Since it is known that the action of many antibiotics can be reversed by cysteine, it was thought that this enzyme system might be affected. However, cystine reduction was not inhibited by streptomycin, fradicin (*10*), or penicillin.

References

1. Mapson, L. W., and Goddard, D. R. *Nature,* **167**, 975 (1951).
2. Conn, E. E., and Vennesland, B. *Ibid.,* 976.
3. ———. *J. Biol. Chem.,* **192**, 17 (1951).
4. Meldrum, N. U., and Tarr, H. L. A. *Biochem. J.,* **29**, 108 (1935).
5. Tunnicliffe, H. E. *Ibid.,* **19**, 199 (1925).
6. Abderhalden, E., and Wertheimer, E. *Pflügers Arch. ges. Physiol.,* **199**, 336 (1923).
7. Brendler, H. *Science,* **114**, 61 (1951).
8. Hogeboom, G. H., and Barry, G. T. *J. Biol. Chem.,* **176**, 935 (1948).
9. Shinohara, K. *Ibid.,* **109**, 665 (1935).
10. Swart, E. A., Romano, A. H., and Waksman, S. A. *Proc. Soc. Exptl. Biol. Med.,* **73**, 376 (1950).

Manuscript received January 4, 1952.

Veralbidine, a New Alkaloid from *Veratrum album*

A. Stoll and E. Seebeck

Research Laboratories of Sandoz Ltd., Basel, Switzerland

After cautious extraction of *Veratrum album* and working up of the alkaloids, it was possible to isolate the already known bases protoveratrine, jervine, and rubijervine. From the mother liquors, by crystallization from ether, we were able to separate a new alkaloid for which we propose the name "veralbidine." Pure veralbidine crystallizes from dilute acetone in pentagonal plates, from dilute methanol in prisms, and from ether in bunches of fine needles. The crystals melt between 181° and 183° C and exhibit a specific rotation of $[\alpha]_D^{20} = -11.7°$ in pyridine and $[\alpha]_D^{20} = +5.4°$ in chloroform. In 84% sulfuric acid, veralbidine gives a colorless solution. It is sparingly soluble in ether, alcohol, and acetone and insoluble in water. It dissolves readily in chloroform. Veralbidine is irritating to the nasal mucosa, causing sneezing.

The empirical formula of the new alkaloid, as determined by chemical analysis, is $C_{37}H_{61}O_{12}N$. For analytical purposes the alkaloid was dried at 110°.

Required: C, 62.44%; H, 8.57%; N, 1.97%.
Found: C, 62.21%; H, 8.53%; N, 2.14%.

Veralbidine yields a crystalline thiocyanate which melts at 235°–236° with decomposition and frothing. It is readily soluble in methanol and acetone, but sparingly soluble in water. The analytical figures obtained after drying at 110° agreed with the empirical formula $C_{37}H_{61}O_{12}N \cdot HNCS$.

Required: C, 59.26%; H, 8.05%; N, 3.64%; S, 4.16%.
Found: C, 59.04%; H, 8.09%; N, 3.59%; S, 4.09%.
C, 59.10%; H, 8.17%; N, 3.54%.

Veralbidine also yields a crystalline hydrochloride which is readily soluble in alcohol and water. The hydrochloride melts at 250°–251° with decomposition and frothing. Empirical formula, $C_{37}H_{61}O_{12}N \cdot HCl$.

Required: C, 59.43%; H, 8.29%; Cl, 4.73%.
Found: C, 59.32%; H, 8.45%; Cl, 4.61%.

It is intended to give a more detailed report on the constitution and pharmacological action of veralbidine at a later date.

Manuscript received December 28, 1951.

The Effect of Experimental Stress upon the Photically Activated EEG[1]

George A. Ulett and Goldine Gleser[2]

Department of Neuropsychiatry, Washington University School of Medicine, St. Louis, Missouri

In the search for neurophysiological concomitants of mental processes it has seemed worth while to augment electroencephalographic investigation with the use of the stimulus of intermittently flashing light (*1*). The ability of such photic stimulation to drive the brain waves was described in 1934 by Adrian and Matthews (*2*). Such stimulation produces visual sensations (Prevost-Fechner-Benham effect) and a variable dysphoria. Walter (*3*) has made the observation that the type of brain response produced seems at times to vary in a complex manner with alterations in the subject's mood and that EEG responses appearing at a harmonic of the stimulus frequency might increase at the expense of the primary response. The ability of photic stimulation itself to produce mood changes (*1, 3*), however, renders such isolated disclosures difficult of interpretation, and hence prompted our investigation of changes in the photically stimulated EEG in subjects whose mental state was deliberately altered under laboratory conditions.

