TOXIC AMBLYOPIA

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With the increased use of chemotherapy, it may be well to call attention to the symptom known to the eye physician as toxic amblyopia. Characterized by the patient as a veil, mist, fog, or haziness of the vision, further questioning reveals that this is in the direct vision and occurs most frequently in the morning. However, it is not uncommon for the cloudiness to increase during the day, usually affecting one eye, then the other, greatly alarming the patient as a rule. These cases comprise the acute group and if the condition is not recognized and appropriate measures instituted, a chronic amblyopia results. Patients in the latter group could be characterized as being apathetic—perhaps the visual fog includes the cerebrum.

References in the literature on this subject began in the middle of the eighteenth century. In 1751 an article by Boerhaave, as cited by deSchweinitz[1] appeared. In 1813 it was noted that drinkers of bitter beer had difficulty with their sight. For almost two centuries alcohol has been a primary factor in the production of toxic amblyopia.

deSchweinitz[1] in an excellent monograph published in 1896, lists some seventy-five drugs that have been known to produce this condition. The agent responsible for the amblyopia is usually designated in its name, such as alcohol amblyopia, tobacco amblyopia, etc.

Casey Wood[2] classified the drugs into two classes:

1. Poisons affecting the optic nerve
   a. Chronic retrobulbar neuritis.
   b. Poisoning producing other forms of optic nerve disease.
2. Poisons which cause symptoms of amblyopia but are unaccompanied by lesions in the retina or optic nerve.
   a. Agents producing mydriasis—dilated pupil.
   b. Agents producing miosis—contracted pupil.
   c. Agents producing irregular symptoms.

I believe that this classification, modified slightly by deSchweinitz, is the best available although it is evident that with our present knowledge of this symptom, no accurate classification is possible. It may be said that any drug can produce an amblyopia if the patient has an idiosyncrasy to that drug and if it is used over a period of time. The individual sensitivity is very important and must be taken into immediate consideration when any drugs are prescribed, whether they be given orally, intravenously, subcutaneously, by suppository, or by innunction. The absorption of the substance is all that is necessary to produce poisoning in certain individuals. The important point is that almost any drug can produce it and any reference to a cloudiness of vision

should be an indication for immediate discontinuance of all possible toxic substances, followed by a careful study to determine the causative agents.

The appearance of the fundus is as a rule normal. In rare instances edema of the macula may be seen, while in others there may be a questionable hazy disc. If the disease has become chronic, one is apt to find a definite greyish-yellow pallor of the inferior temporal portion of the disc which in most cases is rather indefinite. The nerve head in some instances has a "dirty color" with hazy margins and lacks sharp differentiation. It is not like the fairly sharp white or greyish-white seen in the retrobulbar neuritis of multiple sclerosis about which more discussion will be given later.

In every instance of toxic amblyopia, careful study of the eye is indicated as, associated with the loss of vision, there may be disturbances of the extra-ocular muscles, either as isolated paralysis or in nuclear groups. Diplopia is not uncommon. There are also pupillary changes as shown by the classification of Wood[2]. Some drugs dilate the pupil and others contract it. Changes in accommodation are frequently noted, especially in patients using atropine.

Undoubtedly, the most important sign is the change in the visual fields which is usually typical of the disease. First, the central field (foveal field) is as a rule involved—either a relative scotoma (loss that is not complete—a haziness) or an absolute scotoma in which no targets of any size are seen. These field losses may or may not extend to the normal blind spot (the optic nerve) and they may extend out to the periphery of the field. The study of the visual field is important and it is here that changes in the color field are of importance, as loss of red is seen very early in some cases. Progress studies of the fields are the only dependable way to study the results of treatment in this disease. Visual acuity is a second important factor, but without doubt the best sign is the patient's own statement that objects are more discernible and the mist is beginning to clear.

Careful history in regard to the patient's habits in obscure cases may elicit the causative agents. This requires extreme patience and tact as many people forget the fact that they are taking a cathartic daily and this may contain phenolphthalein; others, the self medicators, are not always willing to divulge their home remedies. Another group definitely hide the information, especially those who have been taking ergot or quinine. The mention of the fact that blindness may ensue unless all possible information is at hand is an excellent and truthful means of finding out the toxic agent. In the case of food poisoning, a rehearsal of previous meals may be necessary. All information is of importance and, in my experience, I have never had too much. In most instances,

it is only by sincere effort that sufficient knowledge is obtained.

Associated physical signs may contribute a great deal toward the diagnosis and determination of the etiological factor. A complete physical examination is indicated in all obscure cases and this may reveal the clue to the causative agent. A knowledge of any effect on the peripheral nerves, tissue changes, degenerations, and alterations in the blood, plus the effect on the special senses, such as hearing, are of value. Because the central vision is involved, no effort should be spared in the search for the causative agent. Hospitalization and repeated quizzing and examination are indicated if clues are not forthcoming.

