Acute visual loss in systemic lupus erythematosus

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Systemic lupus erythematosus (SLE) often presents as a multisystem disease that can be difficult to diagnose. Although ocular symptoms are infrequent, actual acute visual loss has been reported. A review of four cases of acute visual loss from a lupus clinic revealed that two patients had visual loss as a presenting sign of SLE. One had bilateral occipital lobe infarctions, the other multiple cotton wool spots and an attenuated retinal vascular system. Of the two patients with documented SLE prior to the onset of visual problems, one presented with a coincidental retinal tear and the other with retinal phlebitis.

Systemic lupus erythematosus (SLE) is characterized by involvement of many organ systems. Although early studies[1-3] indicated that ocular manifestations were common, patients were treated by methods differing from today's standards. More recent reviews[4,5] indicate that ocular symptoms are infrequent. While many patients develop asymptomatic ocular lesions, actual visual loss is quite rare.[6] The lesions can be either local or systemic and can occur independently of hypertension or diabetes mellitus.

We performed a retrospective examination of our SLE population of 150 patients to determine the incidence and causes of all cases of acute visual loss occurring during the past five years, and to ascertain whether any subgroups could be identified to allow early diagnosis and treatment. The four cases of visual loss occurring in our SLE population will be discussed in detail.

Report of cases

Case 1

A 44-year-old woman with well-documented SLE of three year's duration complained of a shadow over the upper half of the nasal field in her left eye, which had been present for two weeks. The patient was normotensive and took no medications. Ophthalmologic examination revealed a tear in the retina (Fig 1), which was thought to be coincidental disease. A scleral-buckling surgical procedure produced excellent results.

Case 2

A 46-year-old woman with well-documented SLE was taking only small doses of prednisone daily. Although she had complained of progressive visual loss in her right eye for several months, her family physician sent her to an ophthalmologist only when she suddenly began to lose vision in the left eye. The retinal findings were venous sheathing (phlebitis) and white-centered intraretinal hemorrhages (Roth's spots) (Figs 2 and 3). We treated her with large doses of corticosteroids plus immunosuppressive medications for retinal vascular inflammation. The vision returned to 20/20 in the left eye but only to 20/200 in the right eye.

Case 3

The third patient was a 24-year-old, previously healthy woman who had no history of connective tissue disease. She suddenly lost vision in both eyes. Examination revealed bilateral occipital lobe infarctions, and the patient was treated symptomatically, but vision did not return. Subsequent computed tomographic scanning showed the large, bilateral occipital lobe infarctions (Fig 4).

Eight years later, the patient presented with cervical transverse myelitis and quadraplegia. At that time, a diagnosis of SLE was made; careful review of her previous records indicated that she probably had this illness at the time of the cerebral infarctions.

Case 4

A 30-year-old woman in previous good health was admitted with an eight-week history of progressive visual loss. Although a diagnosis of connective tissue disease was not documented, it was an associated constellation of admission physical and laboratory findings, including arthralgias, photosensitive skin rash, leukopenia, and active urine sediment, that clearly indicated that this patient had active SLE.

The patient's local physician had treated her only with eyedrops and had not noted the systemic nature of her illness. When her vision failed to improve, he referred her to an ophthalmologist. Her fundi showed many cotton wool spots and an attenuated retinal vascular system (Fig 5). There were large central scotomas bilaterally. She was treated with corticosteroids and immunosuppressive medications with no benefit (Fig 6).

Results

Our retrospective study revealed four patients who experienced acute visual loss. Two patients who

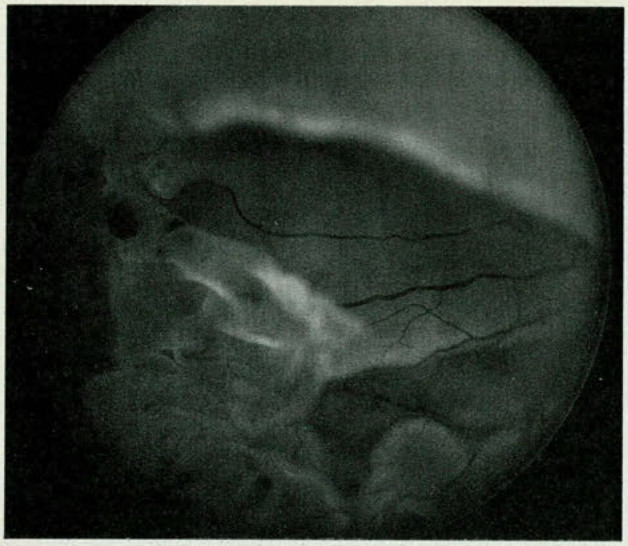

Fig 1. *Funduscopic examination reveals torn and redundant retina (case 1).*

had visual loss as a presenting sign of SLE may have had more severe disease, but the delay in recognizing the systemic nature of their illness, particularly in the patient with retinal arteritis, probably limited the likelihood of a successful therapeutic response. Two patients had established SLE prior to the onset of visual problems. Although one was not referred to an ophthamologist promptly, she still was able to benefit from therapy, primarily because her retinal disease was phlebitis rather than arteritis. The patient who suffered from a detached retina again emphasizes the fact that coincidental and even relatively minor disorders must be considered in the differential diagnosis, because they may require entirely different treatment.

