Clinical investigations

Graefe's Archive for Clinical and Experimental Ophthalmology

Graefe's Arch Clin Exp Ophthalmol (1989) 227:201–205

Central serous chorioretinopathy: an analysis of the clinical morphology using image-processing techniques*

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Abstract. We used a digital image processor to make multiple measurements from the fluorescein angiograms of 53 cases of central serous chorioretinopathy (CSC) associated with single leaks. We determined the area of the base of each serous detachment, the location of its geometric center (CM), the area of the RPE leak, the distance from the fovea to the leak, and the distance from the leak to the CM. The distribution of leaks across the base of the detachments was nonrandom ($P<0.005$) with leaks clustering near the centers of the detachments. When the leak was found within 1 disc diameter from the fovea, the center of the detachment was located virtually at the foveola, suggesting that the central macula is predisposed to the development of CSC. Detachments associated with "smokestack" leaks were significantly larger than those associated with round pinpoint leaks ($P<0.02$).

Introduction

Central serous chorioretinopathy (CSC) is characterized by a serous detachment of the sensory retina in an otherwise healthy patient. The primary lesion has been described as a localized abnormality of the retinal pigment epithelium (RPE) where the affected cells lose their barrier function and pumping ability, allowing serous fluid to leak from the choroid into the subretinal space [2, 3]. The leaks may take several angiographic forms including a profuse plume or "smokestack" of dye, round pinpoint leaks from a focal RPE defect, or diffuse staining of a grossly elevated RPE detachment beneath the serous retinal detachment [11]. Although the disease is usually self-limited, photocoagulation of the leak seen on fluorescein angiography hastens the resolution of the overlying serous retinal detachment [8]. There is disagreement, however, as to whether the disease is caused simply by a focal passive leak from the choroid into the subretinal space or is a manifestation of more widespread dysfunction of the pigment epithelium [5, 6].

We speculated that if the leak itself plays the key role in producing the serous detachment, then the morphologic features of the disease should reflect the location of the leak. For instance, if a detachment originally develops at the leak and then enlarges, the leaks in a series of CSC cases might cluster near the centers of the detachments. Other questions we sought to answer were whether profuse leaks are associated with larger detachments and whether the area of the RPE defect correlated with the area of the detachment.

To study the gross morphology, we digitized the fluorescein images in unequivocal cases of CSC and made computer-assisted measurements to determine the geometric features of each case.

Materials and methods

The fluorescein angiograms of all patients with the diagnosis of CSC in our active photographic files were collected. Prior to review, we elected to only consider eyes fulfilling the following criteria: (1) a serous neuroepithelial detachment whose complete extent could be seen on viewing of stereo pairs; (2) presence of a single, discrete RPE leak located under or in the general vicinity of the serous retinal detachment; (3) no evidence of other retinal disease such as subretinal neovascularization, hemorrhage, retinal vascular abnormalities, or macular degeneration; (4) no evidence or clinical history of previous episodes of CSC; and (5) no history of prior treatment with photocoagulation.

From the review, we obtained 53 studies meeting the selection critera from 53 patients. The age of the patients ranged from 25 to 62 years and averaged 41 ± 9 years (mean $\pm$ standard deviation). Forty patients were male and 13 were female; all were Caucasian. Fifty of the 53 patients had detachments involving the foveola. The angiograms of 12 cases showed classical "smokestack" leaks while 41 studies showed pinpoint leaks.

The best image pair depicting the serous retinal detachment was viewed stereoscopically and the perimeter of the elevation was denoted by tracing it with a fine lead pencil (0.3 mm lead) on the emulsion side of the angiogram film negative. We chose the fluorescein image obtained 10 ± 1 s after the appearance of laminar flow for the determination of the location and area of the leak in each study. The selected images were entered into the optical laser disc image memory of a PAR Systems IS2000 image processor [1]. This was accomplished by placing the fluorescein negatives in a video film strip reader (Tamaron Fotovix) to transform the film image into a video signal. The resultant analog video image was digitized to allow measurements

* Supported by the Lions Clubs of Pennsylvania and an unrestricted grant from Research to Prevent Blindness, Inc. Presented in part at the XVI Meeting of The Club Jules Gonin, Brugge, Belgium, 1988