There are a number of patients who suffer transitory loss of central vision. These individuals undoubtedly have toxic amblyopia. They use certain drugs very infrequently but in sufficient amounts to cause trouble occasionally; however, when they use the drug more regularly, a constant defect in the field may result.

A number of patients have noticed blurring of vision for a long period of time but, because the scotoma was unilateral and not always absolute, they did nothing about it; this is especially true of those patients who suffer with food allergy. Certainly this is true in almost all the cases in which optic atrophy is present. A few patients who have a sensitivity to foods, and probably the same may be said of plants, have had transitory loss of the central field with recovery following proper restriction of the diet. We have seen several patients who have had definite disturbances of the central field while taking vaccine for one reason or another. These patients are difficult to handle and care must be taken that the use of the vaccine be discontinued.

As one sees more of these patients, it becomes evident that any drug, food, or plant may affect an individual who has a sensitivity thereto and thus produce toxic amblyopia. Certain substances, since they are used by many people and have a definite toxicity, are therefore more common offenders than others. Good examples of these are tobacco, alcohol, quinine, and ergot.

Alcohol probably has held the attention of oculists for the longest period of time. The first report was that of drinkers of bitter beer who consumed large draughts of the substance at frequent intervals and in this manner were ingesting large doses of alcohol and possibly other products of fermentation. The drinker of poor alcoholic liquors is apt to be the patient with toxic amblyopia. It is possible, however, for the acute imbiber to have transitory amblyopia after a full night's drinking or a night's full drinking. Carroll[3] has shown that in many of these patients the alcohol is not the cause; rather it is a deficiency of vitamin B due either to inability of the patient to assimilate the vitamin or to a

lack of it. He has given some of these patients vitamin B but allowed them to continue their ingestion of alcohol and they have recovered. This is in keeping with the known action of vitamin B and might possibly be the explanation in some other forms of toxic amblyopia although, in my experience, patients with severe vitamin deficiencies have not shown field losses or visual losses as an outstanding feature of their deficiency.

There is the possibility that alcohol distilled from a grain to which a patient is sensitive might produce a greater reaction than another alcohol. A drinker of corn liquor may be sensitive to corn and not to alcohol. It is also known that poorly distilled alcohol contains too many and too much of the higher toxic alcohols. This is also true of the green or under-aged alcohols. The patients I have seen have mostly been drinkers of large amounts of alcohols over a long period of time although this has been associated with a definite lack of appetite and not infrequently with the use of tobacco.

Tobacco amblyopia presents itself more frequently than one is led to believe and probably will be seen even more often when women, who are notorious "chain-smokers," begin to suffer the effects of overindulgence. The worst cases of toxic amblyopia we have seen were in patients who chewed and smoked cigars or stogies—usually at the same time. It is well to remember that the heavy smoker never knows how much he smokes and he usually underestimates the amount. However, he generally carries an array of cigars in his coat pocket so that he will not run out in case of long delays anywhere.

Our worst cases of toxic amblyopia have been in patients who drank and smoked to excess; one man averaged between 25 and 30 stogies a day and these were soaked in corn liquor for flavoring. He also used a pint of liquor daily as well and to his credit it must be stated that he discontinued both and had almost complete recovery of vision. This occurred in spite of a very "dirty" disc and large field loss.

Chewing tobacco, cigars, and a pipe are the three worst offenders, but contrary to general belief cigarettes can produce toxic effects. Here again it is impossible to secure accurate information from the chronic smoker. By rough estimate three to four packages a day is the outside limit of possibility although a number of patients have used at least three packages. There are several potential dangers in cigarettes—the tobacco itself, toxicity in the paper, and substances used to flavor the tobacco. It is well to discontinue the use of alcohol and tobacco as soon as possible in patients having disturbances of vision. There is, of course, the possibility, as shown by Carroll, that the visual disturbance may be due to other factors. However, the irritating cause is still tobacco or alcohol and they, at the best, are of little value to the patient, radio, newspaper, and magazine advertising notwithstanding.

For treatment of tobacco and alcohol amblyopia, first discontinue the substances as much as possible. Give large amounts of vitamin B, especially in alcohol amblyopia, and increase the elimination from the body either by sweats or catharsis which must not be too drastic, and build the patient up with a diet high in vitamins. It is usually found that patients rarely have a deficiency in a single vitamin, especially if they have faulty dietary habits.

Under faulty dietary habits probably should be classified the individual who knowingly eats foods to which he is sensitive or who makes no effort to find out if transitory attacks of blurred vision need any treatment other than new lens. We have seen a number of patients whose visual complaint was due to food allergy and all the signs and symptoms of toxic amblyopia were corrected by restriction of the diet. Everyone is well aware of the acute toxic effect of certain foods on people with specific sensitivities. The same is possible over a long period of time when the sensitivity is to a food included in the daily or routine diet such as milk, coffee, wheat, or a fairly common offender such as chocolate.

