students. The daylight screen now on the market has several objectionable features: in the first place, its lines are too coarse, thus destroying the details and also producing a glaring streak of light across it; in the second place the greenish tint destroys the true color value in arc-light projection; and in the third place the screen is too expensive. A screen which presents none of these objectionable features can be had in a piece of paraffined tracing-paper, a piece of paraffined tracing-cloth or a ground-glass plate.

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SPECIAL ARTICLES

THE PHOTOACTIVITY OF SUBSTANCES CURATIVE OF RICKETS AND THE PHOTOLYSIS OF THE OXY-PRODUCTS BY ULTRAVIOLET RADIATION

THE demonstration by Huldschinsky[1] and others that radiation with the quartz mercury vapor lamp or sunlight prevented and cured rickets, was a great advance in the knowledge of that disease. It had been proved also that cod liver oil prevents and cures rickets[2] and therefore the dilemma presented itself that two therapeutic agents apparently unrelated cure the disease. The one, a physical force derived from the sun, is absorbed through the skin, the other, an oil taken from the liver of a fish, enters the body by way of the alimentary tract. Nevertheless, investigation soon showed that in their action in rickets and infantile tetany radiant energy and cod liver oil are indistinguishable. No matter which of these apparently dissimilar therapeutic agents is employed, favorable clinical and roentgenological evidences of healing in rachitic subjects are demonstrable. With both, there is a similar latent period; with both, the normal equilibrium of calcium and inorganic phosphorus of the blood is reestablished; and furthermore, with both, the histological changes in the skeleton are identical. The similarity of the action of radiant energy and cod liver oil is so striking as to cause Park, Powers and Guy[3] to conclude, "The similarity between the action of cod liver oil and that of radiant energy in rickets is so close that a connection must exist between them. So far as the calcium and phosphorous metabolism of the body are concerned, cod liver oil seems to be a substitute for radiant energy. It will be most interesting to see if, in the near future, a relation between cod liver oil and radiant energy will not be established of such nature that these effects will be explicable on a single basis."

Investigations were therefore undertaken to determine the possible common property of radiant energy and the various substances curative of rickets. The present data is representative of a series of preliminary experiments for qualitative orientation and serve as a basis for quantitative study.

A. *The Emission of Ultraviolet Radiation by Substances Curative of Rickets.*

Method. Substances curative and non-curative of rickets were tested for their emission of ultraviolet light. They were placed in beakers and covered with specially prepared photographic plate holders. The plates were exposed to each substance for twenty-four hours, developed with pictol,[4] fixed, washed and dried.

The plate holder consisted of a shallow lead box of a size just large enough to admit the four inch by five inch photographic plate and a closely fitting cover of the same material. In the floor of the lead plate holder a hole two centimeters square was cut to allow the formation of a sharp photographic image. A quartz plate, either fused or transparent, was sealed over this aperture in such a way as to prevent the permeation of volatile substances from the test materials. Similar holders were made with glass screens. Ultraviolet sensitive plates[5] coated with a very rapid emulsion (Seed Graflex 60) were placed with the film surface in apposition with the quartz or glass screen and then covered by the lid. Each beaker covered by this plate holder was placed within a light-proof container which in turn was placed within a second light-proof container.

Three series of experiments were carried out on each substance. In the first series the substances were made alkaline with ten per cent. potassium hydroxide and this mixture was oxidized by bubbling through it a current of pure oxygen. In the second series the substances were untreated. In the third

[1] Huldschinsky, K., Deutsche med. Woch., 1919, XLV, 712; Zeitschr. f. Orthop. Chir., 1920, XXXIX, 426.

[2] Schabad, J. A., Zeitschr. f. klin. Med., 1909, LXVIII, 94; Shipley, P. G., Park, E. A., *et al.*, *J. Biochem.*, 1921, XLV, 343. Park E. A., and Howland, J., Johns Hopkins Hosp. Bull., 1921, XXXII, 341.

[3] Park, E. A., Powers, G. F., and Guy, R. A., *Am. J. Diseases Children*, 1923, XXVI, p. 111.

[4] Dissolve 3 oz. of desiccated sodium sulfite in 16 oz. distilled water and add this to a solution of 150 grains of hydroquinone in 8 oz. of distilled water. This constitutes solution A. Dissolve 2 oz. of potassium carbonate and 60 grains of potassium bromide in 16 oz. of water. This constitutes solution B. For use mix three parts of A with two parts of B.

