

at 8 and 12 weeks respectively; the latter, 40% and 48% decreases over the same time periods (Table I). Tretinoin was capable of dramatically reducing microcomedone counts by 12 weeks as seen by comparing Fig. 2 (pre) and Fig. 3 (12 weeks).

DISCUSSION

This limited study bears out what we have previously reported in the human coal tar model. Few chemicals possess comedolytic activity. Human comedones, natural or coal tar induced, are firmly anchored and are dislodged only with great difficulty. Most classic 'peeling' agents such as resorcinol and phenol are ineffective: they are merely irritants which cause scaling. While salicylic acid and tretinoin are also irritants, their efficacy is dependent on specific pharmacologic effects. The former seems to detach horny cells from each other by weakening the intercellular cement. As a result, the comedones tend to undergo disorganization. Salicylic acid penetrates skin readily and increases turnover which also favors exfoliation of the comedo. Tretinoin, on the other hand, does not cause dehiscence of pre-existing horny cells. Rather it affects the keratinization process itself so that horny cells cannot cohere strongly to each other. Consequently, comedones are no longer anchored and eventually fall out.

Not surprisingly, the antibiotic clindamycin did not possess comedolytic activity. Its probable mode of action is to suppress *P. acnes* and this must hold also for benzoyl peroxide.

In a previous study, using the rabbit ear model, we reported that benzoyl peroxide was moderately comedolytic. Assays with various commercial formulations since that time have led us to revise this assessment. The rabbit comedolytic activity of most benzoyl peroxides is insignificant. We found this to be the case in the present study, as well as in the human coal tar model. The softer comedones of the rabbit are much more easily exfoliated; hence, comedolytic activity tends to be overrated. The vehicle itself also becomes a factor. Not only percentage reduction but speed of action can be used to characterize comedolytic drugs. For example, at 8 weeks, tretinoin had produced a 75% reduction, compared with 40% for salicylic acid.

The follicular biopsy technique constitutes a practical method of assessing comedolytic activity.

It takes into account all the microcomedones within five-cm² fields, the large as well as the smaller ones. The accuracy of this method is far greater than clinical counting of comedones. Except for the conspicuous open comedones, many of the closed comedones are barely visible, a source of great variability.

Of course, knowledgeable persons will appreciate that there are agents besides tretinoin and salicylic acid that are effective in acne vulgaris. This assay measures *only* comedolytic activity. Agents whose mode of action is different must be assessed differently.

REFERENCES

1. Marks, R. & Dawber, R. P. R.: Skin surface biopsy: An improved technique for the examination of the horny layer. *Br J Dermatol* 84: 177, 1971.
2. Mills, O. H.: The follicular biopsy. *Dermatologica* (in press).
3. Mills, O. H. & Kligman, A. M.: A human model for assaying comedolytic substances. *Br J Dermatol* (in press).
4. — The follicular biopsy: Methodology and application. *Clin Res* 23: 251A, April, 1980.
5. — Assay of comedolytic agents in the rabbit ear. *In Animal Models in Dermatology* (ed. Howard I. Maibach), p. 176, Churchill Livingstone, New York, 1975.

Age at Menopause of Females with Systemic Sclerosis

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Abstract. Clinical symptoms of menopause were recorded in 27 females with systemic sclerosis, mean age 53.5 years (range 22–68). Five had regular menstruation, and 22 were in the postmenopause, 2 with climacterium praecox. Mean age at menopause was 47.8 years (range 30–59) among the 22 females, and 49.3 years (range 40–59) among the 20 females with a normal climacterium. Eleven had physiological subjective symptoms of menopause. The 22 females had 34 living children, and 13 abortions. It is concluded that the menopause is normal in females with systemic sclerosis. This indicates that the ovaries are normally not involved in the disease.

