Editorials

Change—Threat or Opportunity

STUDS TERKEL, writer and reporter, said recently that change is inevitable but often resisted or even opposed. Although sharing change can be a bond and relishing change can be invigorating, physicians especially resist change forced by others or required by regulations.

Physicians face accelerating pressures to change: challenging scientific discoveries, new techniques, administrative restrictions, patients' demands, new forms of competition, and more rigorous quality assurance. Fox, Mazmanian, and Putnam, in a study of 340 physicians, found that we meet change in several ways.[1] Some accommodate passively and tend to be angry and resentful as they do so. Most make incremental moves. Others find entirely new directions to explore. They transform.

What causes physicians to change? A few change because they want to excel. Many become aware of innovations and react to them gradually. Some seek new solutions stimulated by patients' difficult problems. Regardless of motivation, making modifications requires repetition of new data or circumstances. Learning and changing are not first-pass phenomena. Finally, a variety of sources of information are necessary—experts, colleagues, literature, seminars, courses, and rounds.

One element in a successful approach to change is involvement. Whether change is sparked by scientific advances or imposed by public policy, physicians who adapt are the ones who participate. They ask questions. They request consultations. They vote. They run for office. They study. They write letters to professional organizations, to editors, to political leaders and other policymakers. They make themselves heard. They convert negatives to positives, so problems become challenges. They take risks. They recognize that others are undergoing change during these troubled economic times. To borrow from Arnold Toynbee, they regard medicine as a "movement and not a condition; a voyage and not a harbor."

Physicians who cope well do so by observing, thinking, and acting. They view change as opportunity.

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REFERENCE

1. Fox RD, Mazmanian PE, Putnam RW (Eds): Changing and Learning in the Lives of Physicians. New York, Praeger, 1989

Retinal Vasculitis

DISEASES OF THE RETINAL VASCULATURE are among the most serious problems in ophthalmology. They form a heterogeneous group of disorders that includes such diverse afflictions as the chronic retinal ischemia associated with diabetic microvasculopathy and the sudden, devastating visual loss of a central retinal artery occlusion. In this issue, Rosenbaum, Robertson, and Watzke present an overview of one important, but poorly understood, category of vascular disease: retinal vasculitis.[1]

Retinal vasculitis should not be considered a single disease entity. It appears to be a nonspecific immunologic reaction of retinal arterioles or venules to various antigenic stimuli and is a finding in many different systemic and local disease states. In some patients, vasculitis results in no visual disturbance. The disorder can, however, lead to serious, sight-threatening complications, including vascular occlusion with infarction of the retina, or vascular leakage with retinal edema. Late sequelae may include retinal neovascularization leading to vitreous hemorrhage or tractional retinal detachment.

Because retinal vasculitis can be a manifestation of systemic disease, it is often evaluated and managed best by an ophthalmologist and internist working as a team, drawing on each other's special skills and experience. An organized approach to retinal vasculitis is clearly needed to ensure the best patient care.

Included in this approach should be the appropriate use of terms to facilitate communication, yet even the designation "vasculitis" has been a source of confusion. Strictly speaking, the adjectival ending "-itis" indicates inflammation, but in practical terms, many vascular disorders have been called vasculitis by ophthalmologists, whether or not they are characterized histopathologically by the presence of inflammatory cells in vessel walls. Confusion arises because the signs and complications of retinal vasculitis may be mimicked by noninflammatory disorders. Vascular sclerosis, for example, can occasionally be confused with inflammatory sheathing of vessels. Furthermore, vascular occlusion by inflammation, thrombus formation, and embolization can all result in a similar clinical picture. Although ophthalmologists have the unique opportunity to view retinal vessels through transparent media, the tissues are not available for routine biopsy and clinicopathologic correlation.