[5] These are being replaced by Schumann plates for photographing the extreme ultraviolet region since gelatin exercises a very powerful absorptive influence upon rays of short wave length.

series they were reduced by ammonium ferro-tartrate. The beakers covered by the plate holders were placed in desiccators containing alkaline pyrogallol and were subsequently evacuated. These three series will be referred to as oxidized, untreated and reduced.

TABLE I

RESULTS OF THE FOGGING OF PHOTOGRAPHIC PLATES EXPOSED TO SUBSTANCES CURATIVE AND NON-CURATIVE OF RICKETS

Reaction	Substances Curative of Rickets			Substances Non-Curative of Rickets		
	Quartz screen	Glass screen	No screen	Quartz screen	Glass screen	No screen
Oxidation	+	0	+	0	0	+
Air Autoxidation	+	0	+	0	0	+
Reduction	0	0		0	0	

Results. The following substances curative of rickets—cod liver oil,[6] non-saponifiable fraction of cod liver oil,[7] oxidized cod liver oil treated to destroy Fat Soluble A,[8] egg yolk,[9], bile,[10] hydroquinone,[11] and sperm oil,[12]—when oxidized produced a definite blackening on photographic plate screened by quartz but not on those screened by glass. The substances non-curative of rickets, namely linseed oil,[13] peanut oil,[13] cotton seed oil,[13] lard,[14] the saponifiable fraction of cod liver oil,[7] and also crude oil, albolene and glycerine when oxidized did not affect the photographic plate through either quartz or glass. All oxidized substances examined fogged plates exposed to them without a screen.

The untreated substances curative of rickets blackened a sensitive plate through quartz but not through glass, on spontaneous autoxidation by the air within the beaker. The intensity of the image was not so marked as with the oxygenated substances. The untreated substances non-curative of rickets did not fog the plate through either quartz or glass.

The reduced substances curative and non-curative of rickets did not fog the sensitive plate through quartz or glass. The substances curative of rickets whose absorbed oxygen was removed by bubbling carbon dioxide through them under reduced pressure produced but very slight fogging of the plate.

Blood also fogs the photographic plate through quartz but not through glass. The degree of blackening increases with the rate of oxidation and decreases when oxidation is prevented by passing carbon dioxide through the blood.

B. *The Liberation of Oxygen from the Oxidized Substances Curative of Rickets by Ultraviolet Radiation.*

Oxidation resulted in the production of ultraviolet rays and therefore an attempt was made to determine the reversibility of this reaction. The substances curative of rickets which were oxidized in alkaline media were placed in a quartz test tube connected to a Torricellian mercury column and radiated by ultraviolet light at room temperature for three hours. Under the influence of the radiation a continuous formation of gas bubbles within the quartz tube was observed with a gradual dropping of the mercury caused by the gas formed. This was found to be oxygen.

The photo-chemical equilibrium in an unstirred solution that absorbs all active ultraviolet radiation is independent of the intensity of illumination, as would be expected, but is entirely dependent upon the extent of the surface exposed to the light source.[15]

Photolysis of the oxy-substances curative of rickets was not detectable in solutions that had been exposed to the ultraviolet light through glass test tubes which transmitted none of the shorter wave lengths.

Therefore, the reaction which takes place when substances curative of rickets are radiated with ultraviolet light seems to be the reverse of that obtained in the previous experiments, namely the emission of ultraviolet radiation upon oxidation.

Summary. The data presented show that the substances curative of rickets, upon oxidation blacken sensitive plates through quartz but not through glass screens. This phenomenon is undoubtedly due to the emission of ultraviolet radiation. The interposition of quartz plates excludes the effect of reducing vapors which otherwise blacken the sensitive plate. The non-

[6] *Loc. cit.*

[7] Zucker, T. F., Pappenheimer and Barnett, *Proc. Soc. Exp. Biol. and Med.*, 1922, XIX, 167.

[8] McCollum, E. V., Simmons, Nina, Baker, J. E., *J. Biol. Chem.*, 1922, 53, 293.

[9] Hess, Alfred F., *Proc. Soc. Exp. Biol. and Med.*, 1922, XX, 369; Casparis, H., Shipley, P. G., and Kramer, B., *J. Am. Med. Assoc.*, 81, 818, 1923.

[10] Kapsinow, R., and Jackson, D., *Proc. Soc. Exp. Biol. and Med.*, 1924, XXI, p. 472.

[11] Huston, A. C., and Lightbody, H. D., *J. Ind. and Eng. News*, April, 1924.