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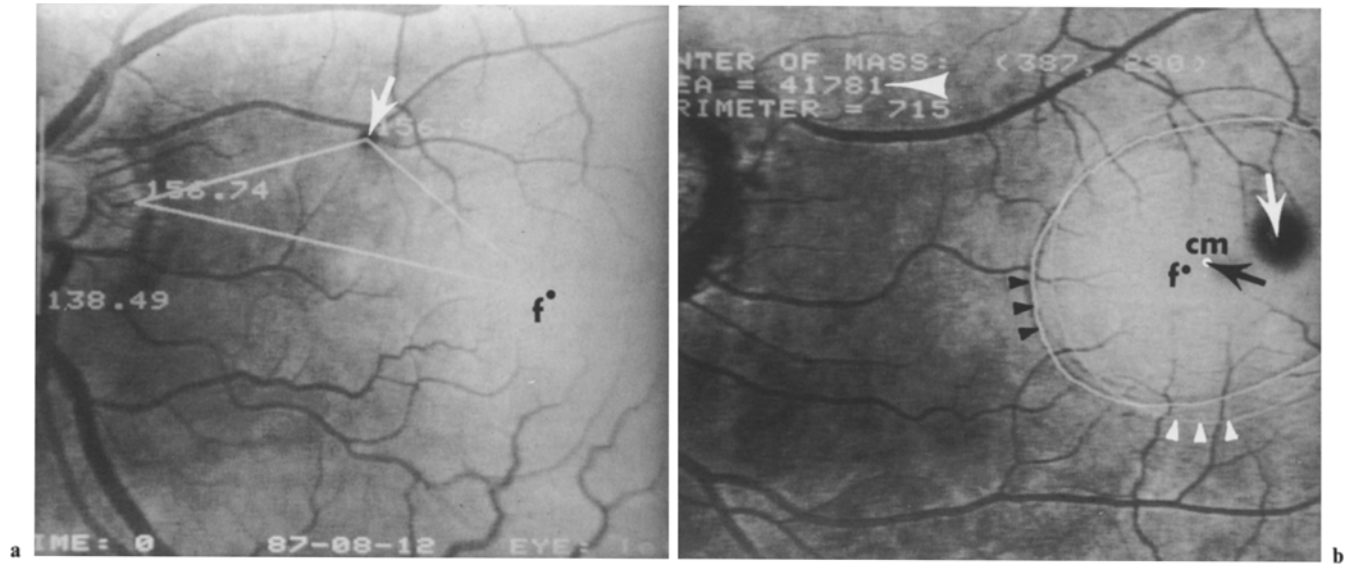

a b

Fig. 1. a Representative measurements made directly from the video image of a selected fluorescein frame. *Arrow* points to fluorescein leak; *f* denotes fovea. Disc to leak, leak to fovea, and vertical disc diameter measurements are given in pixel units. **b** Another case of CSC. Serous detachment perimeter has been outlined (*black arrowheads*) using a mouse-controlled cursor. The image-processor computer has determined the area enclosed (41,781 pixels^2, shown at *large white arrowhead*). The center of mass (CM) has been calculated and is displayed (*black arrow*). *White arrowheads* depict a circle whose center is at CM with the same area as the serous detachment. *White arrow* points to leak

to be obtained using the image processor. Areas were measured by outlining the region of regard on the image processor monitor screen by moving a mouse-controlled cursor; the number of pixel elements enclosed within the outline were summed by computer to give the enclosed area.

We measured the area of each RPE leak and sensory retinal detachment. The position of the geometric center or center of mass (CM) was determined by a computer algorithim for each outlined neurosensory detachment. Line segments were drawn by computer after manually selecting their endpoints with a cursor. The lengths of the following segments were measured in pixels:

a Vertical disc diameter
b Temporal edge of optic nerve to foveola
c Foveola to center of the fluorescein leak (F-L)
d Temporal edge of optic nerve to the center of leak
e Center of mass to the foveola (CM-F)
f Center of mass to the leak (CM-L)

Examples of measured parameters are shown in Fig. 1.

Measurements were made on two separate trials by the same investigator and averaged.