Unfortunately, various vascular disorders that are not primarily inflammatory have been called retinal vasculitis. "Benign retinal vasculitis," for example, is a unilateral condition of young adults characterized by optic nerve head swelling that can mimic central retinal vein occlusion.[2] Although an inflammatory cause is hypothesized by some,[3] abnormal clotting and fibrinolytic mechanisms are thought to be the underlying cause by others.[2,4] Use of the term "vasculitis" for the ocular disease associated with systemic lupus erythematosus (SLE) is particularly confusing. It is usually an occlusive microvascular disease that can lead to cotton-wool spot formation (areas of nerve-fiber layer swelling caused by ischemia) and occasionally to retinal hemorrhage. A more severe vaso-occlusive disease of larger vessels can also occur. Histopathologic studies show that vessels are occluded with amorphous hyaline material without evidence of inflammatory cells in vessel walls.[5] True retinal vasculitis is only rarely a feature of the disease. "Severe retinal vaso-occlusive disease" is probably a preferable name for this disorder.[6]

There are no well-established criteria for the clinical diagnosis of retinal vasculitis. Among the more useful definitions, however, is one proposed by Graham and co-workers.[7] They define retinal vasculitis as the vascular leakage and staining of vessel walls on fluorescein angiography, with or without the clinical appearance of fluffy, white perivascular infiltrates in an eye with evidence of inflammatory cells in the vitreous body or aqueous humor. When called on to examine a patient with "retinal vasculitis," it is appropriate for internists to ask the referring ophthalmologist if, in fact, the vascular disease appears to be inflammatory by these criteria. If

not, and it is solely an ischemic microvasculopathy—as manifested by cotton-wool spots, retinal hemorrhages, or both, without inflammatory signs—disorders such as diabetes, SLE or other connective tissue diseases, and even human immunodeficiency virus (HIV) infection (as discussed later) should be considered.

There are two goals in evaluating cases of retinal vasculitis. Ophthalmologists must assess the intraocular effects of vascular inflammation, and with their internist colleagues they should search for an underlying cause. The severity of damage to the retina and vision will direct the extent to which aggressive evaluation and therapy must be undertaken. Internists will be involved primarily in diagnosing and evaluating isolated cases of retinal vasculitis in which no other focal inflammatory lesions are found. Vasculitis is most commonly seen as an epiphenomenon in patients with other retinal disorders, such as ocular toxoplasmosis, cytomegalovirus retinopathy, or primary ocular disorders such as pars planitis. Because the vasculitis is not necessarily restricted to areas of the retina with primary disease, a careful search of the entire retina for focal lesions is critical in any patient with retinal vasculitis. In persons with toxoplasmic retinochoroiditis, retinal vasculitis has been shown to be an immunologic response to *Toxoplasma* antigens in the eye.[8,9] In this and other retinal infections, the vasculitis resolves without sequelae after appropriate antimicrobial therapy.

If no other retinal lesions are found, systemic inflammatory disease should be looked for. Despite the well-established association between retinal vasculitis and systemic disorders, a systemic illness is found in only a few cases.[10,11] In most large series, Behçet's syndrome and sarcoidosis are the most common systemic diseases identified.[10,11] Isolated retinal vascular inflammatory sheathing can occur in many diseases, but in disorders such as Crohn's disease,[12] Wegener's granulomatosis,[13] and polyarteritis nodosa,[14] it is much less common than are other ocular findings.

The acquired immunodeficiency syndrome (AIDS) has been added to the list of disorders associated with retinal vascular disease. A microvasculopathy similar to diabetic retinopathy is an almost universal finding in HIV-infected patients.[15,16] Infection of endothelial cells by HIV,[17] elevated circulating immune complexes,[18] and hemorheologic abnormalities[19] have all been hypothesized to be contributing factors. Isolated retinal vasculitis has been associated with HIV infection.[15] Although an uncommon manifestation in the United States, isolated retinal vasculitis is seen frequently among African patients with AIDS,[20] making it one of the distinctions between various patterns of HIV infection seen around the world.

