

logical tests, it may be permissible to apply tentatively some of the findings reported for rabies and yellow fever viruses to the dengue problem. Chicks hatching from eggs inoculated with rabies virus between the 15th and 19th day of incubation either died or responded to persisting infection with production of antibody(10). Rabies virus was found to persist in the CNS of one such chick until the 27th day after hatching. Fox and Laemmert(2) did not test the CNS of yellow fever-infected chicks for virus, but found it in blood of several newly hatched chicks. Chicks which had viremia early in life later responded with antibody formation. Further work is required in order to establish whether infection with dengue virus follows a similar pattern.

The failure of hatched chicks to support multiplication of virus after intracerebral inoculation seems to fall in line with the observation that susceptibility of chick embryos decreases with progressing age. In this respect, the Hawaiian strain of dengue virus appears to simulate the 17D strain of yellow fever virus(2).

Summary. 1. The Hawaiian strain of dengue virus has been propagated in chick embryos through more than 90 passages in a series initiated with virus derived from the

101st intracerebral passage in mice. Certain characteristics of the infection of chick embryos have been described in this paper. 2. Susceptibility of chick embryos decreases with increasing age, highest titers being obtained in embryos 4 to 5 days old at the time of inoculation. 3. While sustained propagation of the virus in eggs initially required secondary incubation of more than 5 days, in later egg passages the virus attained maximum titers after 5 days. There was a slight decrease in viral concentration after the seventh day. 4. The infectivity of the virus for chick embryos is of the same order of magnitude as that for mice. 5. Infection with dengue virus does not result in discernible lesions in chick embryos, nor does it appear to affect their growth or their hatchability. 6. The concentration of virus in embryonic brain and spinal cord tissue is 100 to 1000 times higher than in other tissues, with minimal amounts found in extra-embryonic membranes and fluids. 7. Virus has been found to persist in the CNS of chicks until at least ten days after hatching, 22 days after inoculation into the egg. Minimal amounts of virus, much less than present in the CNS, have also been found in the blood of chicks two days after hatching.

Received March 12, 1951. P.S.E.B.M., 1951, v76.

Effect of Light on Urinary Coproporphyrin Excretion in Lead-Poisoned Rabbits.* (18642)

R. PIMENTA DE MELLO.† (Introduced by C. J. Watson)

From the Department of Medicine, University of Minnesota Hospital, Minneapolis, Minn.

Certain effects of ordinary light in patients and experimental animals with lead poisoning have been recorded in the literature. Pincussen(1) observed the effect of ultra-violet light (270 m μ), infra-red light and visible light on lead poisoned rats and mice. He

concluded that the exposure of these animals to the infra-red and visible light produces an increase of 10-20% in the amount of lead excreted in the urine. Pincussen also mentioned certain "chemical" effects of ultra-violet light in these animals, but did not specify their nature, and a further report has not been found. Rapoport and Rubin(2) studied lead poisoned rats and found that the

* Aided by Research Grant No. 345, U. S. Public Health Service.

† Fellow of the Guggenheim Foundation, New York City. (From the Instituto Oswaldo Cruz, Rio de Janeiro, Brazil).

1. Pincussen, L., *Klin. Wchnschr.*, 1933, v12, 275.

2. Rapoport, M., and Rubin, M. I., *Am. J. Dis. Child.*, 1941, v61, 245.

animals kept in the dark showed retardation of growth, but that they appeared "healthy" in that their coats were sleek and they were active. The animals exposed to sunlight were adversely affected in that there were skin and hair changes. They concluded, "the animal experiments further suggest that the photosensitizing action of sunlight on the increased amounts of porphyrin known to be present in persons with plumbism, may contribute in small measure to the seasonal incidence of severe lead poisoning".

The effect of light on urinary porphyrin excretion has also been investigated to a small extent. Thus Hager(3) studied the effect of light of 600-700 $m\mu$ on urinary porphyrin excretion. Although there was some indication of irregular increases, they were of questionable statistical significance. The purpose of the present study was to observe the effect of ultra-violet light and ordinary light on urinary coproporphyrin excretion in rabbits with lead poisoning.

Methods. Four adult rabbits of either sex were injected intraperitoneally with a solution of lead acetate (100 mg/kg body wt) in physiological saline solution. R21 received the lead subcutaneously rather than intraperitoneally. Five control rabbits similarly poisoned with lead were kept in the dark by covering the cages with black paper.

Other rabbits were irradiated with unfiltered light from a CH-4 Mercury arc lamp† of maximum ultra-violet intensity at 365 $m\mu$. The hair was shaved from the animal's back and the shaved area was irradiated for one hour at a distance of 12 inches. Additional control rabbits received the same amount of radiation, but did not receive lead.

The concentration of total urinary coproporphyrin was determined by the method of Schwartz and co-workers(4).

Results. The data for urinary coproporphyrin excretion in the rabbits receiving lead and kept either in ordinary light or in the dark

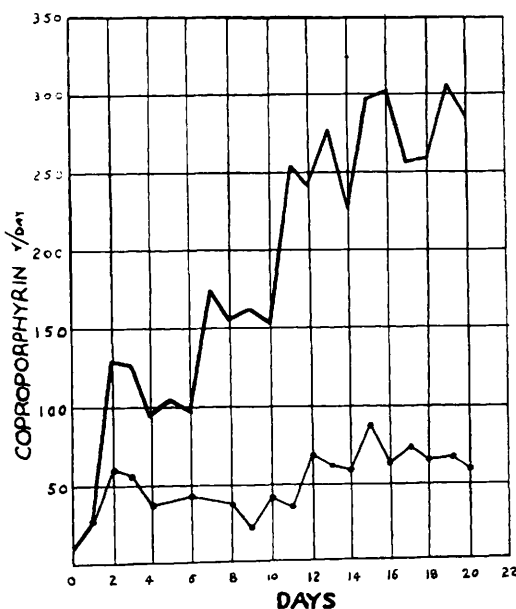


FIG. 1.