Ninety-six subjects 18–35 years of age were used in this procedure. They were divided into three groups. Groups I and II were selected from a larger sample studied for "anxiety-proneness" by psychiatric and psychological examination (*4*). Group I consisted of 30 subjects judged least likely to develop symptoms of anxiety under stress. Group II was composed of 25 psychiatric patients with diagnoses of psychoneurosis or character disorder in which anxiety was the predominant symptom. These two groups were placed under an experimental anxiety-producing situation in an attempt to determine whether such stress could affect the photically driven EEG and whether the two groups might react differently.

Group III (41 subjects) was the control group, consisting of experimentally sophisticated medical

[1] This report was completed under Air Force Contract Number 33(038)-13884. It is one of a series of studies under R and D Project 21-37-002, Development of Psychiatric Screening of Flying Personnel, Department of Clinical Psychology, U. S. Air Force School of Aviation Medicine.

[2] The technical assistance of Rosemary Baessler and Ruth Ellerman is gratefully acknowledged.

students and hospital staff who were known to be without gross psychiatric disturbance. They were subjected to photic stimulation only, without the added experimental stress.

The experimental procedure required approximately 30 min. Following the recording of the basic EEG all subjects were exposed to intermittent photic stimulation at a frequency of 14 flashes/sec. After an initial 3 min the stimulation was interrupted. Instructions for the ensuing procedure were then given. Different instructions were given to several groups:

a) Groups I and II were told that during photic stimulation they would have a variety of subjective sensations. They were told that these were known to the experimenter [untrue!] and that they would be called upon to report these experiences briefly and correctly in response to a bell rung at 15-sec intervals. They were informed each time of the correctness or incorrectness of their answers and told that as an incentive to correct reporting an electric shock would be administered if they gave 10 incorrect replies. The replies were then graded in a predetermined fashion, and all subjects received a shock to the hand after their twentieth (i.e., tenth incorrect) response. The procedure was repeated a second time but stopped just short of another shock.

b) The control groups were exposed to the public stimulation for an equivalent length of time but without experimental stress. Group III_A was told: "Relax, keep your eyes open, and look at the screen." Group III_B was told: "We would like to know what you experience as you look at the light flashing on the screen. You will be asked every few seconds to report as briefly as possible. Accuracy is not important and please be brief."

Photic stimulation was again introduced, and after 1 min recording Groups I and II were subjected to the stress situation for a period of 10 min. At the end of this period, photic stimulation continued for an additional 5 min, but the subjects were informed that they could relax, there would be no more bells or shocks, and they need give no more replies. The controls were recorded for an equivalent length of time.

The EEG's were recorded from a standard placement of bipolar right parieto-occipital needle electrodes made with reference to midline and inion. The critical occipital lead was placed 1 cm above and 1 cm to the left of the inion. All subjects were recorded with eyes open and were seated behind a large opal-glass screen placed some 6–12 in. from the face. The light stimulus was from a tungsten-filament source. It completely filled the subject's visual field with a circle of light of 200 ft-c maximum intensity. This light was interrupted at a rate of 14 flashes/sec by a pendulum-type episcotister. The EEG, recorded through Grass Model II amplifiers, was electronically analyzed by a modified, Walter-type electronic brain wave analyzer which permitted an accurate analysis, by 10-sec epochs, of all changes in power (product of amplitude and number of waves) in the 14-c/sec band of the EEG, as recorded before, during, and after photic stimulation at this frequency.

The brain wave response to photic stimulation was determined by measuring the deflection of the analyzer pen for the 14-c/sec band of the brain wave for representative 10-sec periods during the time of photic stimulation, using as a base line the pen deflection for this band of the brain wave taken with eyes open and without stimulus. Such response is herein called "driving."

The average driving response of Groups I, III_A, and III_B is shown in Fig. 1. Points on the ordinate indicate average millimeters of the analyzer pen deflection. These in turn are directly proportional to the groups' activity in the 14-c/sec band of the EEG at representative periods of time. The period intervals A, B, and C, with their appropriate subnumerals, indicate, respectively, the resting, stress, and post-stress periods of the experiment as previously described. The black line indicates the stressful period, and the arrow the time of shock for Group I.