Most cases of isolated retinal vasculitis remain idiopathic. The classic condition in this category is Eales disease, which may be a group of disorders characterized by peripheral occlusive periphlebitis without prominent inflammatory changes elsewhere in the eye. Described more than 100 years ago, its cause is still unknown. Furthermore, because specific criteria for the diagnosis of Eales disease have varied over the years, the term is not particularly useful.

A detailed description of inflammatory findings in the eye has limited diagnostic value with regard to retinal vasculitis. A distinction between retinal periphlebitis and arteriolitis can be made ophthalmoscopically but has rarely been emphasized in published series. Vascular changes vary widely among patients with any disease, but in most disorders the peripheral venules rather than arterioles are involved.[13,21,22] Syphilis is one disease thought to preferentially involve the retinal arterioles,[23,24] but both venules and arterioles can be affected.[23,25] The location and appearance of vascular lesions are also generally of limited diagnostic use. The term "candle-wax drippings" has been applied to dense, focal, nonoclusive periphlebitis associated with sarcoidosis, but its appearance is neither pathognomonic nor present in all patients with the disease. The occlusive phlebitis of Behçet's syndrome tends to manifest in the posterior pole, although peripheral retinal vasculitis may occur.

The laboratory evaluation should be directed by the patient's history and the findings of the physical examination. It is common for many ophthalmologists and their internist consultants to order a large, routine battery of tests for patients with ocular inflammatory disease, but this approach is rarely productive and can be misleading. For example, tests of anti-*Toxoplasma* antibodies are unnecessary in patients with isolated retinal vasculitis. As stated already, vasculitis can be a secondary finding in patients with focal necrotizing toxoplasmic retinochoroiditis, but the parasite does not cause retinal vasculitis alone. This fact, coupled with the high prevalence of anti-*Toxoplasma* antibodies in the general population, means that false-positive results are common with this approach.

There are very few laboratory studies that should be done in all patients with isolated retinal vasculitis. A VDRL and fluorescent treponomal antibody absorption test, or their equivalents, should always be done. Isolated retinal vasculitis is an uncommon manifestation of syphilis but one that should not be overlooked. A chest x-ray film to look for evidence of sarcoidosis or tuberculosis is also appropriate because these diseases may first be apparent in the eye.

The relationship between retinal vasculitis and *Mycobacterium tuberculosis,* however, is a source of confusion. It is well established that inflammatory sheathing of the retinal vessels can occur in patients with miliary tuberculosis and ocular infection. Retinal vasculitis has even been reported to be the first sign of disease in patients subsequently found to have active pulmonary tuberculosis.[26] A more difficult problem is the patient with isolated retinal vasculitis whose skin tests positive to purified protein derivative (PPD) without other signs of active ocular or nonocular tuberculosis. (Such an association has been described for many patients with Eales disease, but a causal relationship has never been established.) Some investigators advocate antituberculous therapy for such patients,[27] but this recommendation remains controversial. Because tuberculous uveitis without other signs of tuberculosis is extremely rare, other investigators simply refer patients for the management of their positive skin test, as they would do for anyone with this incidental finding. The retinal vascular lesions are then observed closely for the development of associated problems. The same does not apply to patients with both focal granulomatous lesions in the eye and retinal vasculitis; the granulomata would suggest localized infection.

Tests of immune function have been studied in large groups of patients with retinal vasculitis. Regardless of whether or not patients have evidence of associated systemic inflammatory disease, the most frequently identified abnormalities have been elevated circulating immune complexes and antibodies against retinal antigens, especially against the S antigen, a soluble protein located in the outer layers of the

retina.[7,11,28] Although not a universal finding in patients with retinal vasculitis, these abnormalities have given support to the hypothesis that retinal vasculitis is an autoimmune disorder. A causal relationship between such abnormalities and retinal vasculitis has never been established, however, and their role in the pathogenesis of the disorder remains speculative. Because these abnormalities have never been shown to have diagnostic, therapeutic, or prognostic significance,[29] they are probably unnecessary in the routine evaluation of retinal vasculitis.