[12] Personal communication from Professor E. A. Park. —"So far as we are aware, sperm oil has never been tested for anti-rachitic property. However, Drummond (Biochem. J. XVI, 518, 1922) found it to contain Fat Soluble A. It is highly probable that the oils of all fish have anti-rachitic properties."

[13] Mellanby, E., British Med. Research Council Report No. 61, 1921, 22.

[14] Personal communication from Professor E. A. Park. —"Lard has no specific anti-rachitic effect." (Unpublished work).

[15] W. T. Anderson, Jr., *J. Am. Chem. Soc.*, 1924, 46, 801.

blackening through glass screens excludes the emission of both radioactive and visible rays. The necessary conclusion is that upon oxidation ultraviolet rays are produced.

The degree of blackening is apparently a function of the rate of oxidation for the intensity of the image from vigorous oxidation is greater than that from spontaneous oxidation within a given time. The blackening is also a function of the hydrion concentration for the intensity of the image is greater from alkaline medium than from neutral or acid media.

The experimental data further show that the oxidized substances curative of rickets when exposed to ultraviolet radiation liberate oxygen. Therefore the photochemical reaction appears to be reversible and may be expressed by the equation, Oxygen + Rickets-curing Substances $\rightleftarrows$ Oxy-Substances + Ultraviolet Rays.

These experiments point strongly to the common property of emitting ultraviolet rays, of cod liver oil, egg yolk, sperm oil, bile, hydroquinone on the one hand and of sunlight or quartz mercury vapor radiation on the other, as the basis for their identical curative action in rickets.

The experiments recorded may be applicable to physiologic phenomena in general. Not only do they suggest the mechanism common to all rickets-healing processes and imply a method to measure the therapeutic potency of the curative agents but they also disclose the fact that solar energy exerts a hitherto neglected function in the physiology of higher organisms as well as in plants.

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THE EFFECT OF INTRAPANCREATIC ADMINISTRATION OF GLUCOSE ON THE BLOOD SUGAR CURVE

THE normal stimulus to the assumed insulin-producing function of the island tissue of the pancreas is as yet undemonstrated. A possible stimulus is the sugar carried to the gland by the blood. Work already published from this laboratory has paved the way for a direct attack upon the problem.[1] The curve of the change in sugar concentration during the two or three hours following the ingestion of glucose has long been used by clinicians as evidence in the diagnosis of underfunction of the insular tissue. Since the rate of absorption of ingested sugar into the blood stream can not be controlled, however, continuous intravenous injections of glucose at the rate of 0.7 gram per kilo of body weight per hour were used, and the course of the curve of blood sugar concentration was studied during the injection. Dogs were used for the experiments. The sugar was introduced into a superficial leg vein. A total of 30 to 50 blood samples was taken during an injection period of two and a half to five hours. These were analyzed in duplicate by the Schaffer-Hartman method. The blood sugar curve thus determined was of materially different form from curves following the alimentary administration of glucose. The typical alimentary curve, as is well known, rises in the first half hour, then returns to fasting level in about three hours. The curves during continuous administration by vein rose similarly but remained elevated throughout the period of injection. Twenty-two such experiments yielded only one curve that returned to the initial level. Having established the average level reached and maintained by the blood sugar curve during injection into a peripheral vein, it was sought to subject the pancreas to a higher concentration of sugar in the blood without, however, increasing the quantity injected, by introducing the sugar into an arterial channel leading to the pancreas.

The animals were anesthetized with isoamylethyl barbituric acid, a substance reported to be without disturbing effect itself upon the blood sugar level.[2] This report was verified in several experiments in which the original route of injection, into a peripheral vein, was used. In the experiments here reported glucose solution was directed into the blood stream supplying the pancreas by injecting it centrally into a collateral duodenal branch of an artery supplying the tail of the gland, or else by injecting it upstream into the splenic artery, and thus via another branch of the celiac axis into the pancreatic circulation.

Eight technically successful experiments have been performed. Four of the resulting curves were not greatly dissimilar to those obtained during injection into a leg vein. Four others, however, rose to a height either equal to or below the average level reached during peripheral injection, then fell steadily to and below the initial level, despite the continuation of the injection. In form and in duration these latter curves closely resemble those resulting from administration of the sugar by mouth. One of these showed so little elevation as to suggest the type seen after alimentary administration of fructose. These four curves are interpreted as evidence of a greater discharge of insulin than occurred in the experiments in which injection was made by peripheral vein.

Further investigations of the problem are in progress.

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[1] E. C. Albritton, *Am. J. Physiol.*, 1924, in press.

[2] I. H. Page, *J. Lab. & Clin. Med.*, 1923, 9, 194–196.