

THE RECIPROCITY LAW OF UV-IRRADIATION EFFECTS

Damage on mouse skin exposed to UV-light varied over a 10^7 -fold intensity range

STIG CLAESSION¹, LENNART JUHLIN², AND GUNNAR WETTERMARK¹

UPPSALA, SWEDEN

The minimum dose of irradiation with UV-light needed to cause erythema of living skin was thought to be independent of intensity (Hausser and Vahle, 1922). Thus, minimum erythema dose = intensity \times irradiation time = constant. This relation, which was later called the reciprocity law, was studied extensively by Blum and Terus (1946 b). Earlier studies on this subject were carried out by Luckiesh (1930) and by Coblentz et al. (1932). The latter studied the occurrence of erythema at 297 m μ and considered the reciprocity law valid as they found it to apply over a fourfold intensity range (430-108 μ W/cm²). Blum and Terus (1946 b) varied the intensity over a 20-fold range in studying the reciprocity law. They found the law to be valid at 253.7 m μ . However, they called attention to the fact that small deviations from the reciprocity law could not be detected as the dispersion of their values was great. The range in intensity was not sufficient to define the slope of the curve well under such circumstances. With polychromatic light from an intermediate pressure mercury arc and from a carbon arc they obtained systematic deviations from this law.

These previous investigations were all limited to intensities within a very narrow range, i. e. intensities of the order used in common UV-radiation therapy. A wider intensity range would be extremely desirable for more accurate study of the reciprocity law. This was difficult to achieve, however, since erythema is not induced at much lower intensities, and much higher intensities were not available. Recently, UV-light of very high intensity became obtainable with the development of special photolysis flash lamps. This made it possible to investigate the validity of the reciprocity law over a very much wider intensity range.* The following investigation was therefore undertaken to study the effects of UV-light when the intensity is varied from as high as about 100,000 times that of a high-pressure mercury lamp down to somewhat lower than the intensities used by previous workers. The corresponding irradiation time necessary to cause detectable skin damage varied from about $35 \cdot 10^{-6}$ sec. to 500 sec. Thus, it was possible to vary the intensity over a 10^7 -fold range, which is a range over which the reciprocity law has never before been studied. In addition to studying the minimum dose causing damage and used for studies on the reciprocity law we also wanted to compare the effects of higher doses at the different intensities.

* The effects of light with these high intensities are also interesting and might be of importance in studying phenomena caused by an atomic bomb. At a distance of 1 km from a 10-kiloton atomic explosion the intensity of UV-light has been estimated to be of the order of 100 W/cm² (United States Atomic Energy Commission, 1950).

¹ Institute of Physical Chemistry, University of Uppsala.

² Institute of Pharmacology, University of Uppsala.

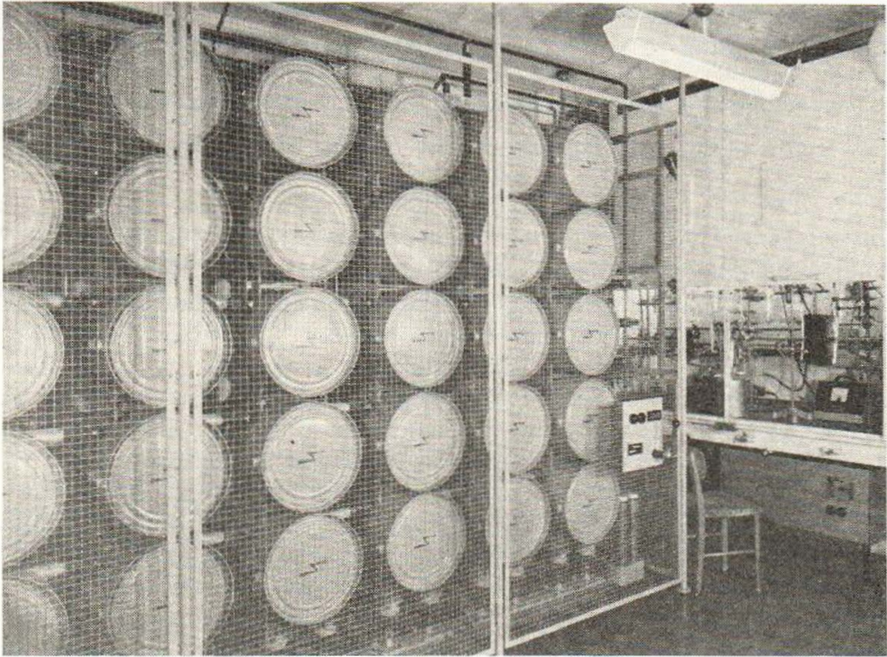


Fig. 1. Photograph of the flash photolysis apparatus with the condenser bank (left) and the lamp pair (right).

Methods

Irradiation procedures

Flash lamp. The high-intensity light pulse was obtained from a flash photolysis apparatus developed by Claesson and Lindqvist (1957). A large condenser bank (1400 μ F, 7 kV) is discharged through a photolysis flash lamp-pair. The units are connected coaxially to get short flash duration times (30–150 μ sec). The lamps consist of straight quartz tubes with a tungsten electrode at each end. The tubes are filled with oxygen at reduced pressure (5 mm Hg). The animals were fixed vertically with head upright at a distance of 4.5 cm from one of the lamps. A filter (see following) was placed immediately in front of the area to be irradiated (figs. 1, 2). The lamps were discharged at a constant voltage of 5 kV. As the duration of the flash varies almost linearly with the capacity (Claesson and Lindqvist, 1957, page 544), different doses at a constant intensity can be obtained by changing the capacity. Flashes obtained at 200, 400, 800, 1000 and 1400 μ F were used. The doses were measured by chemical actinometry, using the ferrioxalate actinometer exactly as described by Hatchard and Parker (1956). The solution was 0.006 M in ferrioxalate. For the quantum yield a value of 1.23 was used in calculating the average light intensity given in table I. The flash duration is taken as the time interval from $1/e$ of maximum light intensity on the rising part of the curve for light intensity plotted as a function of time to the corresponding point on the descending part of the curve.