From Fig. 1 it appears that the experimental group (I), during stress, showed a considerably lower response to intermittent photic stimulation as compared with the control subjects. The difference is even more notable since their driving previous to stress (A_1 and A_2) was the highest. However, it should be pointed out that individuals vary considerably in the extent to which the brain wave may be driven at a given frequency, and the distribution of driving is greatly skewed in that a small number of individuals give very high responses. Also, the amount of response for a single individual fluctuates considerably from time to time, and this fluctuation is greater for high levels of driving. Group averages are affected by large values and may not at all reflect the modal trend.

In order to obtain less skewed distributions with more homogeneous variance, from group to group, and a more accurate picture of group trends, a transformation was made to the square root of the measure of driving. The average values for this transformed variable when the groups were equated as to original driving level (A_2) are shown in Fig. 2. These values were used for all tests of significance. It may be seen that although the differences between the groups are now reduced the general trends persist.

For Group I there was a significant drop in driving level between the response at A_2 and the corresponding response during the period of stress (B_2 through B_6). No such decrease in response was obtained for Groups III_A or III_B. The average response for these two groups was practically identical, indicating that verbalizing in itself did not affect photic driving. The difference between the average change in response for Group I and the change in response for Groups III_A and III_B combined was significant at the 5% level. We can therefore conclude that for normal subjects the introduction of experimental stress tends on the average to lower the driving response. Fig. 3 illustrates this point by means of representative strips taken from the EEGs of an experimental and a control subject at appropriate points in the procedure.

The EEG response of the patients (Group II) was compared with that of the non-anxiety-prone experi-

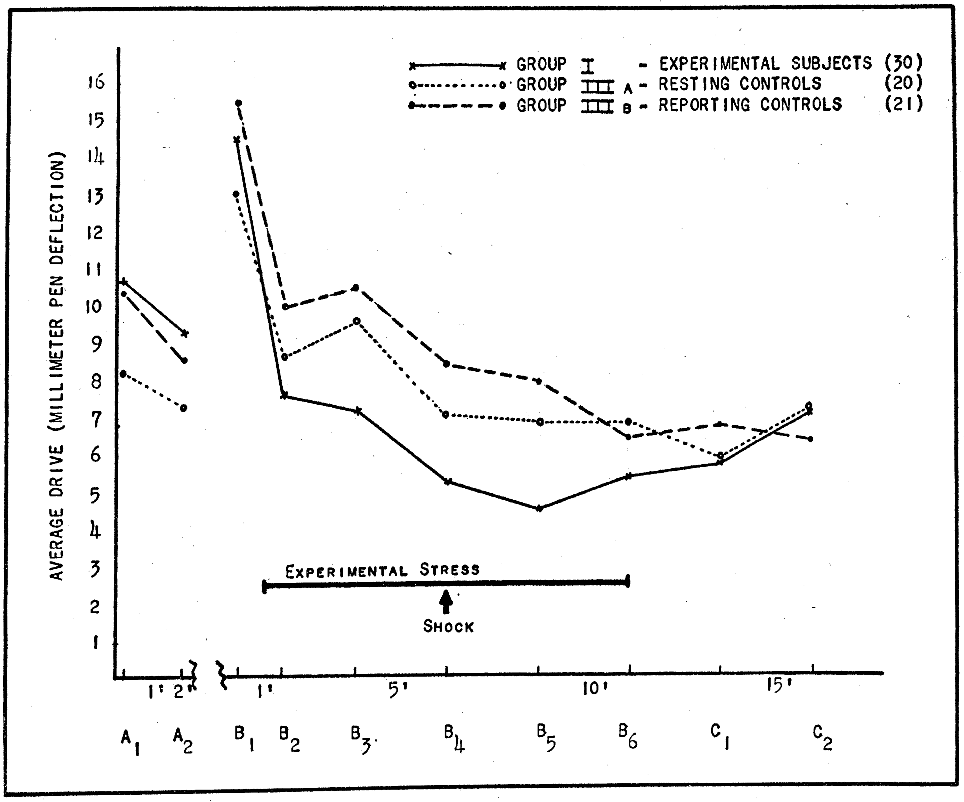

FIG. 1. Average EEG driving response to photic stimulation at 14 c/sec for experimental subjects before, during, and after stress, and for their controls without stress.

