receptors per cell 5 500 vs. 4 400) (5). The PMN receptor was also found to be located to the plasma cell membrane (5).

The characteristics of this binding site correlate well with previous studies on the mitogenic effect of LTB_4 on human keratinocytes in vitro (2, 8). LTB_4 stimulated keratinocyte proliferation in culture at concentrations between 10^{-1} and 10^{-8} M, and half-saturable binding occurs at 1.03 nM of the leukotriene. The presence of one population of specific binding sites for LTB_4 on keratinocytes in culture, thus, supports the finding of a direct mitogenic effect of LTB_4 on human keratinocytes in vitro. This may suggest that this arachidonic acid metabolite may directly influence epidermal proliferation in a number of cutaneous inflammatory diseases.

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Skin Extensibility Time in Women. Changes in Relation to Sex Hormones

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The influence of female sex hormones on mechanical properties of the skin has been assessed in an in vivo extensometric study. Twenty young (20±4 years) and 12 middle-aged healthy women (42±3 years) entered the study. Measurements were carried out on the volar surface of the left forearm on the 10th and 25th day of the menstrual cycle. A significantly decreased skin extensibility time in the pre-menstrual phase was found (25th day) when compared with the 10th day in the young group, while the older one did not reveal significant changes. The data are compatible with an increased water content of the skin noticeable in the pre-menstrual phase and more relevant in young women. In studies on mechanical properties of the skin, changes relative to sex hormones and menstrual cycle need to be taken into account. ***Key words: Estradiol; Menstrual cycle.***

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Mechanical and viscoelastic properties of the skin are related to many variables, such as skin thickness (1), age (2, 3, 4), sex (1) and environmental conditions (5). Age-related changes are widely studied (2, 3, 4). Most authors agree that the skin becomes less extensible with age. Leveque et al. (4) and Agache et al. (6), using the same torque method, reported decreased extensibility with age, namely after 30 years, associated with an increase of the elastic modulus. Similar

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Table I. *Skin extensibility and relaxation times (mean values ± SD) in relation to female sex hormones recorded on the 10th and 25th days of the menstrual cycle in young and middle-aged women*

The decrease of extensibility and relaxation times at the 25th day is significant only in the young group (Wilcoxon signed rank test $p<0.01$). Values in hundredths of seconds

	Young		Middle-aged	
Menstr. cycle day ...	10th	25th	10th	25th
Extensibility time	86.4±9.5	79.6±10	100.8±14	104±14
Relaxation time	109.1±11	102±13	121±12	121±13

findings have been reported by Grahame & Holt (7), but not by Sanders (8).

When the skin is stretched by a force there is an immediate deformation (immediate extensibility) followed by a slower phase. Using a uniaxial extensometer to measure the extensibility time of superficial skin layers, our group (2) reported increased immediate extensibility time with age. According to Daly & Odland (9) this result, obtained by using low loads, may be useful in recording the unfolding capability of the skin and skin wrinkling.

Pierard & Lapiere described sex differences (1) with increased skin extensibility and lower elasticity in women. Manschot & Brakkee (5) found greater skin stiffness in winter due to humidity changes. The role of hormones in skin extensibility has been studied by only a few groups: Burton & Shuster (10) showed that intravenous prednisolone produced an increase in skin extensibility. Vogel (11) described decreased viscoelasticity after treatment with prednisolone acetate in vitro on rat skin. The same author (12) showed a strict correlation with human skin between tensile strength and viscoelasticity on the one hand and insoluble collagen content and glycosaminoglycans on the other. The relationship between female sex hormones (i.e. estrogens) and skin extensibility has not yet been demonstrated, despite the various effects that these hormones have on skin (13, 14). The cyclic variations of these hormones in women led us to investigate this.

MATERIALS AND METHODS

Twenty young (age 20±4) and 12 middle-aged (42±3) women, all healthy, entered the study after their informed consent was obtained. Measurements were carried out with a specially built extensometer, described elsewhere (2, 15). The instrument allows non-invasive, in vivo uniaxial measurements of skin immediate extensibility time by using low standard loads (3.9 10^{-3} N/m). Two square plates (1.5×1.5 cm) are applied to the patient's skin by means of cyanoacrilate tape. The initial distance between the extensometer's two plates was 10 mm and the time when the skin resistance was measured was in hundredths of seconds. Displacements could not be measured (were a few mm).

Recordings were taken on the volar aspect of the left forearm with the elbow extended at 180°. Subjects rested 30 min before the test. Measurements were performed on the 10th and the 25th day of the menstrual cycle. Subjects selected had normal 4-week cycles. The parameters investigated were:

1) immediate skin extensibility time at time 1 (immediate extension time after the application of the force. The motor stops automatically when the force absorbed exceeds the preselected value). After the recording of the value at time 1, the probe was left in situ for 5 min, allowing the re-adjustment of the skin to the stretching force, and was then restarted (time 2). The procedure was repeated twice (times 3 and 4).

2) relaxation (difference between time 4 and time 1). This parameter is related to the adapting capacity of the skin following a stretching force.

The results were analysed by means of non-parametric statistical tests (Wilcoxon signed rank test and Mann-Whitney U-test).

RESULTS

The results are presented in Table I. Mean values showed a decrease in skin extensibility time and skin relaxation time in the young group at the 25th day of the cycle. The comparison is highly significant ($p<0.01$). In the older group, no changes related to the variation in sex hormones were detected. The comparison between young and middle-aged women at either the 10th or 25th day showed significant differences related to age, for both extensibility and relaxation times.

DISCUSSION

The most striking change during the pre-menstrual phase is the retention of water and salts, in most women resulting in an increase in weight and rise in temperature which begins during the follicular phase (16). This general water retention is renal.

Estrogens in the dermis increase the hyaluronic acid content and thus the water content (12). These more protracted effects are mediated by dermal estrogen receptors as demonstrated by Bentley et al. (17). In this model, the administration of estrogens and progesterone induced in macaque sex skin increased the hyaluronate biosynthesis and water content. The correlation between the estradiol-induced increase in hyaluronic acid and the number of estrogen receptors in the skin is reported (18) by Uzuka et al. The greater the number of estrogen receptors in skin is, the greater is the increase in hyaluronic acid following treatment with estradiol.

An increased water content in the skin is probably responsible for decreased skin extensibility time and relaxation time detected with our technique in the young group. An increased water content of the skin may cause higher skin tension with flattening of small wrinkles and of skin surface relief. Another factor could be an increase in skin thickness due to the increased water content. This appears less relevant, and our device measures only elastic properties of superficial skin layers. We do not know the exact relationship between extension time, as measured, and extensibility or strain, which was not measured. A reduction in skin extensibility time was not detected in the older group. This behaviour was confirmed by the data on skin relaxation time. Indeed, estrogen receptors in the older group's skin could be reduced, as shown in animal models (18). Furthermore, blood concentration and cyclic secretion of sex hormones is decreased in middle-aged women.

The comparison between young and older subjects (at the same phase) reveals significant differences ($p<0.01$) with an increase of values relative to ageing. The data confirm what we have previously reported (2, 15). Progressive thinning of skin and degeneration of elastic fibres occur in adult life (19).

Further work is needed to confirm and investigate these physiological variations of skin extensibility time. Investigators of mechanical properties of the skin should take into account, besides sex and age differences, extensibility's cyclic changes in young women.

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