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SERIES

Year Book
OF
OPHTHALMOLOGY

VAIL

THE YEAR BOOK *of* OPHTHALMOLOGY

(1957-1958 YEAR BOOK *Series)*

EDITED BY

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THE YEAR BOOK PUBLISHERS
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THE PRACTICAL MEDICINE YEAR BOOKS

This volume is one of the 15 comprising the Practical Medicine Series of Year Books founded in 1900 by G. P. Head, M.D., and C. J. Head, and published continuously since then. The complete list follows:

Medicine: *Infections*, edited by PAUL B. BEESON, M.D.; *The Chest*, by CARL MUSCHENHEIM, M.D.; *The Blood and Blood-Forming Organs*, by WILLIAM B. CASTLE, M.D.; *The Heart and Blood Vessels and Kidney*, by TINSLEY R. HARRISON, M.D.; *The Digestive System*, by FRANZ J. INGELFINGER, M.D.; *Metabolism*, by PHILIP K. BONDY, M.D.

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Dentistry

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INTRODUCTION

The appearance of this issue, the first of the YEAR BOOK series devoted exclusively to Ophthalmology, marks the end of more than 50 years of the annual combined Eye, Ear, Nose and Throat volume, a long and honorable association. "If it were not for the YEAR BOOK OF THE EYE, EAR, NOSE AND THROAT," say the publishers in the Fortieth Anniversary Preface to the 1940 YEAR BOOK, "the Practical Medicine Series could not this year celebrate its fortieth anniversary. For without it there would have been no such series, and the many-volumed record of medical and surgical progress that has served the profession since the turn of the century would not have existed. It was the first of the YEAR BOOKS, antedating the series as a whole; and it provided both the inspiration and the fundamental plan from which the series started."

Before the first world war an ophthalmologist was a rare individual in the United States. The combined field of practice was universal even in large cities, although less so along the eastern seaboard, where there were a few ophthalmic centers. Special hospitals throughout the country were, as a general rule, designated as Eye, Ear, Nose and Throat infirmaries or hospitals and many of the public ones still are. In most of these places, however, the various services were distinct and attended by men practicing their specialties, although here and there there was some overlapping, especially in the private wards. The interns or residents, however, served both services in rotation.

The joint specialty idea was also carried out in professional societies (e.g., American Academy of Ophthalmology and Otolaryngology), in journals (e.g., *The Eye, Ear, Nose and Throat Monthly*) and in the army, navy, air force and public health services; in many instances, there still are Eye, Ear, Nose and Throat units in armed services clinics and wards. The separation of the specialists but not the Eye, Ear, Nose and Throat service was strikingly obvious in World War II, during which it was found almost impossible to locate a

medical officer who was equally versed in ophthalmology and otolaryngology. The commanding officer of a unit was therefore forced to designate the otolaryngologist to handle the eye work and vice versa, often with considerable embarrassment to the individual and to the patient involved.

Since the first world war, and particularly since the end of World War II, the specialty of ophthalmology, sui generis, in the United States, has increased to a most striking degree. Fewer and fewer of us practice ear, nose and throat; indeed, most have never had training in the latter specialty. Those who did, turned away from their ear, nose and throat work in increasing numbers, devoting themselves exclusively or nearly so to ophthalmology, for a number of reasons which are familiar to most of us.

When the Academy of Ophthalmology and Otolaryngology was first established more than 50 years ago, most of the members (more than 80%) were combined specialists. In 1957, the census was as follows: members exclusively practicing ophthalmology, 46%, exclusively practicing otolaryngology, 27% and practicing the combined specialties, 23%. There has been considerable agitation in the past few years to separate the members and make two academies; but at the moment this idea is not being entertained too seriously.

In the rest of the world the story is quite different. Ophthalmology has long had a field of its own, its own societies, journals and hospital services. It is an interesting problem just why the American specialist combined the two fields, which after all have not much in common, much less than ophthalmo-neurology for example. No doubt relatively poor training, lack of opportunity and economic reasons all played a part.

In any event, there has been evidence of increasing desire, mounting in pressure, on the part of ophthalmologists here and abroad to have published a YEAR BOOK devoted entirely to ophthalmology. The publishers have carefully looked into this and, after considerable study, have decided to try it out. The success of this venture, from the publishers' point of view, depends on the support of all ophthalmologists everywhere, for in the past the YEAR BOOK OF EYE, EAR, NOSE AND THROAT has had a world-wide distribution and popularity.

This YEAR BOOK contains more than twice the number

of abstracts and editorial comments as in the past. Most of the articles that are abstracted are of great clinical interest and importance; a few are of experimental ophthalmologic interest. These latter were chosen for the most part because they had some clinical bearing, and will be found scattered throughout in the various appropriate sections. With the rapid growth of experimental ophthalmology it is possible that in the future a special section will be devoted to it in the YEAR BOOK OF OPHTHALMOLOGY. At present, I think it wiser to maintain the high clinical value of the YEAR BOOK for handy use in daily clinical work. Opinions on this point are solicited for future guidance.