The treatment of patients with retinal vasculitis should be directed toward the underlying systemic problem, if one is identified. Management of the vasculitis per se is necessary only if it is leading to vision-threatening complications. It is important to distinguish between vaso-occlusive inflammatory disease and simple vascular sheathing; fluorescein angiography is a useful tool in making this determination. Aggressive anti-inflammatory therapy is not indicated for patients with asymptomatic vascular sheathing; the use of steroids in such therapy may produce glaucoma and cataracts.

The treatment of occlusive vasculitis has generally been disappointing regardless of the modality used, but corticosteroids have been its mainstay. If there is no systemic disease, the periocular administration of long-acting corticosteroids such as triamcinolone acetonide should be considered to avoid systemic side effects. Topically applied corticosteroids cannot reach the retina.

Immunosuppressive therapy is usually a treatment of last resort, but the literature contains little evidence that it is beneficial for the long-term retention of vision in severe idiopathic retinal vasculitis. The use of immunosuppressive agents for intraocular inflammatory disease is generally reserved for patients with bilateral disease whose vision has fallen below 20/40 in the better eye. Occlusive vasculitis in patients with Behçet's syndrome is the one form of uveitis for which most authorities agree that immunosuppressive drugs are the treatment of first choice. They are best administered by an internist experienced in their use, with monitoring of treatment effect by an ophthalmologist, again indicating the importance of a team approach.

Sometimes complications cannot be avoided despite aggressive therapy. When complications arise, treatment with laser therapy for neovascularization or vitrectomy for hemorrhage is required.

More effective management of retinal vasculitis must await a better understanding of its associated disease mechanisms. Rosenbaum and colleagues have shown that progress is being made toward that understanding. In the meantime, they have provided an excellent framework for developing a rational approach to the current evaluation and management of the disorder.

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REFERENCES

1. Rosenbaum JT, Robertson JE Jr, Watzke RC: Retinal vasculitis—A primer. West J Med 1991 Feb; 154:182-185

2. Hart CD, Sanders MD, Miller SJH: Benign retinal vasculitis. Br J Ophthalmol 1971; 55:721-733

3. Hayreh SS: Optic disc vasculitis. Br J Ophthalmol 1972; 56:652-670

4. Savir H, Wender T, Creter D, Djaldetti M, Stein R: Bilateral retinal vasculitis associated with clotting disorders. Am J Ophthalmol 1977; 84:542-547

5. Graham EM, Spalton DJ, Barnard RO, et al: Cerebral and retinal vascular changes in systemic lupus erythematosus. Ophthalmology 1985; 92:444-448

6. Jabs DA, Fine SL, Hochberg MC, Newman SA, Heiner GG, Stevens MB: Severe retinal vaso-occlusive disease in systemic lupus erythematosus. Arch Ophthalmol 1986; 104:558-563

7. Graham E, Spalton DJ, Sanders MD: Immunological investigations in retinal vasculitis. Trans Ophthalmol Soc UK 1980; 101:12-16

8. Newman PE, Ghosheh R, Tabbara KF, O'Connor GR, Stern W: The role of hypersensitivity reactions to *Toxoplasma* antigens in experimental ocular toxoplasmosis in nonhuman primates. Am J Ophthalmol 1982; 94:159-164

9. Webb RM, Tabbara KF, O'Connor GR: Retinal vasculitis in ocular toxoplasmosis in nonhuman primates. Retina 1984; 4:182-188

10. O'Day J, Shilling JS, ffytche TJ: Retinal vasculitis. Trans Ophthalmol Soc UK 1979; 99:163-166

11. Wakefield D, Easter J, Penny R: Immunological abnormalities in patients with untreated retinal vasculitis. Br J Ophthalmol 1986; 70:260-265

