

MEMO ROUTING SLIP		NEVER USE FOR APPROVALS, DISAPPROVALS, CONCURRENCES, OR SIMILAR ACTIONS		ACTION
1 TO Ch/Surgical Rsch Br.	INITIALS	CIRCULATE		
	DATE	COORDINATION		
2	<i>New Suspense DATE</i>		FILE	
	<i>26 NOV 65</i>		INFORMATION	
3	<i>6/11/65 COORD with 1504 CDC</i>		NOTE AND RETURN	
			PER CONVERSATION	
4			SEE ME	
			SIGNATURE	
REMARKS <p>Per our conversation it is requested that extensive comments be obtained for a definitive answer to CDC if you feel that this should remain a research objective and not a Qualitative Materiel Development Objective (Exploratory Development).</p> <p><u>Footnote:</u></p> <p>Per telecon L/Col Williams, CDCMSA, Col Taylor, MMDD, 3 Nov 65, L/Col Williams stated that: "CDCMSA recognized the extreme difficulty in reaching the objective of the QMDO, i.e. to produce a drug to raise the threshold level for flashblindness and/or accelerate the reformation of affected visual pigment and thereby decrease the duration of flashblindness. CDC, however, wishes to use the QMDO as a means to instigate and financially support research to determine the feasibility of the objective."</p>				
FROM EMERSON B. TAYLOR Colonel, MSC Ch/Med Materiel Dev Div		DATE 3 Nov 65	PHONE	

WNRC: 21 Nov 94
 RG: 112
 Accession # 67A-4873
 Box #36
 File Name: Flash Blindness
 Correspondence

MEDDH-RS

UNCLASSIFIED AND FORN DISSEMINATION RESTRICTIONS REMOVED
Mitigation, Individual

Ch/Med Materiel Dev Div

Surg. Resh. Br.

1 Dec 1965
Lt Col Kovaric/rk/66082

1. A review of the proposed QSDO has been completed by appropriate consultants.
2. It is agreed that the operational need for just such protection exists. However, the basic research done to date does not support the hypothesis that a protective substance or drug exists.
3. The amount of visual pigment present in the retina does not determine the severity of flashblindness, nor can the amount of pigment influence the return of visual performance to normal, to a significant degree.
4. Choriorretinal burns, a form of flashblindness, can be produced by atomic flash or laser irradiation. No drug could possibly be effective in preventing this type of retinal destruction. The term "flashblindness" needs defining to limit the scope of the QSDO.
5. The lack of success to date should not deter further studies to modify the effects of flashblindness. It is conceivable that additional basic research will open new possibilities. Because of this we agree that the subject should be pursued.

JOHN J. KOVARIC
Lt. Colonel, MC
Chief, Surgical
Research Branch

THE ZARET FOUNDATION, INC.
1230 POST ROAD
SCARSDALE, NEW YORK

MILTON M. ZARET, M. D.
DIRECTOR OF RESEARCH

CODE 914 GREENLEAF 2-2882

November 23 1965

John J. Kovaric
Lt. Colonel, MC
Chief, Surgical Research Branch
U. S. Army Research and Development Command
Washington D. C. 20315

Re: MEDHH-RS of 15 November 1965 concerning Draft QMDO for
Flashblindness Treatment and/or Mitigation, Individual

Dear Colonel Kovaric:

The draft objective referenced in your letter of November 15th is very interesting and intriguing and I want to thank you for giving me the opportunity to review it.

Regarding your inquiries, I am assuming that individuals knowledgeable in the field of photopigments were involved in the preparation of the draft. Therefore, I will confine my comments to some of the adverse factors which should be considered before embarking on the proposed research.

1. As regards the existing literature, there is little evidence that a drug is already available which could significantly alter the rate of recovery from flashblindness. There are, however, isolated reports suggesting that some agents can influence the recovery of visual sensitivity and/or the absolute threshold, --but no research, in depth, has been reported.

2. A visual pigment is characterized by the union of a chromophore (retinal) with a protein (opsin). While the chemistry of isomerization and bleaching of the retinal (the aldehyde of vitamin A) and the kinetics of its resynthesis are known to some extent, relatively little is known about the formation, transport and pathways of the associated protein synthesis. Thus, if one were to develop a catalyst to push the reaction rate of chromophore production in the appropriate direction, this does not ensure equally rapid production of the visual pigment. However, protein kinetics may not be an important factor in this regard. We simply do not know the answer.

THE ZARET FOUNDATION, INC.
1230 POST ROAD
SCARSDALE, NEW YORK

MILTON M. ZARET, M. D.
DIRECTOR OF RESEARCH

CODE 914 GREENLEAF 2-2552

Lt. Colonel John J. Kovaric

3. Assuming for the moment that an effective drug can be produced, the likelihood that it can be administered after a flash and react quickly in the visual pigment cycle is remote. It seems more probable that the agent would have to be introduced some time prior to exposure. Furthermore, its effect on the function of other body tissues must be seriously considered.

4. Perhaps the most significant factor to be considered involves the role of visual pigments in the visual process itself. That they are essential to vision is self evident; but, the question arises as to how much bleaching takes place at flashblinding levels of illumination. That is, can we have a nearly full complement of visual pigment and still be visually incapacitated?

Surprisingly, the answer seems to be in the affirmative. From the experiments by Aguilar and Stiles we know that complete rod saturation (i. e., rod threshold raised to infinity) occurs at illumination intensity levels below that which would bleach even 1% of the visual pigment rhodopsin. And, in the dark-adaptation curve itself, Rushton has shown that rod vision begins to appear (i. e. the break in the dark-adaptation curve) only after 90% of the rhodopsin has been regenerated. Apparently, neural factors (e. g. activity of neural elements which mask signal detection) play a more important role than pigment quantity in determining whether perception can occur. Thus, if following a high energy bleaching exposure, one could manage to cause 95% of the visual pigment to regenerate in an infinitely short time, it would influence only slightly the rate at which visual performance is restored to normal.

5. In item 6a, page 2, the proposal reads "...it is conceivable that a pharmacological means can be developed to raise the threshold level for flashblindness...". This implies that the photosensitivity of the pigment can be reduced by means of the drug. That a drug can alter either the extinction coefficient, α , or the quantum efficiency, γ , (since photosensitivity = $\alpha\gamma$) without seriously impairing the nature of the pigment is highly improbable.

6. Finally, from a practical standpoint, the development of such a pharmaceutical for protection against flashblindness would not preclude the need for individual protective devices, one of the stated aims of the proposal. Protection against chorioretinal burns from

THE ZARET FOUNDATION, INC.

**1230 POST ROAD
SCARSDALE, NEW YORK**

**MILTON M. ZARET, M. D.
DIRECTOR OF RESEARCH**

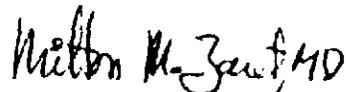
CODE 914 GREENLEAF 2-2852

Lt. Colonel John J. Kovaric

atomic flash (or laser irradiation) could not be afforded by the proposed drugs and this would require protective devices. In fact, for some forms of radiant energy (e. g. the neodymium wavelength), retinal burns will be produced before a significant amount of pigment is bleached, owing to the low absorptivity of the visual pigments for the emission spectrum of the source. Thus, it is possible to produce a chorioretinal burn without flashblindness.

I hope that the above is of value to you. Should you have any additional questions, please feel free to express them. The concept has merit but it requires much basic research before the goals can be realized.

Sincerely yours,



Milton M. Zaret, M. D.
Director of Research

MMZ:fd