We performed linear regression analyses to determine whether relationships existed between: (1) the area of the RPE leak and the area of the serous detachment; (2) between the fovea to leak and the fovea to center of mass distances; and, (3) between the fovea to leak and leak to center of mass distances. A goodness-of-fit chi-square test of the distribution of leaks with respect to their location in the macula was determined by dividing the macula into superior nasal, inferonasal, superior temporal, and inferior temporal quadrants with the intersecting axes at the foveola. A *t*-test was used to compare the detachment areas associated with "smokestack" leaks to the detachment areas associated with round, focal leaks.

We standardized the distance from the geometric center of each detachment to its associated leak (CM-L) by dividing the CM-L distance by the radius of the circle having the same total area as the serous retinal detachment. A standard detachment of radius R was divided into ten annuli of equal area and the distribution of all the leaks within these zones was analyzed by a goodness-of-fit chi-square test.

Table 1. Morphology of central serous chorioretinopathy (CSC)

Parameter	Average measurement (Mean ± SD)[a]
Distances	
Center of detachment of radius R to leak	0.52 ± 0.01 R
Leak to foveola	0.83 ± 0.59 DD
Foveola to center of detachment	0.46 ± 0.51 DD
Areas	
Leak	$7.86 \pm 4.67 \times 10^{-3}$ DD^2
Base of detachment	4.43 ± 2.7 DD^2
"Smokestack" leaks	6.32 ± 3.08 DD^2 ($n=12$)
Round, focal leaks	3.81 ± 2.31 DD^2 ($n=41$)

[a] $n=53$ unless otherwise indicated DD, Vertical disc diameter

Results

The results of the measurements are shown in Table 1. The locations of the leaks in the 53 cases are shown in Fig. 2. The distribution of leaks by quadrants was significantly nonrandom ($P<0.01$) with more leaks occurring in the superior nasal quadrant and the fewest in the inferior temporal quadrant. The locations of the centers of the detachments are shown in Fig. 3. For all eyes, 85% of the centers of mass were located within 1 disc diameter (DD) from

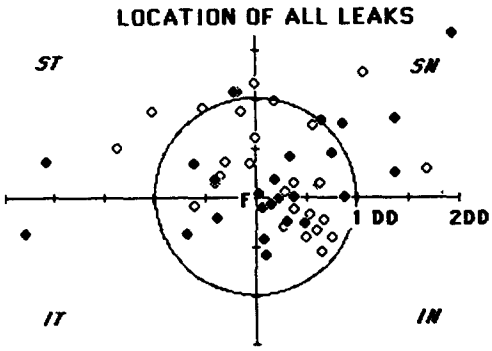

Fig. 2. Composite plot showing location of leaks by quadrants with respect to fovea (standardized to right eye). *Open diamonds* represent right eyes, *closed diamonds* left eyes. Plotted to scale; circle 1 DD in radius is drawn for reference

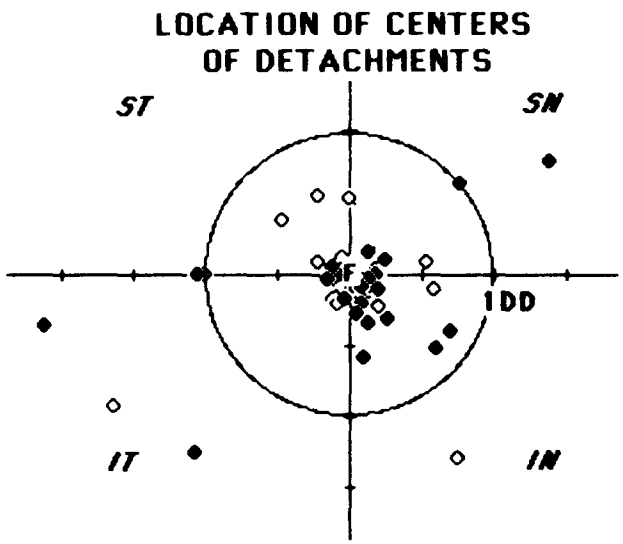

Fig. 3. Composite plot showing locations of the calculated center of each serous detachment with respect to fovea (standardized to right eye). *Open diamonds* represent right eyes, *closed diamonds* left eye. Plotted to scale