Every patient who has a toxic amblyopia due to alcohol or tobacco should be thoroughly checked for other substances with which he comes in contact each day, as these are likely to be predisposing factors.

Certain individuals have been seen who have had specific sensitivity to substances where they worked; for example, a boy packing plants in moss in a commercial greenhouse had a severe unilateral amblyopia with a slight haze in the other eye. He had a cecocentral scotoma, a large blind spot by virtue of pure edema of the disc which looked like a hive of the nerve head. This was associated with loss of the central field. Removing him from that one location was all that was necessary to clear his sight. However, had he been allowed to continue in this work, I am certain that permanent changes would have taken place.

Toxic amblyopia is supposedly rare in women. This, I believe, is a statement not borne out by our present day experience. The women of today indulge in as much tobacco and in some instances as much alcohol as do the men. Several of our most acute and severe cases were in young women who had used ergot preparations in an attempt to correct failure to menstruate. In this type of case, the toxic effect is transitory. It may be necessary, however, to use sweats and elimination to shorten the period of toxicity to a minimum.

Another instance in a woman was when one individual, in an effort to cure a cold, took nearly a dozen cold tablets containing a salicylate and quinine. We used elimination and sweats as well as deep diathermy to the orbits. This patient responded slowly to treatment as

did a second woman with recurring headaches and a constant habit of taking empirin to relieve them.

It is more than likely that, if field studies were made in more instances, many more cases of toxic amblyopia would be found in women suffering from blurred vision. I am convinced that, in at least several of our patients with optic atrophy of unknown etiology, allergy was the cause as they were suffering with severe general allergy.

Two other substances which are commonly used and which have produced amblyopia are lead and arsenic. Lead is used in industry by painters and plumbers, and others use lead products to which they may be susceptible. A fairly large number of these cases have been reported in the literature.

Arsenic, whether given as a toxic agent or in one of the combination arsenicals used in the treatment of syphilis, has produced amblyopia in a number of instances and attention must be called to the toxic effects of some of the arsenic compounds on the optic nerve. Certainly some preparations are more toxic than others but there is a large factor of individual sensitivity which probably is as important to realize and know.

Mention must be made of the use of belladonna (atropine) and its derivatives. A very high percentage of people are sensitive to atropine and complain of visual disturbances. In most of these individuals, the eye disturbance is due to relaxation of the muscles of accommodation with pupillary dilation. In a few, however, the disturbance is in the macula or optic nerve and study of the field should be made, as in the latter group atropine should be discontinued, whereas a mild pupillary and accommodative disturbance is of no consequence.

Retrobulbar neuritis and toxic amblyopia have been used as synonyms. However, when one thinks of retrobulbar neuritis, one is apt to have in mind that change as seen in multiple sclerosis. The most bizarre, unusual, and untrustworthy fields are those in multiple sclerosis. Rarely are fields taken at intervals found to be the same and the fundus picture ranges from a severe neuritis to a normal nerve head.

The atrophy seen in multiple sclerosis is a white atrophic change and usually by the time atrophy has taken place other physical signs such as scanning speech and the loss of abdominal reflexes are present. Early cases of multiple sclerosis present a very definite problem in diagnosis, but every case of retrobulbar neuritis is not multiple sclerosis nor should every case of optic neuritis or retrobulbar neuritis be so classified without a thorough search for the etiological factor and a complete study for allergy.

Multiple sclerosis offers a poor prognosis whereas toxic amblyopia

may definitely be benefited by proper management. It is well to remember that in 50 per cent of all cases of multiple sclerosis there is involvement of the optic nerve in one form or another.

There is a condition classified as pseudo-sclerosis which simulates multiple sclerosis but which produces no changes within the eye at all.

No effort has been made to discuss the pathological processes underlying the loss of vision. It might be well to draw attention to the usual changes taking place. There is usually a cellular edema which is a transitory process in most instances. This, when chronic, is replaced by round cells or small lymphocytes and eventually by connective tissue which is the final stage of permanent loss or atrophy.

Summary

Toxic amblyopia might be classified in two types: (1) acute and (2) chronic. These two types can be further subdivided according to the action of the substance. In both types there is similar loss of vision. In the chronic type, there is usually atrophy.

Immediate withdrawal from or removal of the offending drug, food, or chemical is important. The treatment is more that of management, as further use of drugs may add to the difficulty during a severe stage of hypersensitivity.

Elimination and sweats are indicated. Deep diathermy to the orbits should be attempted.

Use of the eyes should be restricted.

The prognosis is good in most of the acute cases. In chronic cases with atrophy, more vision tends to be lost before the process is completely halted.

References

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3. Carroll, F. D.: Acute alcoholic amaurosis, Arch. Ophthal., 20:797-803, (November) 1938.