Discussion

Local and systemic ocular complications

The ocular manifestations of SLE can be grouped in many ways. We have chosen to categorize them into four areas: local disease, ocular complications of systemic disease, medication side effects, and coincidental disorders.

Local ocular complications are listed in Table 1. Cotton wool spots are the classic retinal lesions associated with SLE, but they also are present in many other conditions, particularly hypertension. These lesions usually are asymptomatic; therefore, their exact incidence is difficult to determine. Many other local conditions also are quite common. Three local lesions—uveitis,[5] scleritis,[7] and optic neuritis[8]—have been associated with acute visual loss.

The ocular complications of systemic disease also are detailed in Table 1. Of the seven entities in this list, only four (retinal vasculitis, central retinal vein occlusion, intracerebral vasculitis, and pseudotumor cerebri) have been associated with acute visual loss. Three conditions in this category (myopathy and cranial neuropathy[9] and migraine-like syndrome)[10] are quite uncommon.

The retinal vasculitis of SLE can occur independently of systemic hypertension, diabetes mellitus, or infection.[11] It can affect vessels of various sizes in the vascular network, and, although some

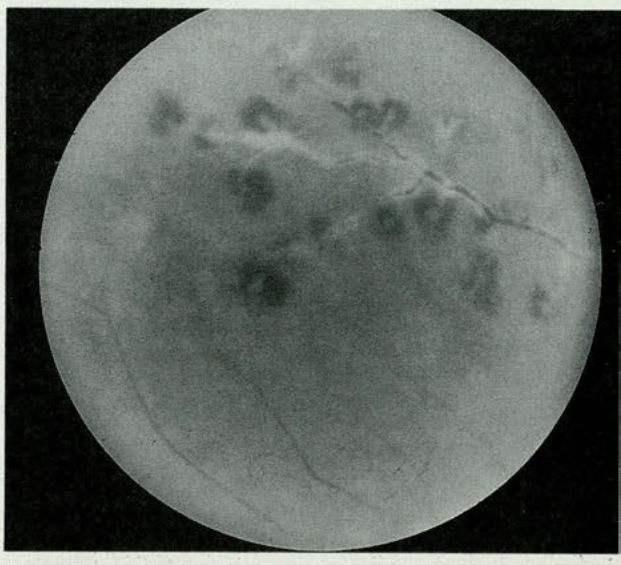

Fig 2. *Venous sheathing is demonstrated by the white areas noted around the vein on funduscopic examination. White-centered intraretinal hemorrhages also are present (case 2).*

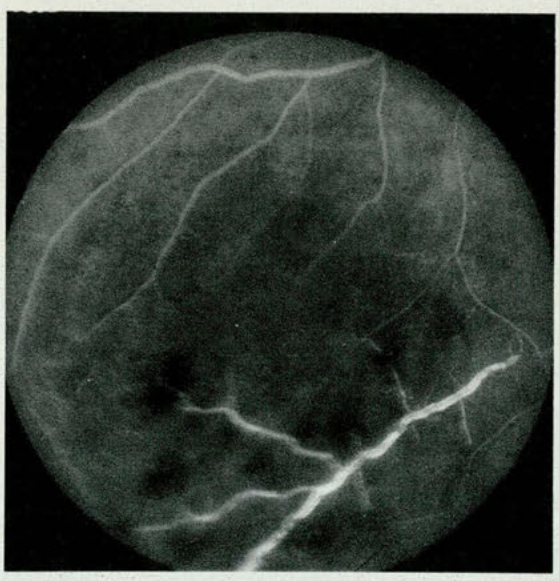

Fig 3. *Fluorescein angiogram of the same vessel pictured in Fig 2 shows the sluggish flow in the veins, as represented by the accumulation of dye in the vessel. By contrast, a normal vein, in which the dye has flushed out normally, is seen at the top of the figure.*

authors[12] think that it can be distinctive, others[13] have observed a somewhat similar type of pattern in many other conditions.

Although the lesions of retinal vasculitis commonly are thought to occur more frequently in those lupus patients who are more acutely ill,[14] in a study by Santos and associates,[15] retinal microangiopathy was found in one-fourth of their ambulatory patients who were not seriously ill. They stated, however, that a majority of these patients previously had had evidence of vasculitis in other areas of their bodies, when they had been acutely ill, and perhaps the retinal damage simply was residual.