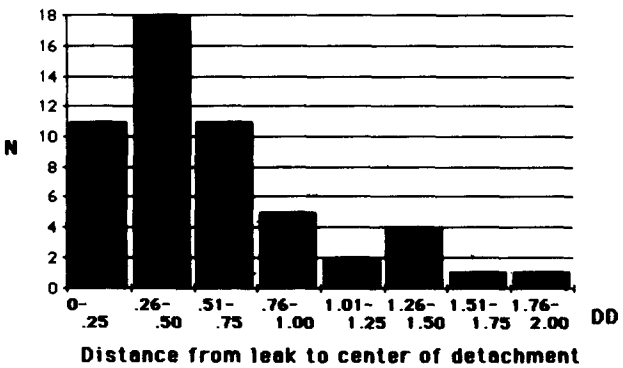

Fig. 4. Distribution of the leak to center of detachment distances

the foveola. The distribution of the leak to center of detachment distances is shown in Fig. 4. In 39 of 53 cases, the geometric center of the detachment was located below the level of the leak. The standardized distances from the leaks to the centers of the detachments are plotted in Fig. 5. (In three cases, the RPE defects were located outside the base of the sensory detachment and were excluded.) The distribution of leaks across the base of the detachments was non-

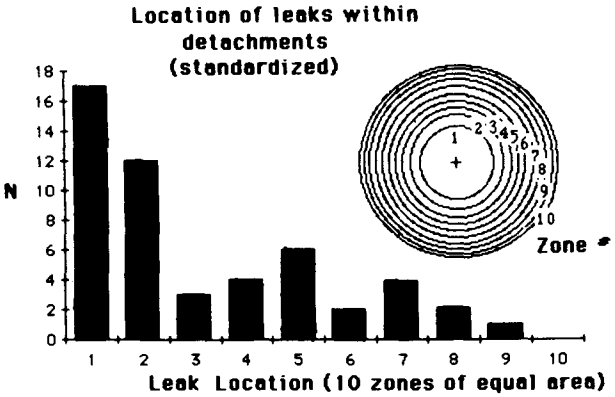

Fig. 5. A standardized detachment of radius R has been divided into ten regions of equal area. Each center of detachment to leak distance was divided by the radius R of its associated detachment to standardize the data between cases. The number of cases with leaks in each of the respective zones is plotted. This distribution is not random ($P<0.005$) with a clear trend toward the leaks being found near the center of the detachments

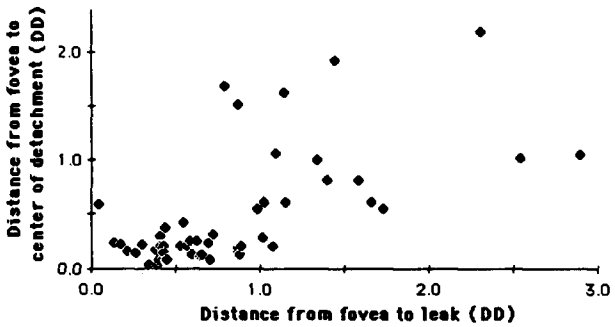

Fig. 6. Distance from the fovea to the center of the detachment versus the distance from fovea to the leak (DD)

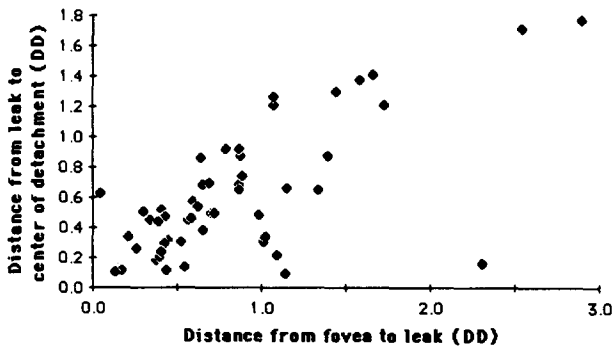

Fig. 7. Distance from the center of the detachment to the leak versus the distance from the fovea to the leak (DD)

random ($P<0.005$) with a clustering of leaks near the centers of the detachments. There was a poor correlation between the area of the leak and the area ($r=0.18$) of the detachment.

Cases associated with "smokestack" leaks had significantly larger detachments than those with round, focal leaks ($P<0.02$, see Table 1).

The distance from the fovea to the center of the detachment versus the distance from the fovea to the leak for each case is plotted in Fig. 6. The distance from the center of the detachment to the leak versus the distance from the fovea to the leak for each study is shown in Fig. 7. As the fovea to leak distance increased, the leaks tended to

be located further away from the centers of the detachments ($r=0.70$).

