SOME REMARKS ON THE HORMONAL TREATMENT
OF KRAUROSIS-CANCER VULVAE

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Useful informations have been obtained in clinical gynecology by the modern endocrin laboratory tests, viz.
1) endometrial biopsy,
2) vaginal smears,
3) examination of the a) bacterial flora, b) the pH, c) the glycogen content in the vagina and d) examination of the cervical mucus,
4) biological and chemical hormone analyses of gonadotrophins, oestrogens, androgens, progesteron and 17-ketosteroids.

Until recently it was considered that the action of the ovarian sexual hormones were completely abolished in women past the menopause, but research using various endocrin tests has in later years shown that the female organism even after the menopause is under stimulation of oestrogens, androgens and in rare cases of progesteron.

At the menopause the ovulatory cyclic ovarian activity ceases but the sexual stimulation persists more or less continuously, normally decreasing. The origin of the sexual hormones after the menopause may be the ovaries (granulosa cell tumors, thecomata, stromal cell hyperplasia of the ovaries, etc.) but in the majority of cases it is the X-zone of the suprarenal cortical area which takes over the secretion of sexual hormones after the menopause. This zone in the suprarenal bodies has therefore been called »the third gonade« (Botella Llusia, 1956).

Endometrial biopsy and vaginal smears after the menopause show great individual variations in the sexual hormonal stimulation of the female genital organs (Pundel, 1952). It has been declared that »chaque femme fait sa ménopause a sa façon comme le dormeur fait ses rêves« (Dalsace, 1956). Pende has differentiated certain characteristic postmenopausal types or endocrine syndromes: 1) Cushingoid, 2) myxoedematous, 3) hyperthyreoid, 4) acromegaloid, 5) dia-
betic types, and as to the sexual hormones the 6) hyperestrogenic, 7) viriloid and 8) the senil atrophic types (Pendle, 1956).

Certain pathological hormonal deviations during and after the menopause have in later years been put in relation to the genesis of cancer of the female genital system.

With the exception of cervical cancer which is of obvious exogen etiology, cancer of the ovary and tubes and the breasts seem to be hormone-dependent cancers. As to endometrial cancer clinical and experimental research suggest that the genesis may be associated with a continuous estrogen stimulation.

Cancer of the vulva is a rather rare form of cancer and occurs predominantly in women after the menopause with complete lack of any hormonal sexual stimulation of the genital mucous membranes. Its tendency to develop in known precancerous lesions – vulvitis senilis, leukoplakia, kraurosis – makes it exceptional among tumors of the genital tract (Way, 1951).

Its tendency to multiple separate primaries and the tendency to recur after radical surgery is very interesting (Mouloungut, 1954). This high frequency of recurrences does not occur due to microscopical residues left after radical surgery but must be considered as new cancers. Clinical findings suggest that the pathogenesis must be associated with a persistence of a hypo-hormonal state of the genital mucosas.

A very important question arises hereby. May the precancerous lesions or cancer and its tendency to recurrences be prevented if the morphology of the mucosa can be changed by adequate endocrin therapy?

To elucidate this problem a case history is presented:

A 37 year old married woman had in 1941 an X-ray menopause because of heavy menstrual bleedings. The menopause provoked severe climacteric symptoms and an atrophic state of her genital organs with infectious complications: vulvitis, kopolitis. Her chief complaints were: itching, discharge, dyspareunia. Various treatments were performed, but in vain. At last she developed the typical leukoplacik-kraurotic appearance of the vulvar mucosa and was admitted in 1947, 43 years old, to the Norwegian Radium Hospital suspected of cancer of the vulva. A vulvectomia was made. The histologic examination did not show any invasive cancer, but only epithelial hyperplasia, and therefore no other treatment was given.

The surgical treatment had only a temporary effect. The earlier symptoms reappeared and she suffered much during the subsequent years. She had no sexual life, but in 1955 sexual activity came into question. She was not able to have intercourse due to severe dyspareunia and her condition became more intolerable. First seen. October 1955, she looked forward for some miraculous endocrin treatment.