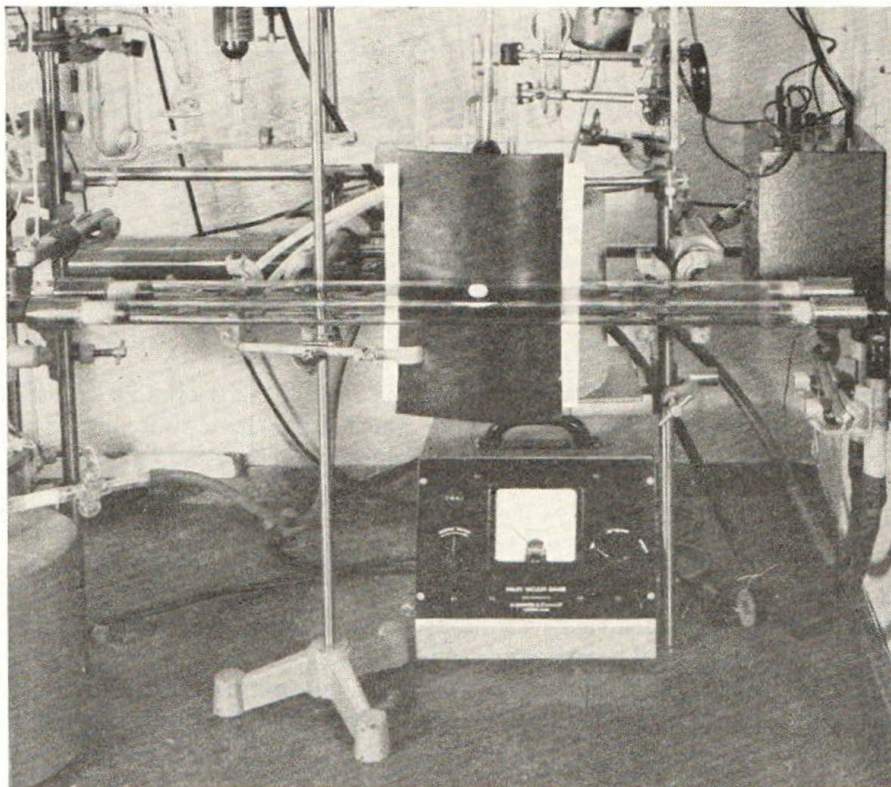


Fig. 2. Photograph showing the mounting of the animal behind the flash lamp pair.

Mercury arc. The lower light intensities were obtained from a commercial water-cooled high-pressure mercury arc (Philips SP 500 W). The same filter was used as with the flash lamp. With working distances from lamp to animal of 10, 12, 40 and 140 cm the exposure time was varied for given doses from $2.5 \cdot 10^{16}$ hr/cm^2 to $80 \cdot 10^{16}$ hr/cm^2 for six different intensities. (At the 10 cm distance two lamps with different light output were used.) The doses were measured by chemical actinometry, using a uranyl oxalate actinometer according to Forbes and Heidt (1934). The solution was 0.001 M in uranyl oxalate and 0.004 M in oxalic acid. Titrations with ceric sulfate were made exactly as described by Claesson and Lindqvist (1957). A quantum yield of 0.56 was used in calculating the values for the intensities at the various distances shown in table I. The fluctuation of the average light intensity of the mercury arc between different irradiations was less than 5 per cent.

Filters. The transmission curve for the filter (2 mm Jena WG 7 + 10 mm $\text{NiSO}_4 \cdot 6 \text{H}_2\text{O}$ 500 gm/l) is shown in figure 3 (heavy line). This transmission curve has been multiplied by the actual spectral distribution of the flash lamp (Claesson and Wettermark, 1957) and of the high-pressure mercury arc expressed in number of quanta (fig. 3, dotted lines a and b). These curves give the spectral distribution of the light to which the skin is exposed. Rather mono-

Table 1.

Lamp	Distance cm	Intensity		Irradiation time seconds
		$\text{hr/cm}^2 \cdot \text{sec.}$	W/cm^2	
Flash	4.5	$1.3 \cdot 10^{21}$	860	0.000030—0.000150
Philips SP 500 W	10 a	$3.1 \cdot 10^{16}$	0.021	2—30
	10 b	$5.1 \cdot 10^{15}$	0.0034	10—100
	12	$3.6 \cdot 10^{15}$	0.0024	5—200
	40	$7.1 \cdot 10^{14}$	0.00047	100—1000
	140	$1.0 \cdot 10^{14}$	0.000066	250—6000

chromatic light with a maximum at about 310 $\text{m}\mu$ is thus obtained with this filter. The curves from the two types of lamps differ somewhat, but the difference is assumed to be of negligible importance in this investigation.

Animals

The mice, a commercial albino stock, weighing 20—25 g, were shaved on the back with barium sulfide paste (Österlind, 1948) 24 hours before the experiments. They were fastened rigidly without anaesthesia by means of black rubber sheets to plane wooden boards and irradiated on the back through 20 mm circular openings in the sheets. Each animal was normally irradiated with alternating doses at two positions over the spine with about 25 mm between their centres.

Estimation of the damage to the skin

The degree of tissue damage was estimated by studying the leakage into the irradiated areas of intravenously injected Evans blue. A volume of 0.3 ml of the dye solution (0.5 % in physiologic saline) was injected intravenously 20 hours after irradiation. The animals were killed 15 min. after dye injection. The skin was then dissected free, fixed on a cork sheet and dried.

First all the experiments were performed and all the skins dried. Then the skins were arranged in an ascending order of blueing. The strongest blue was arbitrarily assigned the value 7.5 and the just perceptible blueing the value 0.5. The intermediate degrees of blueing were divided into subjectively even steps and the values noted for each skin. This procedure was repeated independently by four persons. The mean of their values was used. Usually, when the degree of blueing was plotted as a function of the irradiation dose (see following), each point represented the average of the results from eight independent irradiations on different animals. The vertical lines indicate the standard error of these averages.