Discussion

The pathogenesis of CSC has been debated. Gass [2] and Yannuzzi [11] have suggested that a focal loss of RPE barrier function results in accumulation of fluid beneath the sensory retina. Spitznas [10] has hypothesized that the pigment epithelial pump is "reversed" at the leak, forcing fluid beneath the sensory retina. Others have argued that CSC is not caused simply by a passive leak through the RPE barrier, and that a diffuse area of RPE dysfunction is a necessary condition to maintain the serous detachment [6].

Using image-processing techniques, we determined that the center of the typical detachment in CSC was located at a distance 0.52 R from the leak, where R is the detachment radius. The average location for randomly distributed leaks should tend toward a distance of $0.7R$ from the center, as this radius separates the total detachment area into two concentric zones of equal area. The nonrandom distribution of leaks near the center of the serous detachments in our study supports the generally held concept that the leak plays a principal role in the development of CSC. However, it does not answer the question of whether diffuse RPE dysfunction is also necessary for the development and maintenance of such a detachment.

In 38 of our 53 cases, the leaks were located within 1 DD of the foveola, implying that the central posterior pole is predisposed to the development of CSC. One explanation offered for this apparent susceptibility is the high rate of blood flow through the posterior ciliary arteries, placing the area under increasing hydrodynamic stress [3]. Our study revealed an additional reason why central vision is often affected by CSC. We discovered that when a leak was found even as far away as 1 DD from the foveola, the center of its associated detachment was located virtually at the foveola (Fig. 6). The reason for this apparent propensity for the foveola to detach is unclear. The binding of the retina to the RPE may be weaker in the central macula, possibly because of reduced adhesivity between the outer segments and the photoreceptors or perhaps because of a less effective RPE pump in this region.

Leaks located several disc diameters from the central fovea were associated with more elliptical-shaped detachments than leaks located nearer the fovea. The centers of these elliptical detachments were also found further away from the leaks (Fig. 7). The more peripheral detachments were not necessarily larger, however, as there was a poor correlation between the fovea to leak distances and the areas of the detachments ($r=0.36$). However, our selection of detachments which could be photographed on one photographic field eliminated the consideration of very large detachments, a bias which may well have influenced our results.

The physical factors involved in the development and maintenance of a serous retinal detachment in CSC are multiple. Tending to detach the sensory retina from the RPE is the fluid flow beneath the retina induced by the hydrostatic pressure gradient between the choriocapillaries and the subretinal space. Tending to prevent accumulation of fluid beneath the retina are the osmotic gradient between the subretinal fluid and the choriocapillaries, the ionic pump of the pigment epithelium, the elastic rigidity and

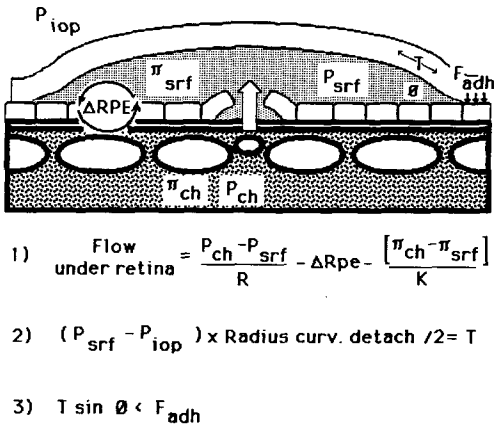

Fig. 8. The physical parameters potentially influencing the development of a sensory retinal detachment in CSC. P_{SRF}, Π_{SRF}, P_{ch}, and Π_{ch} are the static and oncotic pressures in the subretinal fluid and choroid, respectively. ΔRPE represents the total fluid pumped by the RPE, R is the resistance to fluid flow across the leak, and K is the resistance to oncotic fluid flow. The tension T in the retina is related by the Laplace equation to the pressure gradient between the subretinal fluid and the intraocular pressure P_{iop}, and the radius of curvatuve of the detachment. The adhesive force F_{adh} between the sensory retina and the RPE must be greater than the component of tension acting to separate them. The relationship between the parameters is given in the three equations. Equation 1 represents the net flow under the retina

tensile forces within the retina, and the adhesive forces between the retinal outer segments and the pigment epithelium [7]. Formulas relating these factors to each other can be developed using physical principles (Fig. 8). A detachment would be expected to enlarge until sufficient RPE is exposed to allow removal of fluid at a rate equal to the inflow rate through the leak.