In this issue is found a special article by Irving H. Leopold, M.D., of Philadelphia, world-wide authority on ocular pharmacology and therapeutics. The rapid growth in the past few years in this field demands a critical sorting out for us of the wheat and chaff. I trust that you will agree that Dr. Leopold has done this most adequately. His article immeasurably increases the value of this volume to all practicing ophthalmologists, and I am most grateful to him for his fine contribution.

It is planned to have some outstanding authority and investigator prepare a special review article in his particular field of activity in ophthalmology in each forthcoming annual number of the YEAR BOOK. The author will be chosen from experts, no matter in what country he may reside. Next year we are promised such an article by Bernard Becker of St. Louis on Glaucoma.

I approach the task of editing and helping to launch the first YEAR BOOK OF OPHTHALMOLOGY, to be sure, with some temerity, but with confidence that it will meet with your approval, and that you will find it useful in our great and separate specialty.

DERRICK VAIL

Special Article

RECENT ADVANCES IN OCULAR THERAPY

by IRVING H. LEOPOLD*

DURING THE PAST YEAR, as in preceding ones, new drugs have been introduced and old ones have received more consideration. The year's experience has allowed one to become familiar with important features of new and old drugs in current use so that their application and limitations are understood more completely.

HEPATOLENTICULAR DEGENERATION

An increased concentration of copper in both liver and brain of patients dying of Wilson's disease, hepatolenticular degeneration, was noted by Haurowitz, Luthy and Glazebrook. These observations were all made in single cases and were confirmed and extended by Cummings, who reported a series of 3 patients who died of hepatolenticular degeneration. It is now known that in addition to the copper in the tissues there is increased excretion of copper in the urine, low plasma copper concentration and a very low level of ceruloplasmin, the copper-binding globulin. This last is believed to be the primary biochemical defect in Wilson's disease. Removal of excess copper from patients with hepatolenticular degeneration may be brought about by parenteral use of BAL. This was first reported by Mandlebrote and Thompson and has been confirmed by many subsequent workers. Given in repeated courses over long periods, BAL may lead to marked clinical improvement, although in the more acute forms of the disease the results have been less satisfactory. Intravenous versene and amino acids have also been shown to increase copper excretion, as have high protein diets and cortisone. Absorption of copper from the intestines can be reduced by oral administration of potassium sulfide or carboresins. A new form of oral treatment with

*From Wills Eye Hospital, Philadelphia

penicillamine (beta, beta, dimenthylcysteine) has been described. Given in doses varying from 0.5 to 1.5 Gm. daily to 6 patients with Wilson's disease, it provoked a very large increase in excretion of copper. It appeared to be more active than BAL in this respect (Walshe). No toxic reactions were noted in the short-term trials described. From Dr. Walshe's report it seems apparent that penicillamine deserves further study not only in Wilson's disease but, as he pointed out, in the treatment of lead, gold and mercury poisoning.

THERAPY OF VASCULAR LESIONS

There are various collagen diseases which may produce changes in the fundus. Affecting the arteries are periarteritis nodosa, temporal arteritis and disseminated lupus erythematosis. Pathologically, all these conditions are closely related. The differences are largely of degree, i.e., severity and location of the vascular lesions. The typical lesion is an alteration of collagen in the vessel wall leading to inflammatory reaction. The onset occurs with edema of the vessel wall, followed by fibrinoid necrosis of the media and elastic lamina which then spreads to involve the intima and adventitia with cellular infiltration. Polymorphonuclears predominate at first, but later lymphocytes and giant cells appear. The acute lesions may so weaken the wall as to lead to aneurysms and/or hemorrhages, whereas the chronic lesions lead to proliferation of fibrous tissue which may predominate, causing narrowing and occlusion of the lumen.

The cause of temporal arteritis is unknown. Deaths have been recorded. Although many vessels of the body may be involved such as the temporal, carotid and pulmonary arteries as well as the peripheral and visceral ones, the chief structure affected of serious importance is the visual apparatus.

The treatment recommended in the past has consisted of excision of the vessel, injection of procaine along the course of the involved artery, use of histamine, chlortetracycline, anticoagulants, vasodilators and stellate ganglion block. Steroid therapy in sufficiently large doses may stop progression of the disease (Birkhead, Wagener and Schick; Bennett). It appears to be the best therapy of the moment, but it also fails to control all patients.