Very rarely in SLE can the central retinal vein be affected and cause blindness. Silverman and colleagues[16] reported the case of a young male SLE patient with central retinal vein occlusion whose blindness occurred in the absence of CNS involvement. Three of the four lupus patients discussed by Gold and coworkers[17] demonstrated occlusive retinal arterial disease; all three seemed to have CNS involvement of a varied nature.

Intracerebral vasculitis can cause visual loss, usually from infarction of the occipital lobes of the brain. This results in cortical blindness, which consists of a diagnostic triad of blindness, intact pupillary responses, and normal ocular funduscopic examination.[18] Often these lesions are unilateral and cause homonymous hemianopsia, but they can be bilateral and result in complete blindness.

Pseudotumor cerebri has been reported in SLE patients by several authors.[19,20] Visual hallucinations and blurred vision can occur. Both increased intracranial pressure and papilledema may be present without localizing signs.

SLE also has been associated with multiple types of cerebral visual disturbances.[21] Toxic encephalopathy, severe aseptic meningitis, or even basilar artery vasculitis or intracerebral vasculitis in the occipital region could result in transient visual aberrations or visual loss. It has been suggested that

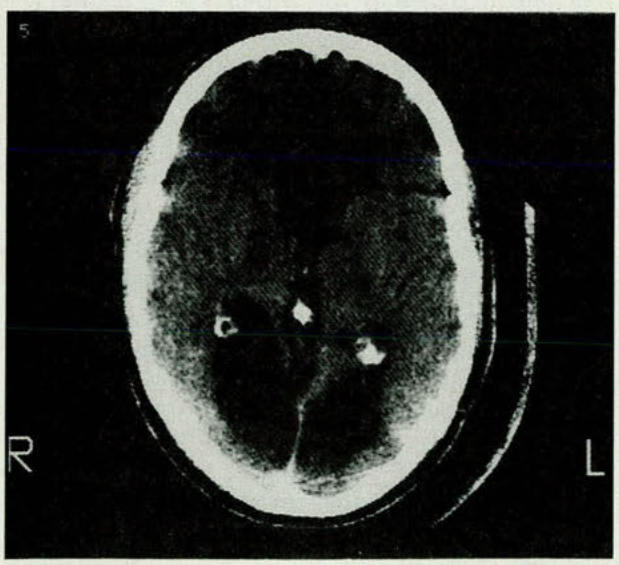

Fig 4. *Computed tomographic scan reveals large, bilateral occipital lobe infarctions, which are represented by the large areas of decreased density in the lower portions of both cerebral hemispheres (case 3).*

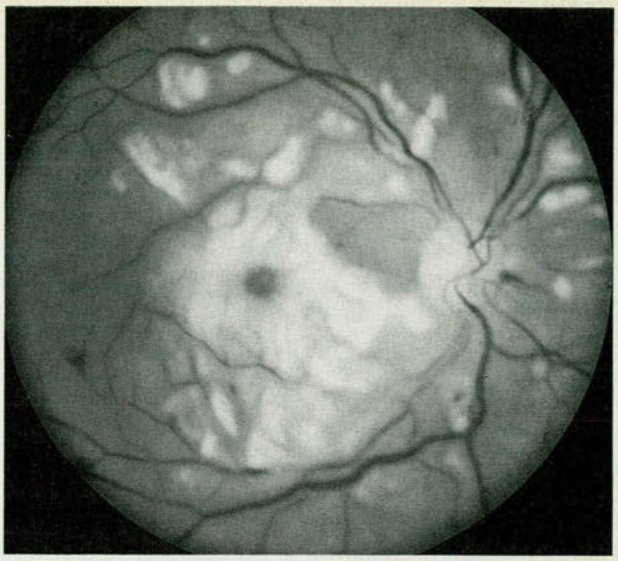

Fig 5. *Funduscopic examination reveals the large number of cotton wool spots, which are infarctions of precapillary arterioles, form the equivalent of a central retinal artery occlusion (case 4). This area of the fundus contains the macula and provides the anatomic reason for the visual field loss. Also, note the generally attenuated vascular system, particularly the arteries.*

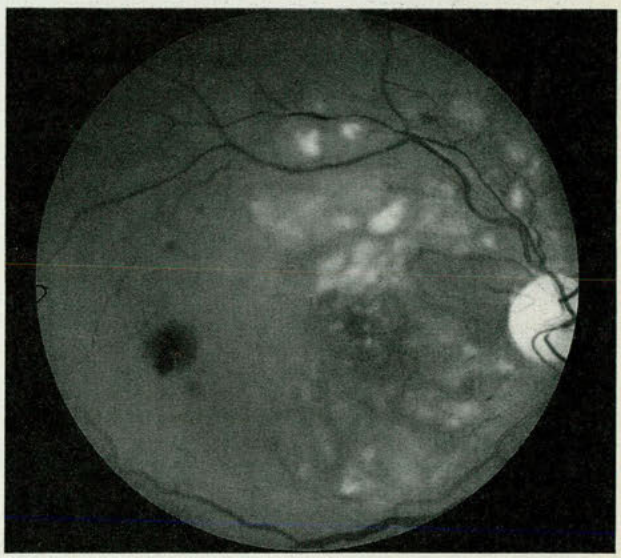

Fig 6. *The same eye seen in Fig 5, some weeks later, following therapy continues to show some cotton wool spots. There also is severe residual retinal scarring.*

TABLE 1. LOCAL AND SYSTEMIC OCULAR COMPLICATIONS OF SLE.

