INFLUENCE OF ULTRAVIOLET IRRADIATION UPON EXCRETION OF SEX HORMONES IN THE MALE

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INFLUENCE OF ULTRAVIOLET IRRADIATION UPON EXCRETION OF SEX HORMONES IN THE MALE

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A wealth of studies on the influence of light upon the sexual cycle, pituitary activity, fertility, etc., have been carried out in recent years (1). Among the external factors which are susceptible of influencing sexual activity, light varying according to seasons and climates is included by Benoit (2) as of first importance. Observations by Bissonnette and Csech (3) that hens with additional light during the night start egg laying several months earlier than breeds of the same age but without additional light, have been confirmed and are now completely accepted.

Bissonnette, as well as Benoit, stresses the opinion that stimulation of the pituitary is the primary effect of increased light, and that the pituitary in turn increases the activity of the gonads. Hoskins and Rioch (1), discussing Bissonnette’s paper, object to this idea, believing that there are different ways of explaining the experimental results.

The work of Witschi (4), and of Riley and Witschi (5), is important in several respects. These authors conclude from their experiments that there is only a low degree of responsiveness of the female pituitary to light if a 100-watt incandescent bulb is applied. Light applied for long periods gave no greater results than when applied for short periods. One result of the investigation of these authors may be stressed, namely, that “it appears that the ovary of the bird is harder to stimulate than the testis.” Moreover, Witschi (4), in his earlier work, mentions several of his own observations in different groups of birds which indicate that “if light has any influence, then this group of birds reacts to shortening and not to lengthening the day.” Marshall (6) reports similar observations in birds as well as in sheep and deer. Thus, although there is little or no doubt that light exerts an influence upon the sexual cycle, there still is doubt as to the manner in which its influence in different species is exerted, and whether increasing or decreasing light is of importance.

It must be stated that there is no agreement concerning the question whether irradiation of the skin is important in exerting an influence upon the sexual cycle or not. Parkes (7), in a different connection, states that the peculiarity of the Seabright Bantam lies in the skin which is highly sensitive to estrogens. Bissonnette (1), on the other hand, states that irradiation of the bare skin is negligible in its effect in comparison with the mode of entrance of the light rays through the eyes (photopituitary reaction).

More closely related to our own experiments is the controversy whether ultraviolet irradiation is more potent than other forms of irradiation. While Bissonnette found that ultraviolet irradiation is not effective or necessary in starlings, Marshall

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(6), on the contrary, found that ultraviolet irradiation was much more effective than luminous irradiation; that ultraviolet irradiation caused a prolonged result after the irradiation had ceased. "The presumption is that ultraviolet irradiation has a semi-permanent influence on the hypophysis which is thereby made to undergo a prolonged period of hyperpituitarism in regard to the production of the gonadotropic hormone." Baker (according to Marshall) suggested that a similar influence may account for the two breeding seasons of many tropical birds, "these seasons occurring at times when the ultraviolet radiation from the sun is probably at its greatest." Rowan (8) in his recent paper states that a standard electric light gives the same results in sparrows as an ultraviolet sun-lamp.

Applying these physiological results in animals to man, we are thus faced with the following questions.

a), Does ultraviolet irradiation exert an influence upon the formation and excretion of sex hormones?

b), If so, is the irradiation of the skin the most important single factor, or is the photo-pituitary reaction of greater importance?

c), The third question with which this paper deals is, what influence is exerted by ultraviolet irradiation of presumably indifferent parts of the skin as compared with irradiation of the genital region?

PROCEDURE

A small, quartz, mercury lamp, now on the market, was used. According to the information from the factory, the spectrum of this lamp consists of 52% infrared, 20% luminous and 28% ultraviolet rays. The duration of exposure to the light was 8, 10, 12, 15, 18 and 20 minutes, each succeeding exposure being increased over the preceding one. There was in the majority of cases a marked erythema but no undesirable skin reaction and the procedure of increased exposure could be applied in all cases.

We started with a group of patients, improvement of whose general condition by ultraviolet irradiation we believed would have a beneficial influence upon their mental state as well as bearing upon the experimental problem. All patients suffered from depressive states; 3 patients were 54 years of age, representing depressive phases of manic-depressive psychosis; 2 patients were 28 and 45 years of age respectively, psychopathias with depressive features. The history of the cases may be omitted.