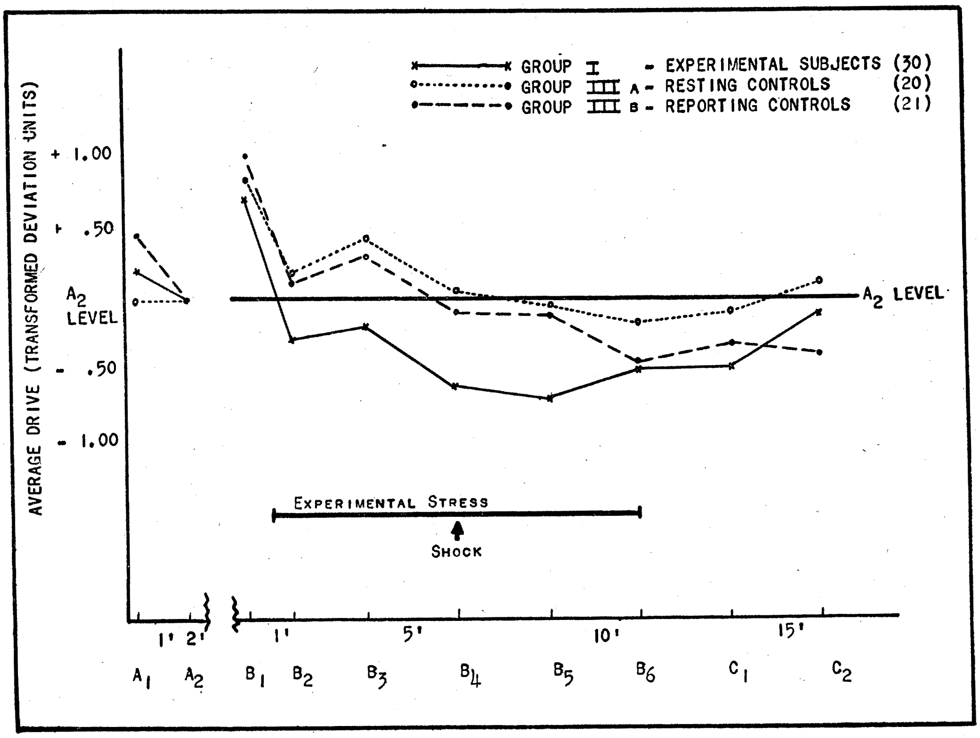

FIG. 2. Square root of average EEG driving response adjusted for differences in initial driving level for experimental subjects before, during, and after stress, and for their controls without stress.