Experimental Results

Flash irradiation

We shall first consider the results of experiments with the flash lamp (fig. 4 F). We observe that almost maximal blueing appears at $14 \cdot 10^{10} \text{ hr/cm}^2$, whereas no blueing at all is found at half this dose. The blueing then abates with a

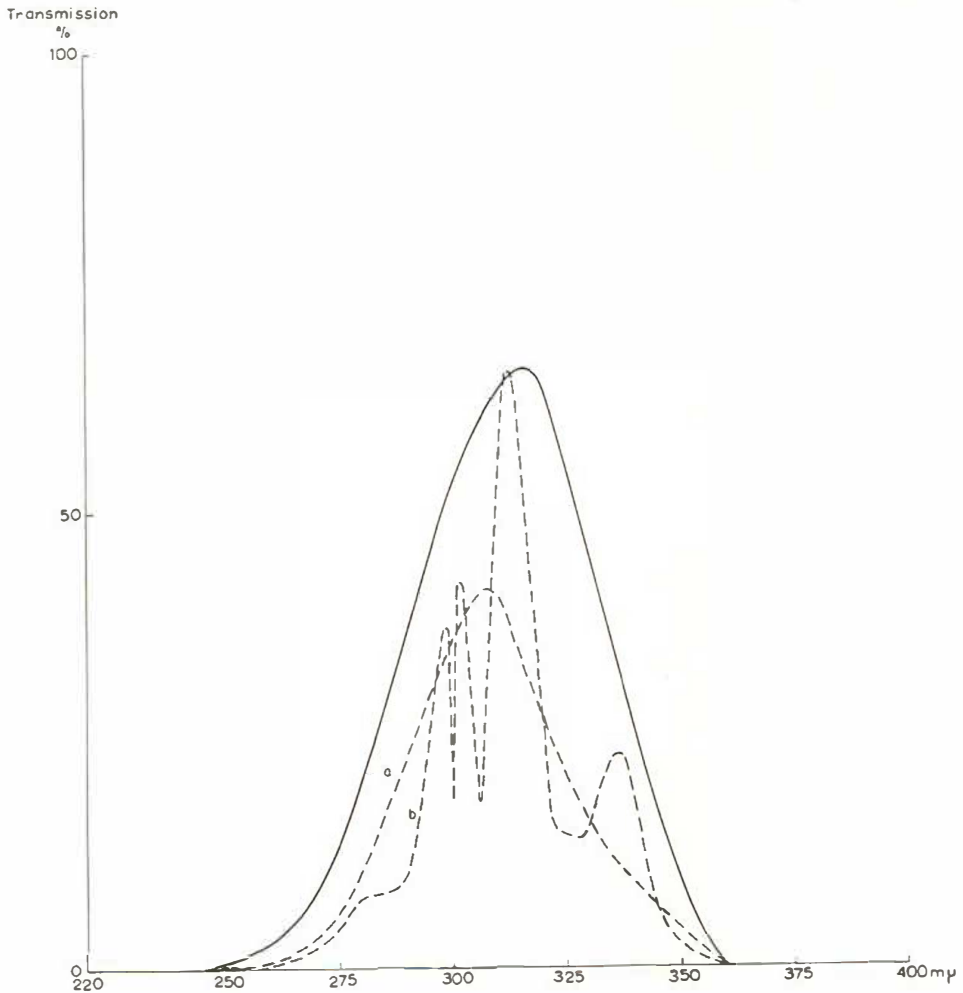


Fig. 3. Heavy line: Transmission curve for the filter. Dashed lines: The product (in arbitrary unit) of the transmission for the filter and the intensity from the lamps a) flash lamp b) high pressure mercury lamp. The dashed curves have been normalized to have the same area.

further increase in the dose and is quite inappreciable after very high doses of irradiation.

The method used here for study of capillary permeability by measurement of the leakage after injection into the circulatory system of a dye solution that is rapidly bound to the blood protein has been used earlier in different connections (cf. Menkin, 1940, 1956). The method is considered one of the most sensitive signs of capillary damage (Halpern, 1956). The factors determining the degree of blueing seem to be the increase of permeability in the capillaries together with the width of the capillaries and the capillary pressure. Intravascular block or constricted vessels can therefore prevent the increased permeability to the dye-protein complex from appearing or cause it to appear inhibited. It has been assumed by Dekansi (1949) that the action of histamine in