Average per diem excretion of urinary coproporphyrin in lead-poisoned rabbits kept either in daylight (upper curve) or in the dark (lower curve).

are summarized in Fig. 1. Average values for each of the 2 groups are plotted for the 20 days following the injection of lead.

In the group of lead poisoned rabbits exposed to unfiltered light from a CH-4 Mercury lamp, the urinary coproporphyrin excretion increases by about three fold after the first exposure. The subsequent exposures, however, produce but relatively slight increases. The data are given in Table I.

Three similarly irradiated control rabbits who were not injected with lead showed no increase in urinary coproporphyrin excretion; values ranged from 5-12 μg coproporphyrin per day during the subsequent 6-day period. The average pre-irradiation value was 7.5 μg per day.

Discussion. The present data clearly demonstrate the effect of daylight and of ultra-violet light in materially increasing the urinary coproporphyrin in rabbits with acute lead poisoning. The reason for this increase is not clear, but two possibilities are considered: (1) that the light in some way mobilizes excessive porphyrin already formed and present in the tissues, as a result of the lead poison-

3. Hager, B. G., *Klin. Wchnschr.*, 1939, v18, 1045.

† Black Light Products, Inc., Chicago, Ill., Model No. BL-2.

4. Schwartz, S., Hawkinson, V., Cohen, S., and Watson, C. J., *J. Biol. Chem.*, 1947, v168, 133.

TABLE I. Effect of Irradiation with Unfiltered Light from a CH-4 Mercury Lamp on Excretion of Urinary Coproporphyrin in Lead-Poisoned Rabbits. Urinary coproporphyrin in $\mu\text{g}/24$ hr.

Day	R18	R21	R23
10		250	210
11		275*	220*
12		950	550
13			520
14		480	480
15	110	450*	350*
16	150*	650	655
17	650	550	400
18	330	470	380
19	180	270	360
20	250	270	250
21	110	273	280*
22	160	150	360
23	80	80	200
24	110	82*	
25	180	200	
26	170*	90	
27	350	88	
28	390	88	
29		60	
30	150	60	
31	150*	50	
32	180	50	
33	210	50	
34	110		

* UV light exposure on day indicated. Lead given on day 0 in each instance. No analyses were made on days 1-14 on rabbit R18 and days 1-10 on rabbits R21 and 23.

ing, (2) that the light stimulates or brings about a rapid increase in coproporphyrin formation. The observation (Table I) of diminishing effect of repeated ultra-violet exposures, is compatible with either possibility,

as in the first instance it could be regarded as exhaustion of stored porphyrin, and in the second, of the cellular potentiality to make the excessive porphyrin. In a recent study of the urinary coproporphyrin in lead poisoned rabbits, carried out with the aid of glycine containing N^{15} (5) the findings indicated that the increased porphyrin was more likely formed as a result of the lead, rather than a heightened excretion of preformed porphyrin. In the present study, however, it is entirely conceivable that the effect of light is to increase the excretion of preformed porphyrin.

Summary and conclusions. 1. Light exposure increases the urinary coproporphyrin excretion in rabbits with lead poisoning. 2. The increase is especially marked after ultra-violet radiation. Subsequent radiation, however, fails to cause a renewed rise or is followed by only a small increase. 3. Whether the increase following light is due to mobilization of preformed porphyrin, or to increased porphyrin formation, has not been determined.

I am deeply indebted to Dr. C. J. Watson and Dr. Samuel Schwartz for many valuable suggestions, and interest in this work.

5. Grinstein, M., Wikoff, H. N., Pimenta de Mello, R., and Watson, C. J., *J. Biol. Chem.*, 1950, v182, 723.

Received September 25, 1950. P.S.E.B.M., 1951, v76

Sulfhydryl Inhibition as a Mechanism in the Effects of ACTH and Cortisone.* (18643)

GEORGE E. ANDERSON, LEON L. WIESEL, ROBERT W. HILLMAN, AND WILLIAM M. STUMPE. (Introduced by S. Seifter)

From Department of Medicine, Brooklyn Hospital, Brooklyn, N. Y.

Suppression or partial inhibition of cellular enzyme systems seems to be at least one widespread mechanism of action of the C_{11} -oxygenated adrenal-cortical steroids. The demonstrated disrupting effect (1) of these steroids on phases of carbohydrate metabolism may

well be mediated thru inhibition of enzyme systems essential to the normal processing of glucose by the organism. If such inhibitory effect is as widespread as is suggested, it

* Aided by a grant from the Mezger Pharmacal Co. Ascorbic acid supplied by Hoffmann-La Roche.

1. Conn, J. W., *J. Lab. and Clin. Med.*, 1948, v33, 651; Lazarow, A., *PROC. SOC. EXP. BIOL. AND MED.*, 1946, v61, 441; Conn, J. W., Louis, L. H., Johnston, M. W., *Science*, 1949, v109, 279.