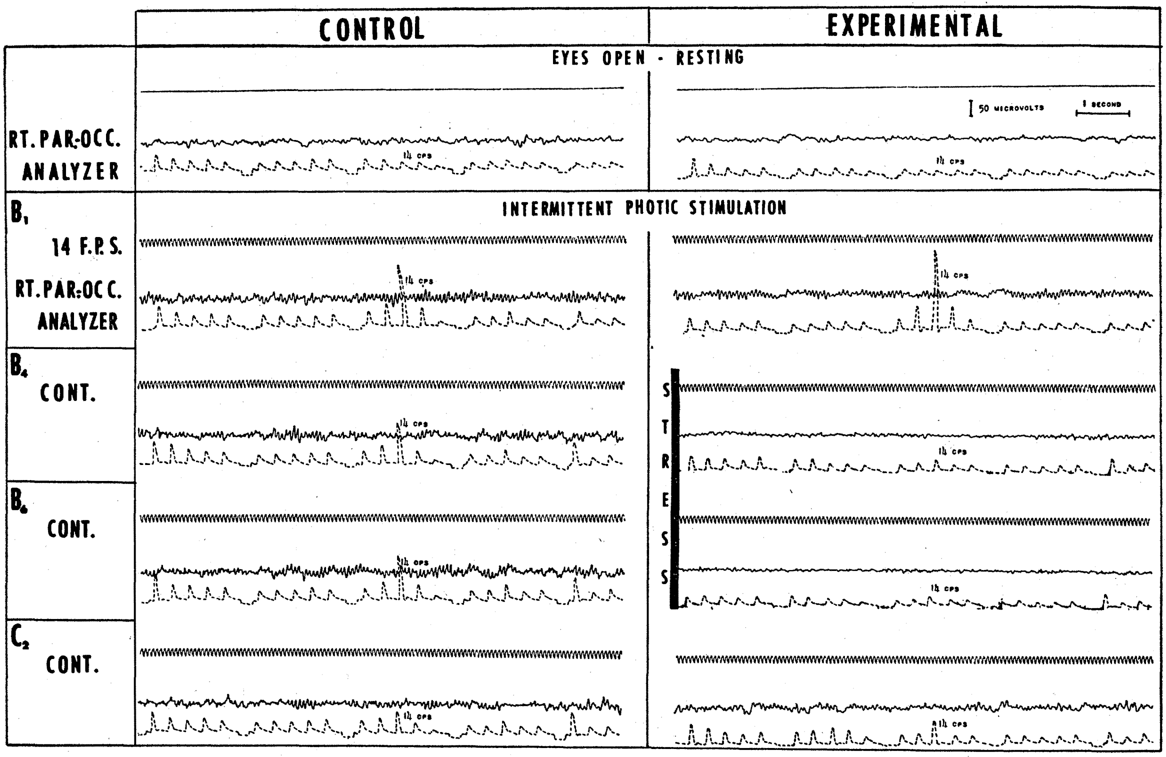

FIG. 3. Representative samples of EEG records from an experimental subject exposed to stress and a control at corresponding periods of rest and photic stimulation.

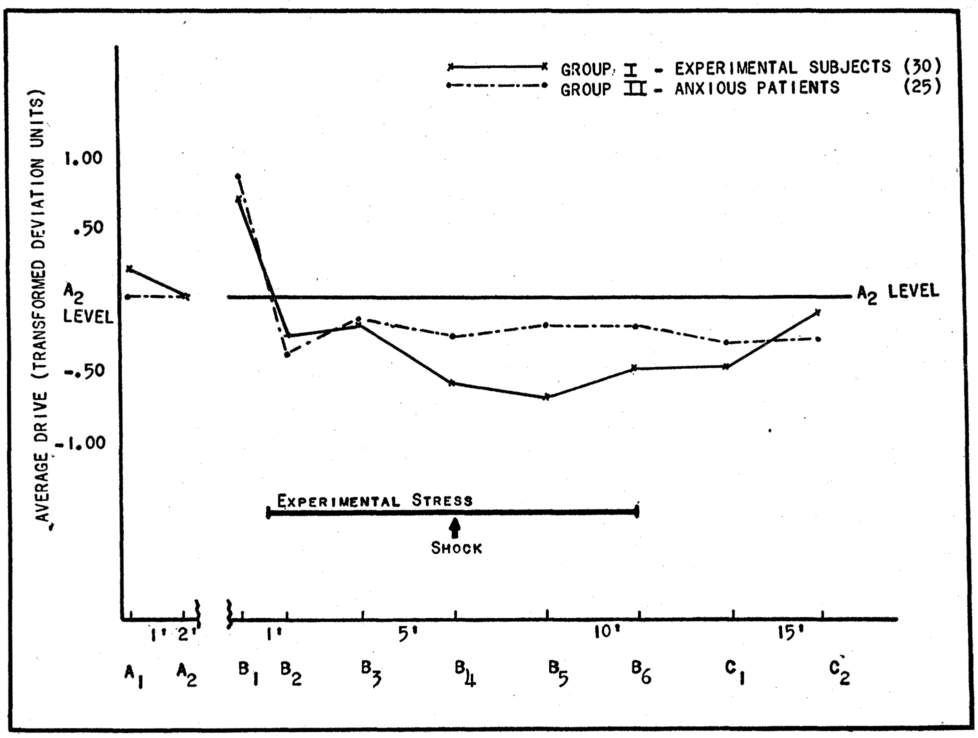

FIG. 4. Square root of average EEG driving response adjusted for difference in initial driving level (A_2 level) for experimental subjects and anxious patients before, during, and after stress.

mental subjects (Group I). Both of these groups, when subjected to experimental stress, showed a decrease in driving below their original level. However, the average drop for the patient group was not as pronounced as for the experimental subjects (Fig. 4). The difference between these two curves was not significant, and yielded no measure for differentiating between patients with anxiety and individuals who were not anxiety-prone.

Group I showed a considerable rise in driving after the stress period was over, so that at C_2 they were at the same or a slightly higher level than the normals who reported their sensations while under no stress (Fig. 2). The increase in driving between B_6 and C_2 for Group I was significant beyond the 5% level ($\bar{d} = .393$, $\sigma = .161$, $t = 2.44$). Thus the normal subjects showed a recovery in driving after the tension was removed. No such increase was evident in the patient group (Fig. 4). Unfortunately, however, this difference in response was not discovered until all data had been collected; hence, we do not know whether the patients also would have shown an increase in driving if allowed a longer period of recovery.