As shown below, successively different parts of the body were irradiated, namely, the anterior part of the body including chest, face and genitalia; chest and head alone; genital region alone; total back; and a small portion of the back in the region of the scapulae corresponding in size to the area of the genitalia. The non-exposed parts of the body were covered either by the garments and underwear of the patients or by dark clothes.

For the determination of sex hormone excretion, we followed the method recently published by one of us (9). A similar colorimetric method was published a few months ago in England by Callow (10). The advantages of colorimetric methods over biological assays for serial examinations are manifold. The exactness of the colorimetric assay is as great as that of the biological methods and probably in the near future will be greater.

We have collected some data on 'female' hormones, but this report deals only with the formation and excretion of androsterones in urine. Since nothing is known at the present time about the storage of male sex hormones in the body, their greater excretion may be regarded as an indication of their greater formation in the body, although this is not certain.
EXPERIMENTAL RESULTS

The results in our group of patients up to the present have been surprisingly uniform. Figure 1 demonstrates the typical reaction. The androsterone excretion, determined twice before starting irradiation, was about 70 I.U. androsterone per liter (and approximately per day). After 5 irradiations of the chest, the hormone output was raised to 155 I.U. per liter, that is, an increase of 120%. These 5 irradiations were given in 5 consecutive days in the usual manner of application of ultraviolet light for medical purposes, namely, the eyes are closed and, in addition, covered with dark glasses. In this particular case, head, chest, genitalia and thighs were exposed to irradiation, the light being focussed on the lower thorax and upper abdomen. After an interval of 8 days without irradiation, the hormone output went back to its previous level of about 70 I.U. androsterone per liter. Three more irradiations, given over a period of 5 days, raised the hormone level from 70 to 140 I.U. per liter (fig. 1). After an interval of 5 days without treatment, the output fell back to 80 I.U. per liter, and another examination 2½ weeks later showed it to be again 70 I.U. per liter.

The next series of irradiation was applied solely to the genital region and its immediate vicinity, the remainder of the body being carefully protected from all rays. After 5 irradiations during 6 days, the androsterone excretion was raised from 70 to 205 I.U., nearly 200%. Five more irradiations during the next 5 days did not further raise the hormone output, but it persisted at nearly the same level. After another 10-day interval without irradiation, the hormone output went back to its 'normal' level of about 70 I.U. per liter (fig. 1).

The findings in this case merit the emphasis of repetition, namely, that 5 irradiations are more effective than 3 irradiations; furthermore, that 10 irradiations are not more effective than 5 irradiations. We must assume that the peak of the reaction is reached either by 5 irradiations or at about that number. Finally, it is to be stressed that irradiation of the genital region is more effective than irradiation of other, even much larger, parts of the body.
In all cases in which irradiation was applied on consecutive or nearly consecutive days, a peak was found after about 5 irradiations. A case in which irradiations were applied twice weekly at first and later only once weekly did not show the peak after 5 irradiations, but rather a continuous rise during the whole period of treatment which reached the number of 12 irradiations.

That the greater response after irradiation of the genital region is not caused by a previous sensitization of the pituitary is shown by figure 2, in which the series of irradiations of the genital region was first applied, and in a second series head and thorax were exposed and the genital region covered. As on the previous occasions, irradiation of the genital region proved to be more effective (a rise from 110 to 320 i.u. per liter after 6 irradiations), than irradiation of even much larger, non-genital parts of the body.

Although irradiation of the head, thorax and abdomen gave an appreciable rise (from 90 to 240 i.u.), it was impossible to raise the level of hormone output by further irradiation of the chest to the height reached by irradiation of the genital region (fig. 2).

Irradiation of various non-genital parts of the body gave identical results if the size of the irradiated parts was identical, for example, a rise from 70 to 150 i.u. per liter after irradiation of the front of the body from the forehead to the umbilicus or a rise from 90 to 180 i.u. per liter after irradiation of the neck and back.