Local complications
Cutaneous involvement of adjacent skin
Cotton wool spots
Keratoconjunctivitis sicca
Conjunctivitis
Subconjunctival hemorrhage
Periorbital edema
Uveitis
Scleritis (episcleritis)
Optic neuritis
Systemic complications
Myopathy
Cranial neuropathy
Migraine-like syndrome
Retinal vasculitis
Intracerebral vasculitis
Pseudotumor cerebri
Central retinal vein occlusion

TABLE 2. MEDICATIONS USED FOR SLE THAT HAVE BEEN ASSOCIATED WITH VISUAL LOSS.

Common causes
Corticosteroids[24-27]
Antimalarial agents[30,31]
Rare causes
Aspirin[24]
Ibuprofen[34]
Indomethacin[35]

either computed tomography[22] or magnetic resonance imaging[23] may localize intracranial lesions in lupus patients who have clinical evidence of CNS disease.

Causes of SLE-related visual loss

Several medications used in the therapy of SLE have been reported to cause visual loss (Table 2). This ocular toxicity may occur rapidly or gradually. The commonly used drugs that may cause visual disturbances include corticosteroids and the antimalarial agents.

Both topical and systemic corticosteroids have been associated with visual loss.[24] Topically applied corticosteroids can cause a decrease in the outflow facility of aqueous humor and lead to a corresponding increase in intraocular pressure.[25] Although systemic corticosteroids may increase intraocular pressure, apparently few cases of actual glaucoma have been reported.[24] Visual loss, when it occurs, can be relatively rapid.

Posterior subcapsular cataract formation seems to be related to both the amount and duration of corticosteroid used.[26] Cataracts appear to cause a gradual decrease in vision,[27] and, therefore, they would not be expected to be in the differential diagnosis of acute visual loss in SLE.

Although attempts are constantly made to lower the dosage of corticosteroids, this must be done gradually, because pseudotumor cerebri has been documented following the rapid tapering of corticosteroids in both adults[28] and children.[29]

The antimalarial drugs chloroquine and hydroxychloroquine have well-known and potentially serious side effects.[30,31] Shortly after beginning antimalarial therapy, SLE patients may complain of poor vision and of seeing halos around lights. Both of these symptoms can be reversed if the medication is stopped, but usually this is unnecessary. The symptoms are relatively mild and do not indicate retinal toxicity.

The dreaded complication of antimalarial treatment is irreversible retinal toxicity leading to blindness.[31] Reviews[32,33,34] have indicated that although ocular toxicity occurs uncommonly at the drug levels that are prescribed currently, routine ophthalmologic screening still is recommended. This should include funduscopy on dilated eyes, central visual field testing using a red object, visual acuity testing, and peripheral visual field examination.

Several of the nonsteroidal, anti-inflammatory medications that may be used to treat lupus patients have been reported to have adverse ocular effects.[35,36] These cases are somewhat rare; however, other newer nonsteroidal, anti-inflammatory drugs may yet be associated with ocular toxicity, and, therefore, caution is advised.

Finally, there are many other disorders that may lead to reduced vision but that have little or nothing to do with either SLE or its treatment. This was demonstrated by the patients with retinal detachment in our study. Therefore, it is always imperative to obtain complete medical and ophthalmologic evaluation in SLE patients who complain of visual symptoms.

Conclusions

We recommend rapid ophthalmologic evaluation of all patients with SLE who complain of visual changes, so that appropriate therapy can be instituted immediately. As we found, it is difficult to predict the etiology of visual loss in any given patient, but, if the problem is diagnosed promptly, therapy may be beneficial.

