To the Editor:

In a recent Report, the authors state that in their 20 cases of rhegmatogenous retinal detachment (RRD): "the lipid concentration of the subretinal fluid has no specific correlation with the protein concentration, based on visual inspection of the data (Table I)." They conclude that since protein concentration in subretinal fluid (SRF) reflects permeability of the ocular vessels following retinal detachment, the lack of correlation between protein and lipid concentrations indicates that the major portion of lipid in SRF does not result from a nonspecific leakage of ocular vessels. They buttress their argument by citing the very low SRF concentration of beta-, pre-beta-, and alpha-lipoprotein, which represent the bulk of serum lipids.

I must disagree with both the analysis and the interpretation of these data. A plot of SRF [protein] against SRF [lipid] from their cases (data from authors' Table I) showed that lipid concentration tended to increase with protein concentration, the correlation coefficient being significantly different from zero (Fig. 1). Partitioning the data in various ways and applying a variety of statistical tests also suggested such an association. The authors' conclusion that there is no correlation between the SRF protein and SRF lipid concentrations is therefore not supported by their own data.

Furthermore, contrary to the authors' statement, the low SRF concentration of beta-, pre-beta-, and alpha-lipoproteins is not convincing evidence against a plasma origin for the other lipids in SRF. There is a progressive breakdown of the posterior segment blood-ocular barrier as RRD's age, allowing progressively heavier serum proteins to enter SRF. However, the large IgM macroglobulins, with molecular weight ~ 900,000, never enter SRF—not even in longstanding RRD's. The beta- and pre-beta-lipoproteins, which together generally constitute around 70 to 80 per cent of serum lipoproteins, are heavy molecules, with molecular weights ranging from the neighborhood of one to several million. Therefore, while molecular weight is but one factor governing passage of a substance across normal or abnormal vessel walls, one might expect the heavy beta- and pre-beta serum lipoproteins to be largely excluded from SRF in RRD's of all durations. The alpha-lipoproteins, constituting only about 20 to 30 per cent of serum lipoproteins, while somewhat lighter, are also heavy molecules, with molecular weights in the

![Fig. 1. Total protein concentration vs. total lipid concentration in SRF samples from 20 RRD cases of Lam and co-workers.](https://iovs.arvojournals.org/pdfaccess.ashx?url=/data/journals/iovs/933066/)

The various alpha-lipoproteins might or might not be present in SRF, the presence and amount of each depending on its molecular weight and plasma concentration, and the duration of the detachment. Since one would expect less alpha-lipoprotein in SRF from more recent detachments, it may be pertinent that 11 of the authors' 20 cases were of four weeks' or less duration, and 9 of those 11 were of three weeks' or less duration. Furthermore, in view of the wide variety of cellular debris and cytoplasmic enzymes previously identified in SRF, the presence of enzymes capable of breaking down serum lipoproteins. Therefore, the low concentrations of alpha-, beta-, and pre-beta-lipoproteins in SRF do not rule out a plasma origin for other, lighter weight lipids in SRF.

The origin of the various components of SRF, and what information SRF analyses can give us about the pathophysiology of RRD are exceedingly complex questions. The authors and I agree that the protein concentration in SRF following RRD reflects to some degree the permeability of the posterior ocular segment. The association of higher SRF [protein] with higher SRF [lipid] found in the authors' reported data (Fig. 1) therefore suggests that the lipid content of SRF is related to the permeability of the posterior ocular vessels. This could be because SRF lipid originates from plasma leaking into the subretinal space. Alternatively, SRF lipid could arise...
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from degenerating retina and other tissues, as suggested by the authors. However, if one accepts this latter concept, one must also accept that the degree of retinal degeneration is somehow related to the degree of vascular permeability. Such a relationship is plausible.5

The present consensus regarding SRF proteins is that many originate from plasma (probably via leakage through an abnormally permeable choriocapillaris Bruch's membrane and retinal pigment epithelium6), some from degenerating retina, and some from other sources.5, 6, 7 Most probably, SRF lipids have a similar dual or multi-compartmental origin.

To the Editor:

We did realize that there is some correlation between lipid and protein concentration. Our statement "... no specific correlation... based on visual inspection..." referred to the scattering appearance of the data. For example, a sample showing a high lipid concentration of 2.06 has a protein concentration of only 11.6 mg. per milliliter. The 20 cases selected in our study are far from a complete representation of the complicated clinical variations. If more data were collected, one might see a nonlinear correlation, or other phenomena not indicated in our data. That is the reason we did not attempt to discuss the statistical analyses.

We also agree that part of the lipid is derived from the blood. The portion derived from the blood could be more significant in samples having high protein concentration. The statement "... lipid in subretinal fluid does not result from a nonspecific leakage..." referred to simple diffusion of original serum constituents, where molecules equilibrate reversibly on both sides of the blood vessel. We have not excluded the unknown mechanism where large molecular weight lipoproteins are actively transported into the subretinal space. We have not been able to demonstrate any lipase activity in the subretinal fluid. It seems to us that the degradative processes occur inside the macrophages and tissue cells.

The subretinal esterases described in our previous paper (Lam et al., INVESTIGATIVE OPHTHALMOLOGY, 1972) are not concerned with degradation of lipids.

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Clean Start For The Retinal Pigment Epithelium

To the Editor:

One of the chief purposes of publication of research results is to provide the research community with data that can be used as a basis for the next logical attack on the unknown. Ideally, experiments performed in one laboratory should be reproducible in another one, thereby facilitating progress toward solving problems of common interest. It is an axiom of both science and philosophy, however, that ones conclusions are only as valid as ones assumptions, and therein lies many problems. The assumptions of one laboratory may not be the same as those of another; data cannot be shared or transferred, and experiments must be repeated.

The recent National Eye Institute Symposium* on "The Pigment Epithelium: Its Relationship to

*Oct. 15 through 17, 1975, Bethesda, Md.