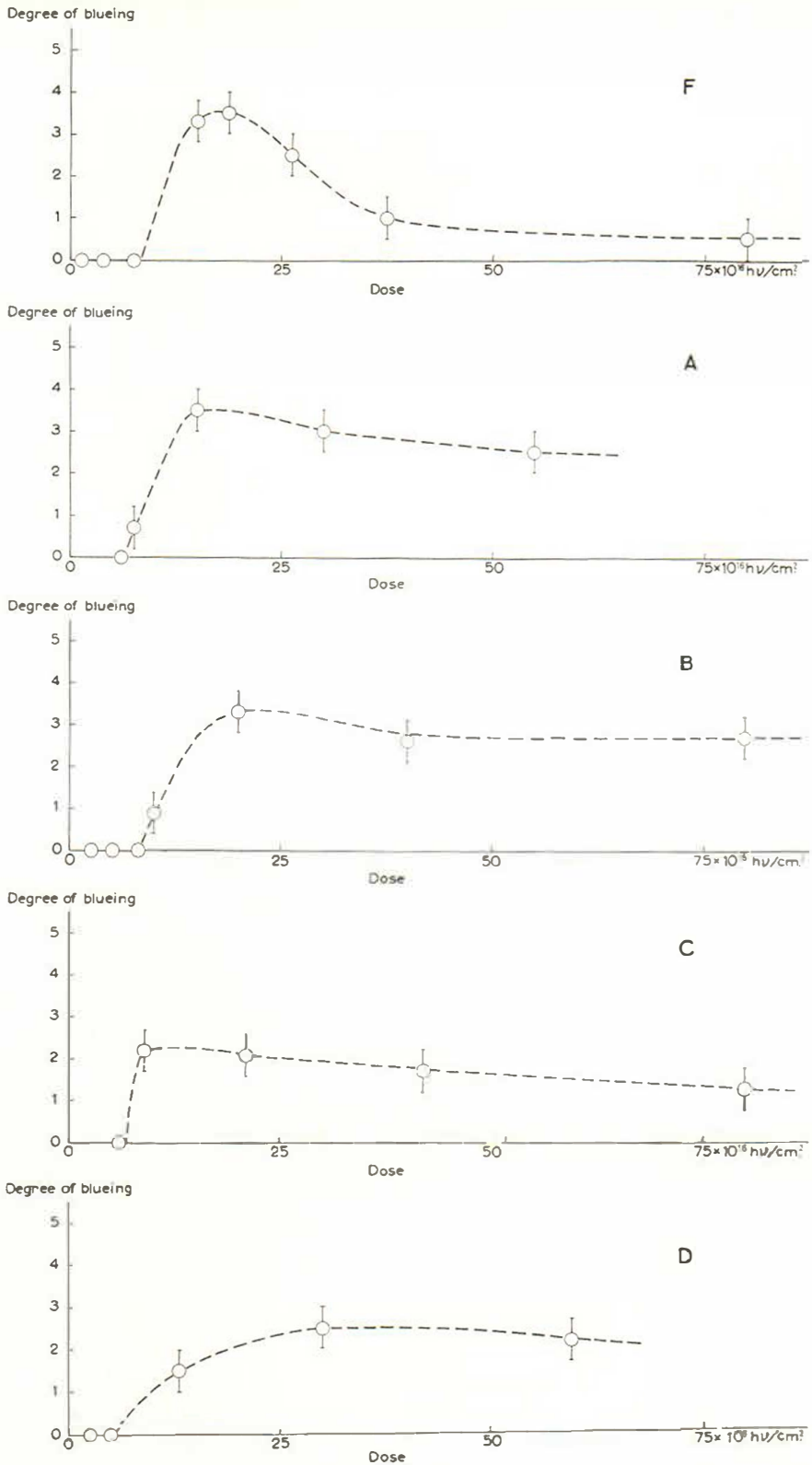


Fig. 4. Degree of blueing as a function of the dose for animals with thin skin irradiated at different intensities with filtered light ($\lambda = 280 - 330 \text{ m}\mu$). F) Flash lamp: Intensity 860 W/cm^2 . A, B, C, D) High pressure mercury lamp: Intensities $0.0034, 0.0024, 0.00047, 0.000066 \text{ W/cm}^2$ respectively.

causing the appearance of a blue skin area does not necessarily indicate an effect on capillary permeability but may simply be a result of vasodilation. This seems scarcely probable, however, because, among other reasons, of the rapidity with which the blueing appears (Miles and Miles, 1952).

The results obtained, which show that an increase in the irradiation dose in excess of that producing maximum blueing gives weaker blueing, might be explained by a vasoconstriction following larger doses. This might inhibit the leakage of the dye from the circulatory system. It should be noted that only with respect to blueing and erythema is there such an optimum dose. If we consider the macroscopic changes in the skin such as peeling, for example, that occur after a few days, we find that they increase with increasing doses. Accordingly, the diminished blueing does not mean that the damage has been checked but rather that it has increased since even the finer blood vessels are engaged.

Thus, the results are similar to those obtained in studies on erythema in man 20 hours after irradiation with UV-light (296—313 $m\mu$ at low intensity) (Blum and Terus, 1946 a). Erythema was demonstrated to be optimum at a certain dose but decreased when the dose was further increased. Blum and Terus (1946) discussed possible causes of this phenomenon and assumed the cause to be as follows: Erythema is caused by damage to the epidermal cells elaborating a dilator substance (Lewis and Zotterman, 1926), which penetrates to the superficial vessels in the papillary layer and frees them from their normal constriction. The inhibition is explained by a direct effect of the UV-light on the papillary layer that results in its vessels' not being affected by dilator substance from the epidermis.

It is also interesting to note in this connection that Miles and Miles (1952) demonstrated that there is an optimum dose for erythema and blueing in intracutaneous histamine injections. They injected 0.1 μg histamine intracutaneously and pontamine sky blue (5 %) intravenously in guinea pigs. This histamine dose was sufficient to give blueing. The blueing increased subsequently with increasing doses up to 1 μg histamine, when it began to abate in the centre. When 4 μg or more histamine was injected, the centre remained completely uncoloured. The reason for this was assumed to be an intense arteriolar constriction persisting at least 10 minutes. In consequence, the centre was not blueed during that interval and, by the time the blood supply was restored, the central capillaries had regained their normal impermeability to the dye-protein complex and were partially immune to a new histamine administration. That the capillary permeability may be refractory to histamine and that this is not dependent upon obstruction of the vascular lumen by blood corpuscles was demonstrated by Lewis and Grant (1924). Miles and Miles (1952) therefore assumed alternatively that "the reaction of the vessels with high concentrations of histamine may proceed so rapidly that the immune stage is reached before the preceding stage of permeability can manifest itself by the escape of dye". A similar mechanism is conceivable with UV-light irradiation. The "active substance" would then conceivably occur in conjunction with irradiation with large doses in a quantity that would keep the capillaries refractory to permeability-increasing substances for 20 hours. With the somewhat smaller doses, on the other hand, the refractoriness would have come to an end before this time.