The driving response at the second harmonic (28 c/sec) was also examined for all groups. There was found to be an average increase in harmonic response in those subjects who were exposed to experimental stress. However, the control subjects showed a similar tendency toward increased response during prolonged stimulation, and thus this phenomenon could not be attributed to the stress situation per se.

From our work it appears that the occipital rhythms induced by intermittent photic stimulation are disturbed by emotional tension in a fashion similar to that in which such stress produces α-blocking. In both instances the synchronized basic pattern is disturbed and the amount of recorded activity is decreased. The mechanisms by which such interruption is accomplished are not fully known, but one assumes from observations such as those of Gellhorn (*5*), Sapirstein (*6*), and Jasper (*7*) that, with the production of anxiety, discharge from diencephalic regions interferes with cortical mechanisms of synchronization by occupying neuronal circuits that are otherwise producing a resting or driven beat.

The finding that screened control subjects and anxious patients do not show a differential decrease of response in the photically activated EEG with the introduction of experimental stress is not entirely unexpected. Malmo (*8, 9*) reported negative results in attempting to differentiate patients from controls on the basis of amount of α-blocking accompanying painful stimulation. It is possible that the stress of our experimental situation could have induced a degree of heightened attention or "vigilance" in the experimental subjects which matched the effect of any anxiety that appeared in the chronically anxious patients. Vigilance may, as Liddell (*10*) stated, be a precursor of anxiety. If this be true its induction in the experimentally stressful situation would hinder the differentiation of our two groups.

The relationship of the neural mechanisms responsible for the photic driving response to those that produce α-activity is as yet undetermined. Observations in which a resting α can coexist relatively unchanged with the appearance of a driving response at another frequency suggest that independent cell groups may be at work. The present study does not answer this problem but does suggest that, whether or not such mechanisms use morphologically different or identical units, at least they react similarly when the subject is placed under emotional stress.

References

1. Ulett, G. A. *Psychosomat. Med.* (in press).
2. Adrian, E. D., and Matthews, B. H. *Brain,* **57**, 355 (1934).
3. Walter, W. G. *J. Mental Sci.,* **96**, 1 (1950).
4. Ulett, G. A., *et al. School of Aviation Medicine Reports* (in press).
5. Gellhorn, E. In P. Hoch and J. Zubin (Eds.), *Anxiety.* New York: Grune & Stratton, 205 (1950).
6. Sapirstein, M. R. *Psychosomat. Med.,* **10**, 145 (1948).
7. Jasper, H. H. *EEG Clin. Neurophysiol.,* **1**, 405 (1949).
8. Malmo, R. B., *et al. Science,* **108**, 509 (1948).
9. Malmo, R. B., and Shagass, C. *Psychosomat. Med.,* **11**, 9 (1949).
10. Liddell, H. In P. Hoch and J. Zubin (Eds.), *Anxiety.* New York: Grune & Stratton, 183 (1950).

Manuscript received January 14, 1952.

Melting Phenomena of a Surface of Monomolecular Thickness[1]

D. E. Beischer

U. S. Naval School of Aviation Medicine, U. S. Naval Air Station, Pensacola, Florida

A number of observations points to the fact that the surface deviates in its melting behavior from matter in bulk. Lord Kelvin (1871) was the first to recognize that the melting point of the first ordered molecular aggregations is lower than that of bigger crystals. This lowering of the melting point with decrease in the size of the particles, corresponding to an increase of the total surface, was often observed thereafter (Ostwald, Freundlich, and Haber). Another group of experimenters noticed that substances absorbed on porous solids like silica may melt, in extreme cases, 40° below their regular melting points (*1*). Recently Hüttig and Lichtenecker (*2*) observed that the surface melting of metal layers 10^{-4} cm thick takes place at a temperature considerably lower than the true melting temperature, the difference sometimes being several hundred degrees. Stranski (*3*) found a "rounding off" which removes rough spots on a solid surface before melting, forming a new "crystal face."

Previous work of this author (*4*), using radioactive monolayers, suggested that these layers would be ideally suited to investigate the phase transition of the topmost layer of a solid material. The radioautographic technique was found to be extremely helpful in such investigations.

[1] Opinions or conclusions contained in this report are those of the author. They are not to be construed as necessarily reflecting the views or the endorsement of the Navy Department.