In order to corroborate the observation made from the above mentioned experiments, namely, that irradiation of the genitals and their vicinity is more important than irradiation of other parts of the skin, the following procedure was carried out in 2 patients. First, the patients received 5 irradiations of the region of the scapulae over an area of about 20×50 cm., the
rest of the body being covered. After an interval of 8 days without treatment, the same patients received 5 irradiations of the genital region, about the same square area being exposed and the rest of the body completely covered. Figure 3 shows this result clearly, namely, that after irradiation of a small area of the back, there is no rise of the hormone excretion in the urine, while irradiation of an area of the same size in the genital region shows a definite rise of the androsterone excretion.

It may be added that the rise in female hormones is slower, lower and more retarded than that of male hormones; but our observations concerning female hormones are only casual and incomplete.

**DISCUSSION**

In discussing our experiments, we may first state that any relation of the depressive mental states of our patients to the formation and excretion of male hormones is not discernible. It may be said, however, that the ultraviolet irradiation and/or the increase of hormones exercised a good influence on the 2 patients who were not true manic-depressives, while the mental state of the other 3 patients remained unaffected.

A question which might be discussed first is whether the observed changes are of any significance at all or whether they are rather physiological variations. Gallagher and his coworkers (11) found in one individual a range of variation from 13 to 69 i.u. androsterone per day, and similar variations in other individuals. From findings of this kind, one might conclude that variations of the degree of our findings were insignificant, but we cannot confirm the findings of Gallagher et al. On repeated urine examinations of the same individual, either on consecutive days or after weeks or months, we obtained results of a highly constant uniformity. Gallagher's and our findings are not necessarily contradictory, although they seem to be. If hormone excretion is partly dependent on external influences, then it is not surprising that there is a range of variation in the free-living individual. On the other hand, we are here dealing with hospitalized patients, all of whom live for months under constant conditions. The uniformity of their living conditions may explain the uniformity of our findings in repeated urine examinations. Therefore, we can regard our patients as living under fairly good experimental conditions, the only change or new variable being the application of ultraviolet irradiation. From the sum total of our experience, we may safely state that under the circumstances in which our patients live, the uniform change in the excretion of androsterones is definitely significant and not coincident.

Another point may be stressed, that is, a possible seasonal factor which might influence our results. Our experiments were carried on from November 20, 1938 to February 10, 1939, a season with a low degree of sunshine. It is a problem for later investigation whether the experiments can be repeated with the same result in the spring or summer.

It is not the purpose of this paper to discuss the value of colorimetric hormone assays in detail. Callow, Callow and Emmens (12) state "that the correlation between biological and colorimetric assays is not much less than that between biological assay and the true amount of androgenic material
present” and later “there remains no doubt, however, that the greater part of the departure of the correlation between colorimetric and biological assays from unity is due to the errors of biological assay.” These citations check with our own experience. We found that the main chromogens in urine which might influence the reaction with Zimmermann’s (13) reagent are removed by the kind of extraction applied. We do not wish to discuss in more detail at this point the value of the colorimetric measurement of androsterone-excretion but only to stress that our experience with this kind of assay is both favorable and reliable. However, a series of biological assays will be carried out as soon as a new series of patients is started.

The next question which merits discussion is whether it is the ultraviolet part of the light band which causes the increase in excretion of androgens. To speak of ultraviolet irradiation in the everyday practice of medicine is to mean the application of the mercury quartz lamp. There are many hints that it is really the ultraviolet part of the spectrum which is of the greatest importance in bringing about the result observed. But a further investigation by the use of narrow and selected spectral bands is planned.

There is plenty of room for speculation as to whether and how the cholesterol and possibly other sterols of the skin are mobilized by irradiation and transformed to sex sterols. But this is mere speculation and our experiments disclose no mechanism of production of sex hormones except that the genital zone is particularly important. The thin and transparent scrotum may not absorb the ultraviolet rays entirely and the testes may be directly stimulated to higher activity. There is no evidence, however, that the pituitary plays an important rôle in the stimulation of increased androsterone formation and output in our experiments.

**SUMMARY**

Ultraviolet irradiation applied with a mercury quartz lamp increases the excretion of androsterone in urine. Measurements were made colorimetrically. Irradiation of the scrotum and its vicinity proves to be more effective than irradiation of other parts of the skin. Our experiments furnish no proof that the pituitary plays a primary rôle in the stimulation of increased androgenic activity.

**REFERENCES**