Low-intensity irradiation

If the flash lamp results (fig. 4 F) are compared with those obtained with different lower intensities from the mercury arc (fig. 4 A—D), we find that the blueing starts to appear at approximately the same dose. With the low intensities the blueing shows no so sharply marked maximum as in the flash lamp experiments.

It seems that the degree of damage from comparable doses decreased somewhat with decreasing intensity. This could have several explanations. At the lower intensities with an irradiation time of several minutes it is easily conceivable that some type of protective mechanism, e. g. a vascular effect, has time to develop. Here it is also possible that injurious agents, which are liberated in smaller quantities per unit of time, are successively removed from the area.

The possibility also exists that the higher intensities might give rise to photochemical reactions of another type and thereby cause greater tissue damage. However, results from more simple systems do not indicate that the primary photochemical process is notably changed at the intensities used here, but, on the other hand, perhaps the concentration of the active intermediate substances becomes so high in the flash experiments that subsequent secondary dark reactions might be affected.

Effect of skin thickness on the results

In continued experiments during later months of the year (October, November) with another commercial albino stock, the animals proved to have thicker skin than those used earlier (May). The increased thickness of the skin was determined, after the skins had dried, by punching out a measured area (3.14 cm^2) and weighing it. The weight of the earlier skin used was $31 \pm 2 \text{ mg/cm}^2$. The later skin weighed $45 \pm 3 \text{ mg/cm}^2$.

The results of irradiation carried out in the manner described earlier are presented in figure 5. The flash lamp gave a more pronounced blueing than earlier, and no decrease was demonstrable with the higher doses. On the contrary, the blueing increased with increasing doses. Lower intensity irradiation (mercury arc) gave less blueing than flash lamp irradiation. As in figure 4 F, the dose-response curve was steep initially up to a maximum blueing, whereafter further increase of the dose gave no increase in blueing but revealed rather a tendency to a decrease. The minimum dose for blueing was, as earlier, approximately the same for the different intensities.

The altered shape of the dose-response curve for the flash may be explained if we assume that the observed thickening of the skin in toto also means a thickening of the epidermis. When the light passes through such a thickened epidermis, the absorption will be greater than earlier. This means both that a greater quantity of 'injurious substance' that might cause vasodilation and increased permeability is formed and that less light reaches the papillary layer where it can exercise its postulated vasoconstricting effect. Of course, a difference in reaction between the different stocks is also conceivable.

The more pronounced blueing at the flash lamp intensity as compared with the mercury lamp intensity might have the same explanations as those offered for thin skin above. However, since irradiation times (with the mercury lamp)

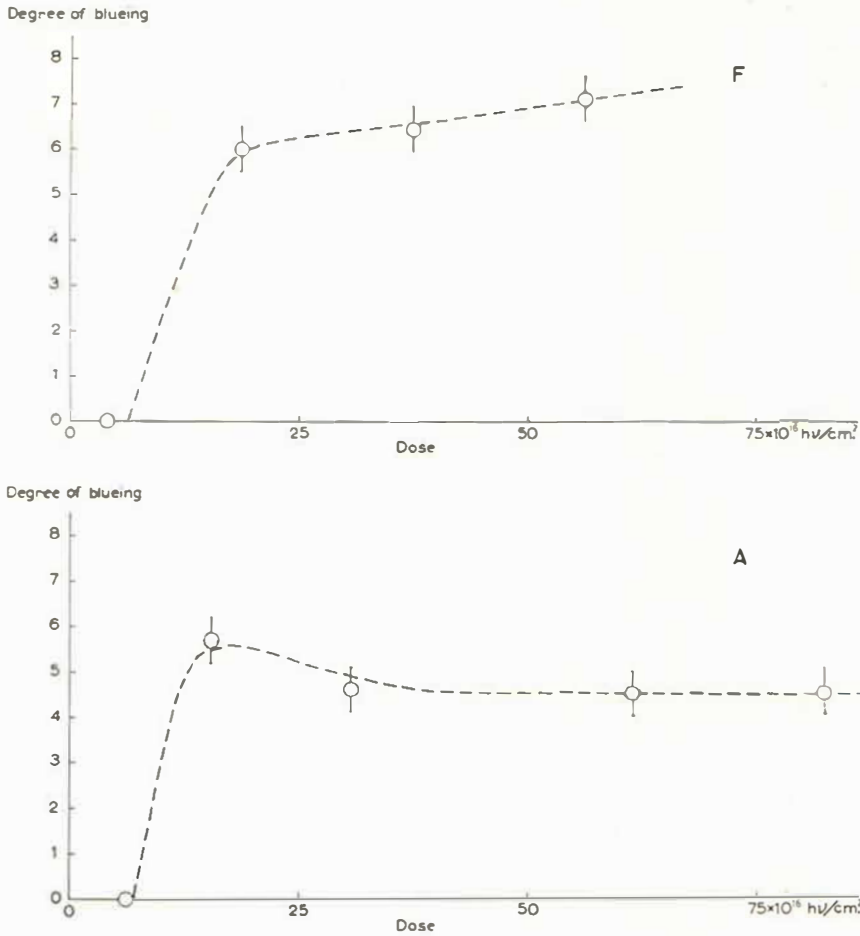


Fig. 5. Degree of blueing as a function of the dose for animals with thick skin irradiated with filtered light ($\lambda = 280 - 330 \text{ m}\mu$) at two different intensities. F) Flash lamp: Intensity 860 W/cm^2 . A) High pressure mercury lamp: Intensity 0.021 W/cm^2 .

of the order of 2 to 30 seconds are now involved, it is uncertain if the less extensive blueing after the mercury lamp irradiation can be explained by the hypotheses that a part of the liberated injurious substance might have had time to diffuse away or that some type of protective mechanism has had time to develop. The irradiation times are not short enough, however, to preclude the possibility of such explanations.