We postulate that the hydrostatic pressure within the extravascular choroid is focally increased in CSC in association with choriocapillaries damage and increased vascular permeability. Such damage has been produced experimentally in primates using an intravenous injection of epinephrine [12, 13]. Choroidal hyperpermeability at the leak has also been described in humans with CSC using indocyanine green angiography [4]. The RPE overlying such a focal choroidal abnormality may lose its barrier function, allowing fluid to be forced beneath the sensory retina through a passive leak. We believe that an RPE defect is therefore necessary but insufficient by itself to cause CSC. This seems likely as the RPE can be damaged by trauma or photocoagulation, or even torn (in association with RPE detachments) without the development of a detachment of the overlying retina.

We are aware of the arguments of Negi and Marmor [6], which are based on animal experiments, that a passive leak at the RPE could not overwhelm the pumping ability of healthy surrounding RPE and that dysfunction of the surrounding RPE in CSC is likely. However, in patients with CSC, other factors may be at work in addition to a defect in the blood-retinal barrier such as increased choroidal permeability and high choroidal tissue fluid pressures. The resultant subretinal fluid flow may indeed the substantial and could deluge even normal RPE in the vicinity of the leak.

The area of the average RPE defect in our study was

0.008 DD^2 while the area under the average sensory detachment was 4.4 DD^2. Assuming that the flow through the leak was the sole source of subretinal fluid, that this fluid was removed uniformly through the surrounding RPE, and that the volume of subretinal fluid was at equilibrium (not changing), the fluid flow per unit area (fluid flux) across the average leak into the subretinal space was about 500 times greater than the average flux back into the choroid through the remainder of the RPE beneath the detachment. We also found that detachments associated with profuse, "smokestack" leaks were significantly larger than those associated with less active pinpoint leaks. In addition, in CSC patients with extensive serous detachments, profuse leaks are, in our clinical experience, the rule. Finally, in cases of CSC without demonstrable leaks, resorption of fluid occurs more rapidly than in cases with active leaks [9]. We therefore believe that the fluid dynamics at the leak are of paramount importance in CSC. While we agree that dysfunction of the RPE may well play a role in the development and maintenance of a serous detachment, just how "sick" the RPE is in the human disease has not yet been determined.

Once a detachment begins, the direction of detachment extension is undoubtedly influenced by the relative strength of the RPE-sensory retina bonding in the regions surrounding the leak and also the relative density of subretinal fluid compared with the density of vitreous. Denser subretinal fluid probably promotes inferior extension of the detachment, assuming that the patients are usually upright. Seventy-four percent of the detachments we studied had their centers located below the level of their associated leaks. We did not find a significant relationship between the area of the RPE leak, as approximated by its size in the arteriovenous phase fluorescein, and the area of the associated detachment. Several explanations are possible. The fluid flow across a leak may not be directly related to the area of the RPE defect alone but may well be a function of the pressure gradient across the leak and the flow resistance at the leak itself. The duration of the disease process may influence the rate of fluid flow across the leak, as profuse leaks may become slow leaks as healing takes place [11]. Alternatively, the pumping ability of the underlying RPE may change throughout the course of the disease.

Compared with the natural history, direct laser treatment to the leak promotes resolution of CSC, but the visual outcome is not altered [8]. Simple debridement of defective RPE with subsequent repair of the RPE barrier has been offered as one mechanism by which laser succeeds. However, photocoagulation of the leak may also increase the mechanical resistance to fluid inflow (Fig. 8, Eq. 1). This could occur if photocoagulation produced a coagulum "plug" at the leak site shifting the equilibrium toward net absorption, and allow the RPE pump and osmotic gradient elsewhere beneath the detachment to remove subretinal fluid. If the rate of fluid inflow is sufficiently reduced by photocoagulation, the RPE cells surrounding the focal RPE defect could then slide over the leak site to reestablish the RPE barrier. Such repair presumably would be inhibited by gross flow of fluid across the RPE during the acute stages of the disease.

Acknowledgement. Paul G. Rehkopf and Joseph W. Warnicki provided technical assistance.

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Received April 13, 1988 / Accepted September 14, 1988