12. Duker JS, Brown GC, Brooks L: Retinal vasculitis in Crohn's disease. Am J Ophthalmol 1987; 103:664-668

13. Sanders MD: Retinal arteritis, retinal vasculitis and autoimmune retinal vasculitis. Eye 1987; 1:441-465

14. Morgan CM, Foster CS, D'Amico DJ, Gragoudas ES: Retinal vasculitis in polyarteritis nodosa. Retina 1986; 6:205-209

15. Holland GN, Pepose JS, Pettit TH, et al: Acquired immune deficiency syndrome: Ocular manifestations. Ophthalmology 1983; 90:859-872

16. Newsome DA, Green WR, Miller ED, et al: Microvascular aspects of acquired immune deficiency syndrome retinopathy. Am J Ophthalmol 1986; 98:590-601

17. Pomerantz RJ, Kuritzkes DR, de la Monte SM, et al: Infection of the retina by human immunodeficiency virus. N Engl J Med 1988; 317:1643-1647

18. Pepose JS, Holland GN, Nestor MS, Cochran AJ, Foos RY: Acquired immune deficiency syndrome—Pathogenic mechanisms of ocular disease. Ophthalmology 1985; 92:472-484

19. Engstrom RE, Holland GN, Hardy WD, Meiselman HJ: Hemorheologic abnormalities in patients with human immunodeficiency virus infection and ophthalmic microvasculopathy. Am J Ophthalmol 1990; 109:153-161

20. Kestelyn P, Lepage P, Van de Perre P: Perivasculitis of the retinal vessels as an important sign in children with AIDS-related complex. Am J Ophthalmol 1985; 100:614-615

21. Jampol LM, Isenberg SJ, Goldberg MF: Occlusive retinal arteriolitis with neovascularization. Am J Ophthalmol 1976; 81:583-589

22. ffytche TJ: Retinal vasculitis. Trans Ophthalmol Soc UK 1977; 97:457-461

23. Morgan CM, Webb RM, O'Connor GR: Atypical syphilitic chorioretinitis and vasculitis. Retina 1984; 4:225-231

24. Crouch ER, Goldberg MF: Retinal periarteritis secondary to syphilis. Arch Ophthalmol 1975; 93:384-387

25. Lobes LA, Folk JC: Syphilitic phlebitis simulating branch vein occlusion. Ann Ophthalmol 1981; 13:825-827

26. Fountain JA, Werner RB: Tuberculous retinal vasculitis. Retina 1984; 4:48-50

27. Shah SM, Howard RS, Sarkies NJC, Graham EM: Tuberculosis presenting as retinal vasculitis. J R Soc Med 1988; 81:232-233

28. Kasp E, Graham EM, Stanford MR, Sanders MD, Dumonde DC: A point prevalence study of 150 patients with idiopathic retinal vasculitis: 2. Clinical relevance of antiretinal autoimmunity and circulating immune complexes. Br J Ophthalmol 1989; 73:720-733

29. Stanford MR, Graham E, Kasp E, Sanders MD, Dumonde DC: A longitudinal study of clinical and immunological findings in 52 patients with relapsing retinal vasculitis. Br J Ophthalmol 1988; 72:442-447

Modifying Physician Practice Patterns—Reflections on Past Deeds

THE PRACTICE OF MEDICINE once enjoyed a purity of focus that has only recently begun to change. The traditional physician knew that maximizing the welfare of patients was the order of the day. The health care system, having identified the physician as the patient's agent for that goal, fashioned itself to serve the physician's needs. What worked for the doctor worked for the patient. What worked for the doctor also worked for the hospital, at least for a while.

Now the picture has changed. Patients, physicians, and hospitals, while not having parted ways, have begun to identify their differences. Why has such a change occurred? Most observers agree on the spectrum of reasons, if not the magnitude of their contribution to the change. The explosion of technology with its heightened emphasis on uncertainty; changes in societal attitudes toward risk-taking, conflict resolution, and regulation; growing tensions between the demand for medical care and the supply of that care; and the