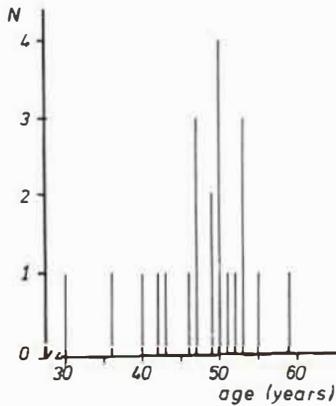


Fig. 1. Age at menopause of 22 females with systemic sclerosis.

Systemic sclerosis is three times more frequent in females than in males, and the mean age at onset is earlier in females than in males. 32 and 42 years respectively in one series (6, 7).

Visceral involvement is a part of the disease, with dysfunction of endocrine organs such as the hypophysis, the thyroid and parathyroids, the pancreas, the adrenals and the gonads in some cases (4).

The physiological menopause is a result of regressive changes and fibrosis of the ovaries.

To the best of our knowledge, the age at menopause of females with systemic sclerosis has not been studied previously.

This study was made to assess if females with systemic sclerosis as an expression of involvement of the ovaries by the disease have reduced menopause age or symptoms not seen during physiological menopause.

MATERIAL AND METHOD

The material consisted of females with a diagnosis of systemic sclerosis, admitted for check-up at the Department of Dermatology.

The following criteria were used for participation in the study:

- 1) diagnostic criteria fulfilling the requirements of the American Rheumatism Association;
- 2) duration of the disease for ≥ 3 years;
- 3) not receiving any hormonal therapy, including oral contraceptives;
- 4) not having undergone any surgical operation on the internal genital organs;
- 5) no known endocrine diseases.

According to the criteria, 27 women could participate in the study. Their mean age was 53.5 years (range 22–68

years), and mean duration of systemic sclerosis was 10.5 years (range 3–30 years). Seven patients could not participate because of earlier hysterectomy.

Registration of information about menstrual bleedings (days of bleeding/interval), age at menopause, bleedings and symptoms during and after menopause, number of liveborn infants born during the fertile period, and number of abortions was made consecutively for all the females participating.

Age at menopause was defined as the age of spontaneous cessation of regular menstrual bleedings for one year or more in a woman aged 40 years or older.

Climacterium praecox is the spontaneous cessation of menstruation in a woman younger than 40 years.

RESULTS

Of the 27 females, 5 had regular menstruation, and 22 were in the postmenopause according to the definition. Of the 22 females, 3 still had irregular menses, 2 with accompanying subjective symptoms of menopause.

The 5 females with regular menstruation had a mean bleeding pattern of 5 days of bleeding (range 3–7 days), and an interval of 26.4 days (range 21–28 days).

The 22 females in the postmenopause had presented a mean age at menopause at 47.8 years (range 30–59 years), (see Fig. 1). Two females had climacterium praecox with cessation of regular menses at 30 and 36 years of age. If the 2 females with climacterium praecox were excluded, the remaining 20 females, who fulfilled the definition of a normal menopause, had a mean age at menopause at 49.3 years (range 40–59 years).

Of the 22 females in the postmenopause, 11 had presented subjective symptoms of physiological menopause such as sweating, sensations of heat, nervousness and general discomfort.

The 22 women had given birth to 34 liveborn infants, mean 1.5 (range 0–4), and they had had 13 spontaneous abortions, mean 0.6 (range 0–3), during their fertile life.

DISCUSSION

The age at menopause at 47.8 and 49.3 years (mean age) found in this study of females with systemic sclerosis does not differ from the mean age at 51.4 years found in 6000 Dutch women with no known diseases (3). No recent Danish studies on physiological menopause exist. In the Dutch study, age at menopause varied in different demographic

groups, and difference may exist among females from different nations, even in Northern Europe (1, 3).

In this study there was 2 females with climacterium praecox (7.4%), which is consistent with a frequency of 5% in the normal population (1).

