Frequent attacks iritis until 1951—All tests repeated: Had become atropine-sensitive. 1955—Healed by cortisone; allergy tests all negative except O.T.1/100,000 +++; desensitized by 10 injections O.T. Retest: O.T. 1/10,000 +; all quiet so far.

Case 5. G.B.L., male (57). 1940-1950—16 attacks iritis. 1951—Iritis and spasmodic bronchitis; all investigations, including allergy tests, negative except *Strept. viridans* protein ++++; treated with cortisone; healed in 3 weeks; auto-vaccine from sputum given for 6 months. 1955—Still symptom-free.

Case 6. B.S., female (40). 1946-1950—6 attacks iritis. 1950—All investigations negative, but treated with course of Lertigon* for 3 months; remained symptom-free for 12 months. 1951—Cortisone tried but not much improvement; Lertigon again; now symptom-free until 1953. 1955—Reported continuous cortisone for past 2 years with some improvement, but never symptom-free; having more Lertigon now.

Psychological trauma due to the sudden acute pain of iritis may precipitate an attack of asthma and so help in the differential diagnosis; but more often a patient has his iritis, his asthma, his migraine, or his dermatitis, as part of a system of alternating allergies, well recognized in the eczema-asthma complex, but not so well known when the manifestations form a migraine-iritis-rheumatoid arthritis syndrome.

The suggestions that some trauma is necessary before any particular tissue becomes a 'shock tissue' for an allergen to act upon leads us to consider those post-accident cases of acute cyclitis. The trauma of the localizing accident may act as a trigger for some allergic response to air-borne dusts or to drugs used in the emergency treatment; or if the lens capsule is torn by a foreign body, the surrounding tissues become sensitized by the escaping lens protein. The stage is now set for an anaphylactoid reaction in this and perhaps also in the other eye, especially if the lens protein is concerned in any operative procedure during the next few days or weeks. Case 7 illustrates such a patient:

Case 7. Male aged 38. Perforating injury of the left eye with lens puncture. No foreign-body found. Routine treatment in hospital, including penicillin locally. Discharged on 8th day. On 10th day reported at out-patients clinic with 'no pain but worried by loss of vision'. Curette evacuation of swollen lens (not whole) and A.C. wash-out. 11th day—Acute cyclitis left eye and some discomfort right eye. 12th day—Severe cyclitis both eyes: routine allergy tests: all inhalants, pollens, foods and drugs negative, uveal pigment negative, lens protein +++ (intradermal). Desensitization by graded doses of lens protein 3 hourly for 3 days. 15th day—Right eye normal in appearance and vision, left eye still slightly injected, but all discomfort gone. 17th day—Further wash-out with A.C. Lens protein disturbed without any flare-up. 23rd day—Vision right eye 6/6, left eye 6/24. 53rd day—Vision right eye 6/6, left eye 6/24.

* Lertigon is Histamine-azo-globulin of Parke Davis Ltd.

Drug Reactions

Compared with other specialities, ophthalmology tends to use few drugs: in iritis, atropine has been the constant friend of both surgeon and patient, except in the odd one in a hundred cases who shows a specific allergy to this drug. Many more than one in a hundred are hypersensitive to atropine, being able to tolerate, and be well-dilated by 1/1,000 or even 1/10,000, although 1/100 causes local stinging and burning. Those who are allergic to the atropine molecule or the tropine ring get reactions in the surrounding tissues. If these are not very intense, and atropine is necessary, one tablet of an anti-histamine given by mouth 20 minutes before each drop of atropine is applied to the eye usually keeps the condition under control for a short attack of iritis; but in severe cases some other mydriatic is necessary.

Case 8. D.L., female (58). Recurrent iritis for 8 years; attacks usually responded to treatment within 4-5 weeks. October 1954—Acute flare-up right eye; given atropine ointment within 12 hours; red, irritating eye with oedema of surrounding tissues and eczema of 2/3rds of face; allergy tests (intradermal): atropine +++, hyoscine +. N.B.—Had 12×1,000,000 units of penicillin for streptococcal pneumonia in March 1954.

In contrast to case 8 case 9 is an example of the production of an acute iritis secondary to glaucoma, presumably by the use of a new drug on this known allergic patient for treatment of his glaucoma.

Case 9. P.A., male (62). 10 a.m.—Admitted to hospital complaining of loss of vision right eye. 11 a.m.—Diagnosed by two senior ophthalmologists as glaucoma without secondary iritis and given eserine drops. 3 p.m.—Intensive pain and smarting and much oedema of lids; acute iritis on examination; intramuscular injection of 2 c.c. of anthisan given *statim* and pain and swelling controlled in 40 minutes. 3 days later—Allergy tests showed: eserine ++, prostigmin ++, pilocarpine −; glaucoma being controlled with pilocarpine as required.

Ideally every patient with a past history of allergy should be tested intradermally with any drug new to this particular patient. These drug reactions are usually of the immediate or extracellular type and show a very definite skin reaction in contrast to a control saline-test within 20 minutes, though it must be remembered that the same patient may at one time have an extracellular reaction and at a later date an intracellular one to the same drug; that is to say, his secondary allergy may be controlled by anti-histamines or may need cortisone.

Are more patients showing allergic manifestations today than 20 years ago? The answer is 'yes' and the reason seems to be not the number of new drugs and foods used daily in this and in other countries but the types of the drugs. Some antibiotics are now known to act as sensitizers, and create or intensify the particular biochemical metabolic upset which is known as the 'allergic state' and is sometimes coupled with that certain hostile outlook on life so often referred to in the study of psychosomatic medicine.

The simplest illustration is the hay-fever patient who has his annual course of anti-pollen injections with good results and no untoward reactions, until he has penicillin

for some intercurrent infection one winter: then next spring the first minute dose of pollen solution produces an attack of hay-fever, accompanied by oedema of the lips, eyelids and occasionally glottis, and may cause a spasmodic wheeze from the chest. Perhaps some of you have patients whose iritis recurs each summer, and heals at the end of the pollen season—and only then, in spite of all your care and attention. Then you would be wise to test for pollen allergy and, if the result is positive, take a careful history of contact with antibiotics, weed-killers and dyes, such as those containing a p-phenylene-diamine group (see case 8).

SUMMARY

Iritis is presented as an occasional manifestation of allergy. It may be of either the extracellular or the intracellular type and may be due to pollen, inhalants, foods, drugs or toxin (bacterial or virus). Both anti-histamines and cortisone have a place in the treatment of the acute stage but take no part in the ultimate prophylactic treatment of recurrent iritis of allergic origin.

REFERENCES

1. Morgan, O. G. (1947): Proc. Roy. Soc., **40**, 598.
2. Walker, V. B. (1950): Ann. Allergy, **8**, 298.
3. Walker, V. B. (1954): Acta allerg., **7**, 138.
4. Pickering, G. W. (1952): Brit. Med. J., **1**, 1207.