CENTRAL RETINAL ARTERY OCCLUSION

This condition demands therapy directed toward bringing about rapid vasodilatation in the involved vessel. There have been an unusual number of studies along this line in the past year (Wudka and Leopold; (Bettman and Fellows, Weerekoon; Staenglen; Wethman). Staenglen and Wethman, with the use of ophthalmoscopic measuring devices, found that a number of compounds such as amyl nitrite and hexamethonium had brief vasodilating effects on retinal vessels but also caused a marked drop in systemic blood pressure. The most effective retinal vasodilator in human eyes in their hands was eupaverine, which at the same time caused the greatest fall of blood pressure. In studies of the choroidal circulation by technics employing scleral windows or scleral dehydration no agents were found which would cause dilatation of the large choroidal vessels. A number were uncovered which would produce vasoconstriction of the long posterior ciliary arteries. Most of the changes observed appeared to be secondary to alterations in general blood circulation rather than to direct responses of the choroidal vessels. By the use of the tagged red blood cell technic, Bettman and Fellows were able to demonstrate that inhalation of carbon dioxide and retrobulbar administration of aminophylline and tolazoline produced increase in blood volume. On the basis of available evidence, it seems advisable to avoid agents which produce general vasodilatation, for this may induce a fall in blood pressure which might nullify any anticipated favorable effects on the ocular vessels. Retrobulbar injections of 25 mg. aminophylline or 25 mg. of 2% procaine of tolazoline or paracentesis of the anterior chamber may improve local circulation and might have a favorable effect on the central retinal artery and its main branches. However, if the point of obstruction lies before the onset of the central retinal artery, it is unlikely that local therapy will have any benefit. Anticoagulants could help by preventing growth of a clot.

Bruce has called attention to the possibility of hypotensive agents inducing central retinal artery occlusion. He has reported a patient in whom central retinal artery occlusion developed very quickly after administration of hexamethonium for hypertension.

Occlusion of the central vein of the retina is difficult to

treat. Anticoagulant therapy was introduced in 1937 for such occlusion, and since then there has been considerable controversy in the literature as to its value. Results obtained by Vannas and Orma were very similar to those previously reported by Duff, Falls and Linman and by Klien and Olwin. Vannas and Orma felt that short-term anticoagulant therapy could be effective if the occlusion was by stagnation, but if sclerosis seemed to be the primary etiologic factor short-term therapy was not sufficient. Their therapy consisted of intensive anticoagulant therapy for 10 days to 3 weeks, preferably with heparin or a corresponding drug. Vasodilator drugs were occasionally used, and any inflammatory conditions were treated. Patients with evident sclerosis were treated with 100 mg. sodium heparin intravenously, or 200 mg. subcutaneously twice a week, and 100 mg. vitamin E by mouth 3 times a day. They continued this therapy for months or years. The vitamin E was used because it was thought that it might increase production of endogenic heparin and might also act as an effective anticoagulant on its own. In Vannas and Orma's analysis of 37 occlusions, 24 were complete, 2 incomplete, and 11 involved a main branch; 59% had good results and 20% had fair results. They therefore concluded that anticoagulant therapy improves the prognosis of central vein occlusion. In some instances short-term therapy might be sufficient, but they were very much in favor of long-term therapy, especially in elderly patients with a possible sclerotic cause for the occlusion.

FIBRINOLYTIC AGENTS

Streptokinase, trypsin, plasminogen and such agents are of theoretic value. Streptokinase activates a serum substance, plasminogen, to plasmin. However, most persons have antibodies against the ubiquitous streptococcus and may possess antibodies against the streptokinase fraction of the streptococcus. This would interfere with this agent's desired activity. Trypsin's mode of action is not known definitely, nor has its value as a fibrinolytic agent in retinal venous occlusion been established. In addition, it has toxic features. Plasminogen has potential value as it is a normal blood constituent, but there is insufficient data on its value for this purpose in ophthalmology or in venous occlusions elsewhere. It is

currently under study. Initial ocular trials have been complicated by fever reactions (Leopold and Bellet).

THERAPY OF MACULAR LESIONS

There is no known therapy which is specific for macular lesions. Central serous retinopathy improves spontaneously in most instances after varying lengths of time. There are favorable reports on the use of cortisone, iodides, thiamine, nicotinic acid, vasodilators and tranquilizers, etc. However, because of the number of cases in which improvement has not occurred a favorable prognosis cannot always be given (Walkowicz).

At present there is no satisfactory therapy for Tay-Sachs and Niemann-Pick disease, nor is there any realistic treatment for the various abiotrophies and diseases of the macula associated with spontaneous resorption of blood vessels. If the changes in the macula are secondary to inflammation of the choroid, and this can be identified as to the specific etiology, i.e., if it is tuberculous or toxoplasmic, specific therapy may be helpful for the identifiable inflammations.

Macular changes due to venous occlusion and central artery occlusion can be avoided only if one succeeds in controlling the occlusion of a vein or artery initially.

The major and increasing problem today is the senile macular degeneration type of lesion for which there has been no satisfactory therapy. With the recent interest in various forms of vascular sclerosis, the relationship to the diet and to agents which alter lipid concentration in the blood (Schroepfer), several possible modes of therapy have been suggested. If it is felt that the lesions are secondary to vascular sclerosis and if development of sclerosis of the vessels which are important to the retinal or choroidal circulation in this area can be favorably influenced, this therapy may prove helpful. Because heparin is thought to have a fat-clearing or lipema-clearing action, it is being used as an antiatherogenic agent. Maumenee suggested the possibility of its use for this purpose, along with Engleberg and, most recently, Rome. Mylius and Stark found an increase of beta lipoproteins in a series of patients with senile macular degeneration. They gave 11 patients heparin intravenously, 100 mg. daily over an average period of 1 month, with definite improvement in 5. Rome used concentrated aqueous heparin,