The females with systemic sclerosis had presented the known symptoms of physiological menopause, and the cessation of menstruation had a normal pattern with no registered bleedings during the postmenopause. The females with menstruation had a normal cyclic bleeding pattern.

In conclusion, this study indicates that the menopause is normal in females with systemic sclerosis.

The fertility of the females with systemic sclerosis, expressed as 1.5 liveborn infants for each female, does not seem to be diminished, since some of the females with this serious disease may have decided to avoid more children. The frequency of recognized spontaneous abortions of 13 (27.6%) out of a total of 47 pregnancies may be higher than a frequency of 10% in the general population (2). An increased rate of pregnancy wastage has been found in other studies, especially in advanced scleroderma (4).

Seven females could not participate in the study because of earlier hysterectomy. This represents a frequency of 20.5% of the entire group before allocation to study, which is no different from the average frequency of hysterectomy in Danish women (5).

The findings in this study indicate that the ovary is not involved in systemic sclerosis.

REFERENCES

1. Bjøro, K.: Klimakteriet. In *Gynaekologi* (ed. K. Bjøro and P. Kolstad), p. 120. Universitetsforlaget, Oslo, 1979.
2. Brody, S.: Abort. In *Obstetrik och Gynecologi* (ed. S. Brody), 1st ed., p. 191. Almqvist & Wiksell, Stockholm, 1970.
3. Flint, M. P.: Sociology and Anthropology of the menopause. In *Female and Male Climacteric* (ed. P. A. van Keep, D. M. Serr and R. B. Greenblatt), 1st workshop report, p. 1, MTP Press Limited, Preston, 1979.
4. Jablonska, S.: Adrenals, hypophysis and gonads. In *Scleroderma and Pseudoscleroderma* (ed. S. Jablonska), 2nd ed., p. 61. Polish Medical Publishers, Warsaw, 1975.
5. Klemp, P. & Crone, P.: Regional variation i hysterectomifrekvensen i Danmark. *Ugeskr Læger* 144: 213, 1982.
6. Medsger, T. A. & Alfonse, T. M.: Epidemiology of

systemic sclerosis (scleroderma). *Ann Int Med* 74: 714, 1971.

7. Rowell, N. R.: Systemic sclerosis. In *Textbook of Dermatology* (ed. A. J. Rook, D. S. Wilkinson and F. J. G. Ebling), 3rd ed., vol. 2, 1209 pp. Blackwell Scientific Publications, Oxford, 1979.

Behçet's Syndrome in Two Brothers

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Abstract. Two brothers, born in 1944 and 1950, had been brought up in separate homes since 1951. In 1978 they were both afflicted with Behçet's syndrome. This condition is uncommon in Scandinavia, and there are no other known reports of familial cases from the Scandinavian countries. The etiology of the disease is obscure and controversial. In our two cases a hereditary disposition seems more probable than an infectious origin.

Key words: Behçet's syndrome; HL-A antigen; Hereditary diseases

Behçet's syndrome is frequently reported from Japan and the Eastern Mediterranean area, but is an uncommon disease in the USA and Northern Europe (9). The syndrome usually displays protean features, making it "a great imitator". The variability in clinical manifestations and the long delay in involvement of various target organs make the diagnosis difficult. There are no pathognomonic symptoms, but a summary of criteria is necessary to fulfil the diagnosis. The criteria are divided into major or minor, according to the Behçet Syndrome Research Committee (9). The four major criteria are 1) recurrent aphthae; 2) skin lesions—erythema nodosum-like eruption, subcutaneous thrombophlebitis, folliculitis; 3) eye lesions—iridocyclitis, chorioretinitis; and 4) genital ulcerations. Minor criteria may include articular, cardiovascular, intestinal, urologic and neurologic involvement (8, 9). The syndrome is considered complete when all four major symptoms appear in the clinical course; otherwise it is called incomplete (9). The complete form is not necessarily more severe than the incomplete variant. The basis for the symptoms