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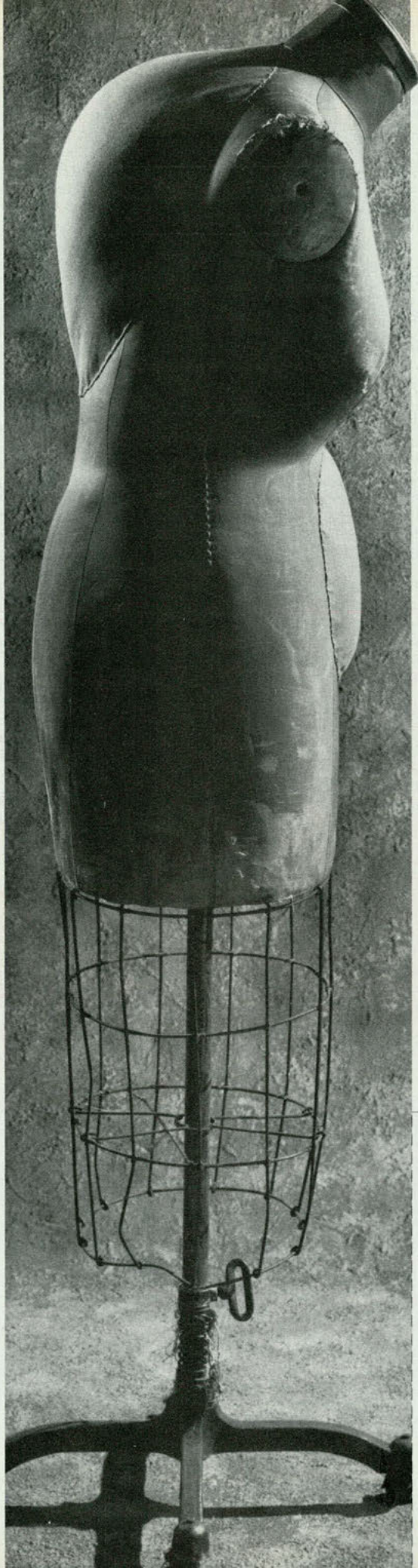

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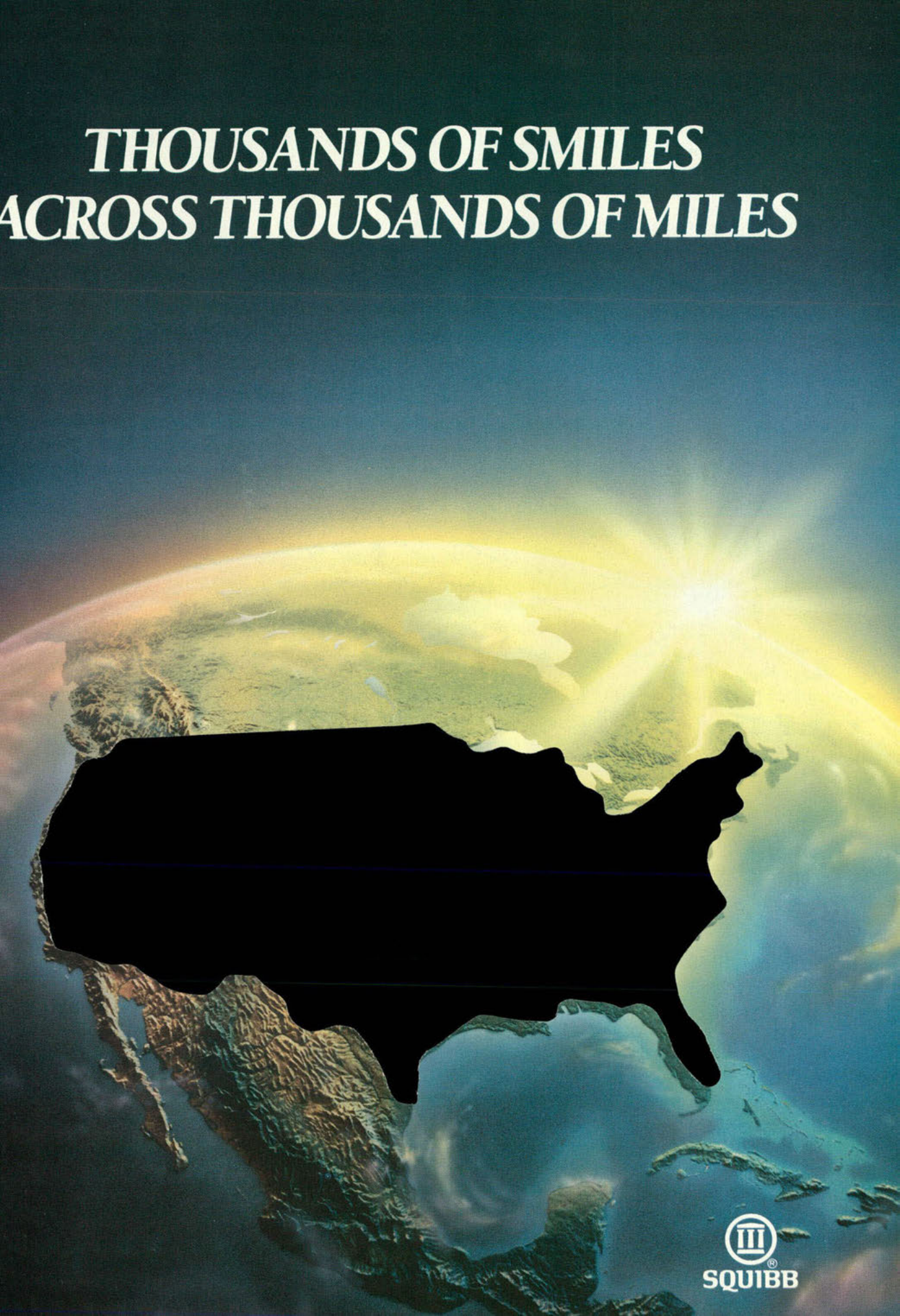