Effect of unfiltered flash irradiation on thick skin

A series of animals with thick skin, of the stock just described, were irradiated with the flash lamp without a filter. The results are presented in figure 6. We obtained a pronounced optimum; blueing was inhibited by increasing doses, similar to the effect obtained with filtered flash lamp irradiation on thinner skin (fig. 4 F). The spectral distribution for this lamp shows that in addition

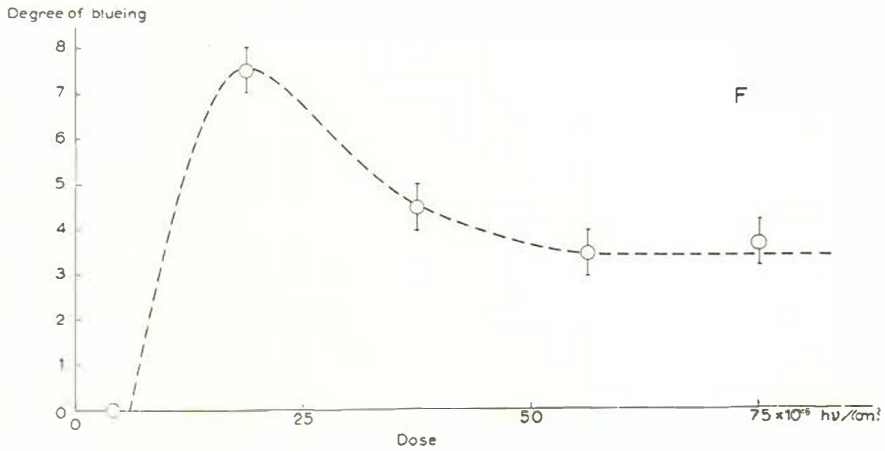


Fig. 6. Degree of blueing as a function of the dose for animals with thick skin irradiated with unfiltered light from the flash lamp. Intensity 1700 W/cm^2 .

to long-wave light we now obtain short-wave light down to shorter than $250 \text{ m}\mu$ (Claesson and Wettermark, 1957). How much short-wave UV-light effects the skin in the unfiltered experiments is uncertain. Short-wave UV-light is known to penetrate only the more superficial layers of the epidermis and should not reach the papillary layer (Blum 1945). It is possible, however, that the shorter wavelengths might have a higher quantum yield for the production of injurious substances. The decrease in blueing could then be explained by a mechanism similar to that produced by histamine (Miles and Miles 1952) and discussed earlier. The amount of injurious substances could then be so high that the papillary vessels are in a state of refractoriness to vasodilating stimuli.

Significance of skin irritation in UV-damage

In the experiments reported thus far the animals were shaved 24 hours before exposure. This precaution was taken as the shaving easily causes skin irritation that persists and affects the results if the irradiation takes place as soon as one hour after shaving. The following experiments illustrate this.

The results are presented in figure 7. The minimum dose is well defined and first appears in flash lamp irradiation in certain cases at a larger dose than earlier. The minimum dose for mercury arc irradiation is the same as before. The dispersion is wide in the results from larger doses, wherefore no conclusion concerning the continued course is possible from this material.

Further experiments are being carried out to determine the significance of skin inflammation in damage from UV-light irradiation.

The Reciprocity Law

From the previous sections it is evident that for wave-lengths around $310 \text{ m}\mu$ the minimum dose required to cause skin damage can be determined with accuracy from the curve giving the degree of blueing as a function of the dose.

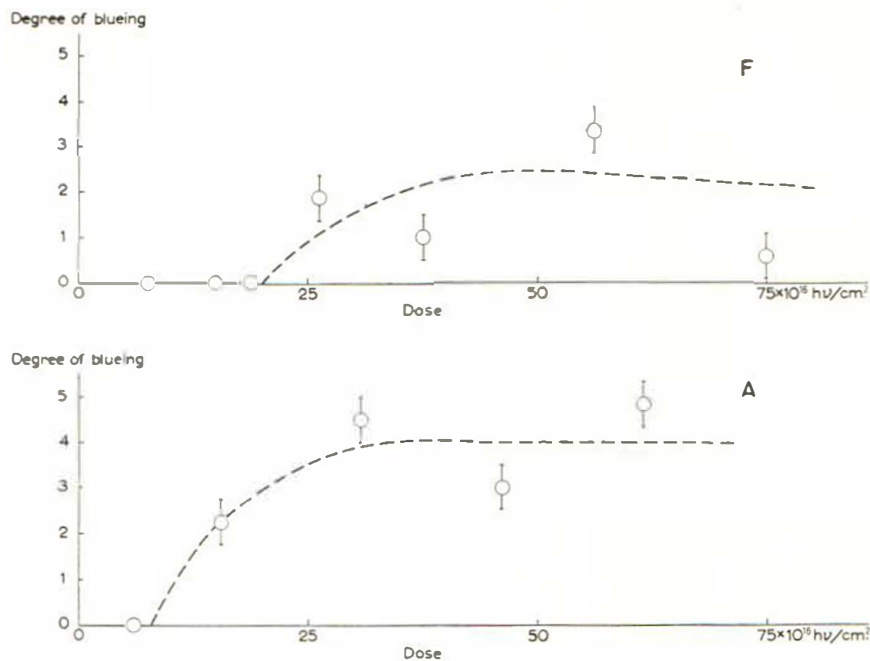


Fig. 7. Degree of bluing as a function of the dose for animals with an irritated (thick) skin, irradiated with filtered light ($\lambda = 280 - 330 \text{ m}\mu$) at two different intensities. F) Flash lamp: Intensity 860 W/cm^2 . A) High pressure mercury lamp: Intensity 0.021 W/cm^2 .