Miraculous effect of endocrin therapy is today an everyday experience. It happened even in the early days of endocrin therapy and we all remember the successful results of pluriglandular extracts and the grafts of Steinach and Voronoff in the early twenties. But in many cases such treatments failed and were replaced first by the natural hormones extracted from the glands and
later by the chemical synthetized hormones and lastly replaced by synthetized products of similar activity but of chemical composition quite different from the native hormone.

In clinical gynecology the failure and even harmful side-effects of a selective "one-hormone treatment" are well known, e. g. the side-effects of androgens and oestrogens. It must be recognised that the hormonal insufficiencies as well as some endocrin hyperfunctions seldom occur due to a single hormone. Some hormones display their action synergistically and in other cases antagonistic hormones may have therapeutic consequences (e. g. the catabolic action of cortison compensated by the anabolic action of androgens, etc.). The tendency of the pharmacological industry of today is to make hormonal combinations. As to the sexual hormones several such combined products have been issued - oestrogen-progesteron, oestrogen-androgen, progesteron-androgen and even oestrogen-progesteron-androgen! This tendency marks undoubtedly a progress. It is already difficult to prescribe one single hormone correctly. To prescribe two or three simultaneously in correct doses must be even more difficult! (Vokaer, 1954).

As to the biology of the vulva and vagina all sexual hormones are involved in the normal and physiological activities. Androgens are predominantly producing a proliferation of the parabasal and intermediate layers of the vagina, progesteron of the intermediate layers, and oestrogens give a proliferation of the superficial layers with cornification. Androgens have also a special action on the subepithelial vascularisation and on the nerve-endings specially in the clitorial region (Pundel, 1952).

As to the patient mentioned above the therapy was based on the following hypothesis: Clinically the vulvar and vaginal mucosa were completely deprived of any hormonal sexual stimulation. This was confirmed by a vaginal smear showing only basal cells and leukocytes. To restore the mucosa to normal physiological thickness and activity it was necessary to give a mixture of androgen and oestrogen in the synergistic ratio of 1/30, a ratio which neutralize the untoward effects of each hormone.

The patient was given stilboestrol - Stilbofollin Nyco 0.1 mg. 3 times daily and methyl-testosteron - Perandren Ciba in linguets - 10 mg. daily, in three weeks. A slight improvement was seen. After one month 2 cc. Femandren Ciba im. was followed by a marked improvement. (Femandren is a aqueous suspension of 2.5 mg. oestradiol-mono-benzoat and 50 mg. testosteron-isobutyrat in microcrystals). All the symptoms disappeared. She got orgasm as in her earlier fertile life. On inspection the mucous membrane of the genitalia showed a approximatively normal appearance as to colour, turgor and succulence, even the remnants of the clitoris had hypertrophied and she had the typical sexual feeling on the skin just over the clitorial region. A vaginal smear showed cells from all layers of the vaginal mucosa. The improvement has remained unchanged without further treatment. It may be presumed that the revival of the physiological activities has contributed to this protracted trophic effect.

Clinical and cytological evidence suggest that the endocrine background of precancerous vulvar conditions and vulvar squamous cancer is a atrophic state.
of the mucosa with complete lack of sexual hormone stimulation. If this condition persists a gradual development from leukoplasia, kraurosis to neoplasia will occur in certain cases. During the earlier stage the condition is reversible and the morphology of the mucosa has a chance to be restored by adequate endocrine therapy. In other words, to prevent tumor formation its endocrine predisposition must be recognised and treated early. This is a therapeutic principle which perhaps has not yet been fully appreciated.

Hormones cannot cure clinical cancers. But by identifying the chief cause which is operating 10–20 years before, endocrine therapy has an important place in the prophylaxis of hormone-dependent tumors.

REFERENCES