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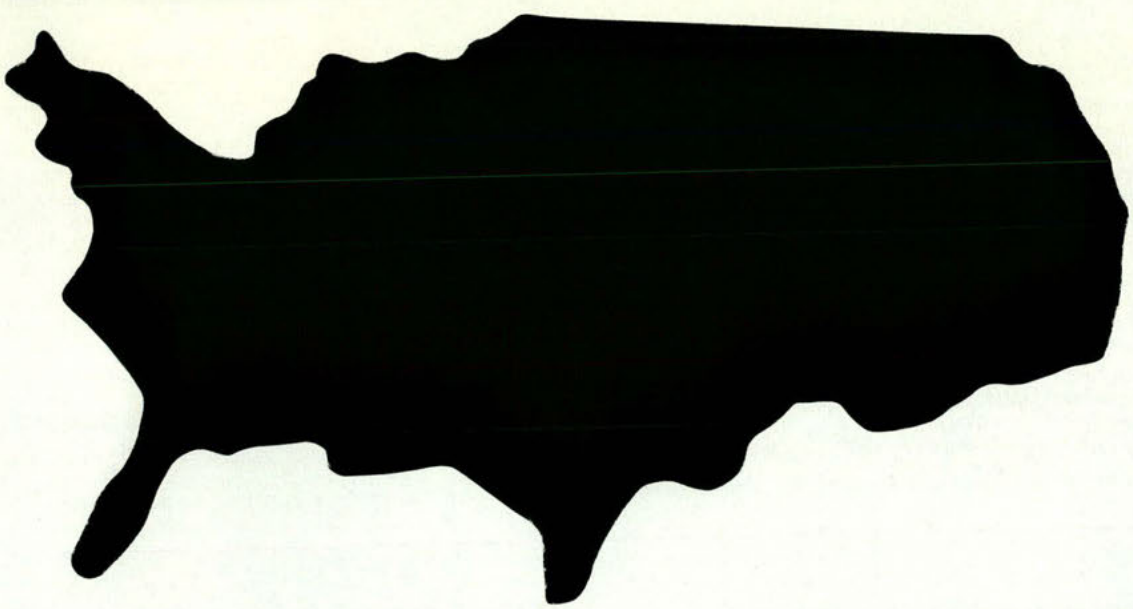

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New study data[1]

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INDICATIONS: Hypertension—CAPOTEN (captopril) is indicated for the treatment of hypertension. Consideration should be given to the risk of neutropenia/ agranulocytosis (see WARNINGS). CAPOTEN may be used as initial therapy for patients with normal renal function, in whom the risk is relatively low. In patients with impaired renal function, particularly those with collagen vascular disease, captopril should be reserved for those who have either developed unacceptable side effects on other drugs, or have failed to respond satisfactorily to drug combinations. CAPOTEN is effective alone and in combination with other antihypertensive agents, especially thiazide-type diuretics.

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CONTRAINDICATIONS: CAPOTEN is contraindicated in patients who are hypersensitive to this product.

WARNINGS: Neutropenia/Agranulocytosis—Neutropenia (<1000/ mm^3) with myeloid hypoplasia has resulted from use of captopril. About half of the neutropenic patients developed systemic or oral cavity infections or other features of the syndrome of agranulocytosis. The risk of neutropenia is dependent on the clinical status of the patient:

> In clinical trials in patients with hypertension who have normal renal function (serum creatinine less than 1.6 mg/dL and no collagen vascular disease), neutropenia has been seen in one patient out of over 8,600 exposed. In patients with some degree of renal failure (serum creatinine at least 1.6 mg/dL) but no collagen vascular disease, the risk in clinical trials was about 1 per 500. Doses were relatively high in these patients, particularly in view of their diminished renal function. In patients with collagen vascular diseases (e.g., systemic lupus erythematosus, scleroderma) and impaired renal function, neutropenia occurred in 3.7% of patients in clinical trials. While none of the over 750 patients in formal clinical trials of heart failure developed neutropenia, it has occurred during the subsequent clinical experience. Of reported cases, about half had serum creatinine ≥1.6 mg/dL and more than 75% received procainamide. In heart failure, it appears that the same risk factors for neutropenia are present.