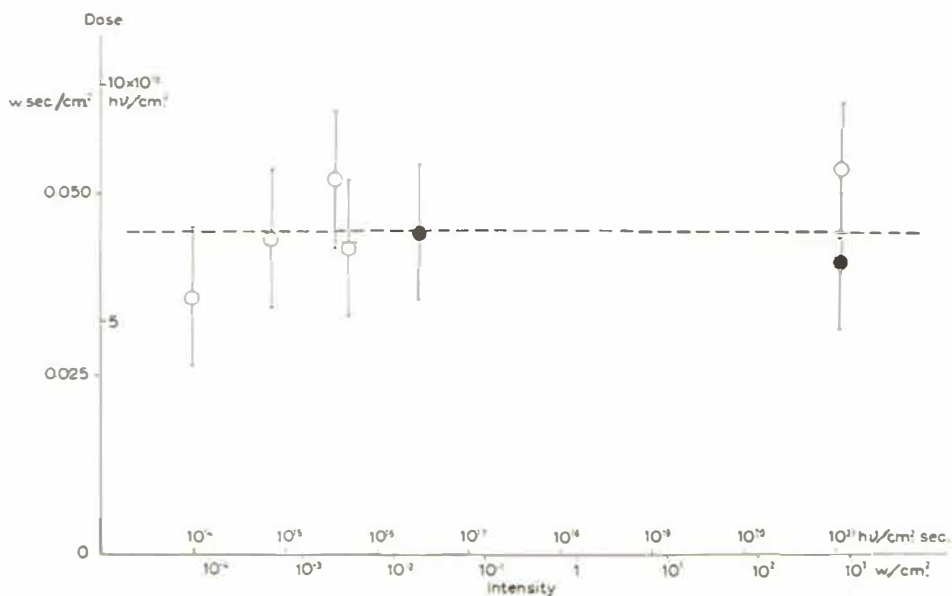


Fig. 8. The relation between light intensity ($\lambda \sim 310 \text{ m}\mu$) and minimum dose to cause tissue injury in mouse skin. \circ Thin skin. \bullet Thick skin.

It was found that this minimum dose and the degree of skin damage were affected if the skin was irritated by shaving or other means shortly before irradiation. However, for animals shaved 24 hours before irradiation the minimum dose was reproducible and was independent of skin thickness within the range investigated here.

It was found that this minimum dose is independent of the intensity of the incident light. This is evident from figure 8, where the minimum dose is plotted as a function of the light intensity. The length of the vertical lines represents an estimation of the errors in the individual determinations. *Consequently, it has been found that the reciprocity law is valid at $\lambda = 310 \text{ m}\mu$ over a ten millionfold variation in light intensity (0.000066 — 860 W/cm²). The minimum dose, 0.04 w/cm² is the same as that found in man at $\lambda = 253.7 \text{ m}\mu$ by Blum and Terus (1946 b) for the intensity range 0.00017 — 0.00001 W/cm².*

Acknowledgement

Part of this research was supported by grants from the *Rockefeller Foundation*. This is most gratefully acknowledged.

SUMMARY

The effect of UV-light on mouse skin has been investigated by studying the capillary leakage of intravenously injected Evans blue. A comparison between the effects of different intensities has been made. By using an extremely high-intensity photolysis flash lamp and a high-pressure mercury arc the intensities have been varied over 10⁷-fold range (0.000066 — 860 W/cm²). Both polychromatic and filtered (280 — 330 m μ) light has been used. The degree of blueing has been determined as a function of the dose at different intensities.

The minimum dose to cause blueing has been found to be independent of the intensity of the incident light over a ten millionfold variation in light intensity. Consequently the reciprocity law (minimum blueing dose = intensity \times irradiation time = constant) is valid at $\lambda = 310 \text{ m}\mu$ for this intensity region.

The importance of skin thickness and skin irritation during irradiation has also been investigated. In thin skin the blueing rapidly reaches a maximum value with increasing dose and then abates. A more sharply marked maximum is obtained with the higher intensities. The decreased blueing does not mean that the damage has been checked but is probably due to engagement of the finer blood vessels i. e. vaso-constriction or refractoriness to vasodilating substances.

In thick skin the filtered light from the flash lamp gave a more pronounced blueing but no decrease was demonstrable with the higher doses. However, when even higher intensities (available here only as polychromatic light) were used, the decrease in blueing at higher doses was again observed. The mechanism of these phenomena is discussed.

RÉSUMÉ

L'effet du rayonnement U. V. a été étudié au moyen du passage à travers les capillaires du bleue d'Evans injecté per voie intraveineuse. On a fait une comparaison entre les effets de différentes intensités. A l'aide d'une lampe de

photolyse de très haute intensité et d'un arc de mercure sous haute pression on a pu faire varier les intensités sur des ordres de grandeurs de 10^7 (de 0,000066 à 860 W/cm²). On a utilisé aussi bien la lumière polychromatique que filtrée (280 — 330 m μ). Le degré de bleuissement a été déterminé comme fonction de la dose à des intensités différentes. La dose minimum provoquant le bleuissement a été trouvée indépendante de l'intensité de la lumière incidente sur une échelle de grandeur de dix millions dans la variation de l'intensité lumineuse. En conséquence la loi de réciprocité: (dose de bleuissement minimum = intensité \times temps d'irradiation = constante) est valable à ≈ 310 m μ pour les intensités utilisées.

L'importance de l'épaisseur de la peau et de son irritation au moment de l'irradiation ont été également étudiés. Sur les peaux minces le bleuissement a rapidement atteint une valeur maximum avec l'accroissement des doses puis ensuite diminué. Un maximum plus fortement accentué est obtenu avec les intensités supérieures. La diminution du bleuissement ne signifie pas que l'agression a été arrêtée mais est probablement due à l'engagement des vaisseaux plus fins c'est à dire soit à une vasoconstriction ou à une résistance à l'action de substances vasodilatatrices. Dans les peaux épaisses la lumière filtrée de la lampe éclair donne un bleuissement plus prononcé mais il n'a pas été possible de mettre en évidence un abaissement avec les plus hautes doses. Cependant lorsque les plus hautes intensités furent employées (dans ce cas sous forme polychromatique) l'abaissement du bleuissement aux hautes doses a été à nouveau observé. Le mécanisme de ces résultats a été discuté.