Neutropenia has appeared usually within 3 months after starting therapy, associated with myeloid hypoplasia and frequently accompanied by erythroid hypoplasia and decreased numbers of megakaryocytes (e.g., hypoplastic bone marrow and pancytopenia); anemia and thrombocytopenia were sometimes seen. Neutrophils generally returned to normal in about 2 weeks after captopril was discontinued, and serious infections were limited to clinically complex patients. About 13% of the cases of neutropenia have ended fatally, but almost all fatalities were in patients with serious illness, having collagen vascular disease, renal failure, heart failure or immunosuppressant therapy, or a combination of these complicating factors. **Evaluation of the hypertensive or heart failure patient should always include assessment of renal function.** If captopril is used in patients with impaired renal function, white blood cell and differential counts should be evaluated prior to starting treatment and at approximately 2-week intervals for about 3 months, then periodically. In patients with collagen vascular disease or who are exposed to other drugs known to affect the white cells or immune response, particularly when there is impaired renal function, captopril should be used only after an assessment of benefit and risk, and then with caution. All patients treated with captopril should be told to report any signs of infection (e.g., sore throat, fever). If infection is suspected, perform white cell counts without delay. Since discontinuation of captopril and other drugs has generally led to prompt return of the white count to normal, upon confirmation of neutropenia (neutrophil count <1000/mm^3) withdraw captopril and closely follow the patient's course.

Proteinuria: Total urinary proteins >1 g per day were seen in about 0.7% of patients on captopril. About 90% of affected patients had evidence of prior renal disease or received high doses (>150 mg/ day), or both. The nephrotic syndrome occurred in about one-fifth of proteinuric patients. In most cases, proteinuria subsided or cleared within 6 months whether or not captopril was continued. The BUN and creatinine were seldom altered in proteinuric patients. Since most cases of proteinuria occurred by the 8th month of therapy with captopril, patients with prior renal disease or those receiving captopril at doses >150 mg per day, should have urinary protein estimates (dip-stick on 1st morning urine) before therapy, and periodically thereafter.

Hypotension: Excessive hypotension was rarely seen in hypertensive patients but is a possibility in severely salt/volume-depleted persons such as those treated vigorously with diuretics (see PRECAUTIONS [Drug Interactions]). In heart failure, where the blood pressure was either normal or low, transient decreases in mean blood pressure >20% were recorded in about half of the patients. This transient hypotension may occur after any of the first several doses and is usually well tolerated, although rarely it has been associated with arrhythmia or conduction defects. A starting dose of 6.25 or 12.5 mg tid may minimize the hypotensive effect. Patients should be followed closely for the first 2 weeks of treatment and whenever the dose of captopril and/or diuretic is increased.

BECAUSE OF THE POTENTIAL FALL IN BLOOD PRESSURE IN THESE PATIENTS, THERAPY SHOULD BE STARTED UNDER VERY CLOSE MEDICAL SUPERVISION.

PRECAUTIONS: General: *Impaired Renal Function*— Hypertension— Some hypertensive patients with renal disease, particularly those with severe renal artery stenosis, have developed increases in BUN and serum creatinine. It may be necessary to reduce captopril dosage and/or discontinue diuretic. For some of these patients, normalization of blood pressure and maintenance of adequate renal perfusion may not be possible. Heart Failure—About 20% of patients develop stable elevations of BUN and serum creatinine >20% above normal or baseline upon long-term treatment. Less than 5% of patients, generally with severe preexisting renal disease, required discontinuation due to progressively increasing creatinine. See DOSAGE AND ADMINISTRATION, ADVERSE REACTIONS [Altered Laboratory Findings]. *Valvular Stenosis*— A theoretical concern, for risk of decreased coronary perfusion, has been noted regarding vasodilator treatment in patients with aortic stenosis due to decreased afterload reduction. *Surgery/Anesthesia*—If hypotension occurs during surgery or anesthe and is considered due to the effects of captopril, it is correctable by volume expansi

Drug Interactions: *Hypotension—Patients on Diuretic Therapy*—Precipitous reduc of blood pressure may occasionally occur within the 1st hour after administratio the initial captopril dose in patients on diuretics, especially those recently placed diuretics, and those on severe dietary salt restriction or dialysis. This possibility be minimized by either discontinuing the diuretic or increasing the salt intake abo week prior to initiation of captopril therapy or by initiating therapy with small do (6.25 or 12.5 mg). Alternatively, provide medical supervision for at least 1 hour a the initial dose.

Agents Having Vasodilator Activity—In heart failure patients, vasodilators shoul administered with caution.

Agents Causing Renin Release—Captopril's effect will be augmented by antihyp tensive agents that cause renin release.

Agents Affecting Sympathetic Activity—The sympathetic nervous system may especially important in supporting blood pressure in patients receiving captopril al or with diuretics. Beta-adrenergic blocking drugs add some further antihyperten effect to captopril, but the overall response is less than additive. Therefore, use age affecting sympathetic activity (e.g., ganglionic blocking agents or adrenergic neu blocking agents) with caution.

Agents Increasing Serum Potassium—Give potassium-sparing diuretics or po sium supplements only for documented hypokalemia, and then with caution, si they may lead to a significant increase of serum potassium. Use potassium-c taining salt substitutes with caution.

Inhibitors of Endogenous Prostaglandin Synthesis— Indomethacin and other non roidal anti-inflammatory agents may reduce the antihypertensive effect of capto especially in low renin hypertension.

Drug/Laboratory Test Interaction: Captopril may cause a false-positive urine tes acetone.

Carcinogenesis, Mutagenesis and Impairment of Fertility: Two-year studies doses of 50 to 1350 mg/ kg/day in mice and rats failed to show any evidenc carcinogenic potential. Studies in rats have revealed no impairment of fertility.

Pregnancy: Category C: There are no adequate and well-controlled studies in pr nant women. Embryocidal effects and craniofacial malformations were observe rabbits. Therefore, captopril should be used during pregnancy, or for patients likel become pregnant, only if the potential benefit outweighs the potential risk to the fe Captopril crosses the human placenta.

Nursing Mothers: Captopril is secreted in human milk. Exercise caution when ministering captopril to a nursing woman, and, in general, nursing should be interrup

Pediatric Use: Safety and effectiveness in children have not been establishe though there is limited experience with use of captopril in children from 2 month 15 years of age. Dosage, on a weight basis, was comparable to that used in ad CAPOTEN (captopril) should be used in children only if other measures for control blood pressure have not been effective.

ADVERSE REACTIONS: Reported incidences are based on clinical trials invol approximately 7000 patients.

Renal—About 1 of 100 patients developed proteinuria (see WARNINGS). Rena sufficiency, renal failure, polyuria, oliguria, and urinary frequency in 1 to 2 of 1 patients.

Hematologic—Neutropenia/agranulocytosis has occurred (see WARNINGS). A mia, thrombocytopenia, and pancytopenia have been reported.

Dermatologic—Rash, (usually maculopapular, rarely urticarial), often with pruri and sometimes with fever and eosinophilia, in about 4 to 7 of 100 patients (depend on renal status and dose), usually during the 1st 4 weeks of therapy. Pruritus, with rash, in about 2 of 100 patients. A reversible associated pemphigoid-like lesion, photosensitivity, have also been reported. Angioedema of the face, mucous m branes of the mouth, or of the extremities in about 1 of 1000 patients—reversible discontinuance of captopril therapy. One case of laryngeal edema has been repor Flushing or pallor in 2 to 5 of 1000 patients.

Cardiovascular—Hypotension may occur; see WARNINGS and PRECAUTIONS [D Interactions] for discussion of hypotension on initiation of captopril therapy. Tac cardia, chest pain, and palpitations each in about 1 of 100 patients. Angina pecte myocardial infarction, Raynaud's syndrome, and congestive heart failure each in 3 of 1000 patients.

Dysgeusia—Approximately 2 to 4 (depending on renal status and dose) of 100 tients developed a diminution or loss of taste perception; taste impairment is rev ible and usually self-limited even with continued drug use (2 to 3 months). Gas irritation, abdominal pain, nausea, vomiting, diarrhea, anorexia, constipation, aphth ulcers, peptic ulcer, dizziness, headache, malaise, fatigue, insomnia, dry mouth, pnea, cough, alopecia, paresthesias reported in about 0.5 to 2% of patients but not appear at increased frequency compared to placebo or other treatments use controlled trials.

Altered Laboratory Findings: Elevations of liver enzymes in a few patients altho no causal relationship has been established. Rarely cholestatic jaundice, and hep cellular injury with or without secondary cholestasis, have been reported. A trans elevation of BUN and serum creatinine may occur, especially in volume-deplete renovascular hypertension patients. In instances of rapid reduction of longstan or severely elevated blood pressure, the glomerular filtration rate may decrease t siently, also resulting in transient rises in serum creatinine and BUN. Small increa in serum potassium concentration frequently occur, especially in patients with r impairment (see PRECAUTIONS).

OVERDOSAGE: Primary concern is correction of hypotension. Volume expan with an I.V. infusion of normal saline is the treatment of choice for restoration of bl pressure. Captopril may be removed from the general circulation by hemodialysi

DOSAGE AND ADMINISTRATION: CAPOTEN (captopril) should be taken one before meals. In hypertension, CAPOTEN may be dosed bid or tid. Dosage mus individualized; see DOSAGE AND ADMINISTRATION section of package inser detailed information regarding dosage in hypertension and in heart failure. Beca CAPOTEN (captopril) is excreted primarily by the kidneys, dosage adjustments recommended for patients with impaired renal function.

Consult package insert before prescribing CAPOTEN (captopril).

HOW SUPPLIED: Available in tablets of 12.5, 25, and 50 mg in bottles of 100 and 1 100 mg in bottles of 100; and in UNIMATIC® unit-dose packs of 100 tablets. (J3-6

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