ZUSAMMENFASSUNG

Es wurde die Einwirkung von UV-Licht auf die Haut von Mäusen untersucht durch intravenöse Injektion von »Evansblau« nach der Bestrahlung und Feststellung des Austrittes des Farbstoffes aus den Hautkapillaren. Der Zusammenhang zwischen Effekt und Intensität der Strahlung wurde festgestellt. Bei Benutzung einer Blitzlichtlampe sehr hoher Intensität und einer Hochdruck-Quecksilberdampf Lampe war es möglich die Intensität über 7 Zehnerpotenzen zu variieren (von 0,000066 — 860 W/cm²). Polychromatisches und gefiltertes (280 — 330 m μ) Licht wurde verwendet. Der Grad der Bläuung wurde bestimmt als eine Funktion der Dosis bei verschiedenen Intensitäten.

Die Minimumdosis die Bläuung verursacht wurde als unabhängig von der Intensität des einfallenden Lichtes gefunden, variiert über 10 Millionen Einheiten der Lichtintensität. Damit wurde das Reziprozitätsgesetz bewiesen (Minimum der Bläuungsdosis = Intensität \times Bestrahlungszeit = konstant) für eine Wellenlänge von 310 m μ und dem vorliegenden Intensitätsintervall.

Die Bedeutung der Hautdicke und Hautstörungen bei der Bestrahlung wurden ebenfalls untersucht. Bei dünner Haut wird schnell ein Maximum der Bläuung erreicht bei wachsender Dosis, die dann wieder abnimmt. Ein schärfer markiertes Maximum wird erhalten bei höherer Intensität. Die Abnahme der Bläuung bedeutet nicht eine geringere Schädigung, sondern ist wahrscheinlich bedingt durch Störungen der Blutgefäße, z. B. Zusammenziehung oder Resistenz gegen gefäßdilatierende Substanzen.

Bei dickerer Haut gab das filtrierte Licht der Blitzlichtlampe eine ausgeprägtere Bläuung, jedoch war kein Abfall bei höheren Dosen feststellbar. Bei Verwendung etwas höherer Intensität (hier möglich nur als polychromatisches Licht) wurde jedoch ein Abfall der Bläuung bei höheren Dosen wieder beobachtet. Die Ursachen für dieses Verhalten wurden diskutiert.

RESUMEN

Se estudió el efecto de la luz U. V. en la piel del ratón mediante inyección intravenosa de azul «Evans» después de la irradiación y comprobación del paso del colorante a los capilares cutáneos. Se confirmó la relación entre el efecto y la intensidad de la irradiación. Empleando una lámpara «flash» de gran intensidad y una lámpara de vapores de mercurio a presión, fué posible variar la intensidad en el orden de 10^7 (0,000066 — 860 W/cm²). Se utilizó luz policromática y filtrada (280 — 330 m μ). Se determinó el grado de intensidad de coloración azul como función de dosis en las distintas intensidades.

La dosis mínima capaz de producir azulado era independiente de la intensidad de la luz incidente, variable en más de 10 millones de unidades de intensidad lumínica. Con ello se comprobó la ley de reciprocidad (mínima dosis de azulado = intensidad \times tiempo de irradiación = constante) para una longitud de onda de 310 m μ y el intervalo de intensidad existente.

La importancia del espesor de piel y la alteración cutánea en la irradiación fueron igualmente investigados. En la piel fina se alcanza rápidamente un máximo de azulado con dosis progresivas, que luego disminuye. Un máximo más manifiestamente marcado se consigue con intensidades mayores. La disminución del azulado no significa una lesión menor, sino que se debida posiblemente a una alteración de los vasos sanguíneos, por ejemplo, a contracción o resistencia a sustancias vasodilatadores.

En piel más gruesa, la luz filtrada de la lámpara «flash» daba un azulado más manifiesto, aunque no se comprobó descenso alguno con dosis más elevadas. Empleando una mayor intensidad (sólo posible con luz policromática) volvió a observarse, sin embargo, una baja del azulado con dosis mayores. Se discuten las causas de este comportamiento.

REFERENCES

- Bachem, A. and C. I. Reed: *Am J. Physiol.* 1931, 97, 86.
 Blum, H. F. and W. S. Terus: *Am. J. Physiol.* 1946 a, 146, 97.
 — *Am. J. Physiol.* 1946 b, 146, 107.
 Claesson, S. and L. Lindqvist: *Arkiv Kemi.* 1957, 11, 535.
 Claesson, S. and G. Wettermark: *Arkiv Kemi.* 1957, 11, 561.
 Coblentz, W. W., R. Stair, and J. M. Hogue: *Bur. Standards J. Research.* 1932, 8, 541.
 Dekanski, J.: *J. Physiol. (London).* 1949, 108, 233.
 Halpern, B. N.: *Histamine. Ciba Found. Symp. London.* 1956.
 Hatchard, C. G. and C. A. Parker: *Proc. Roy. Soc. (London).* 1956, A 235, 518.
 Hausser, K. W. and W. Vahle: *Strahlentherapie.* 1922, 13, 41.
 Forbes, G. S. and L. J. Heidt: *J. Am. Chem. Soc.* 1934, 56, 2363.
 Lewis, T. and R. T. Grant: *Heart.* 1924, 11, 209.
 Lewis, T. and Y. Zotterman: *Heart.* 1926, 13, 203.
 Luckiesh, M.: *Trans. Illum. Eng. Soc. N. Y.* 1931, 26, 706.
 Menkin, V.: *Dynamics of Inflammation. MacMillan Comp. New York* 1940.
 — *Biochemical Mechanism in Inflammation. Ch. Tomas Springfield* 1956.
 Miles, A. A. and E. M. Miles: *J. Physiol. (London).* 1952, 118, 228.
 United States Atomic Energy Commission, 1950.
 Osterlind, G.: *Kgl. Fysiograf. Sällskap. Lund. Handl.* 1948. 59, No. 13.