may give low hybridisation levels. Hence, the test should be used only as a screening procedure, and not for purposes of definitive diagnosis of X and Y chromosome aberrations.

Compared with fetal sex determination by chromosome analysis, the method described here can yield results in 2 to 3 days instead of 2 to 3 weeks. Thus any additional diagnostic studies and genetic counselling can be initiated much earlier in pregnancy. Preliminary data indicate that chorionic villi can also be used for sex determination with the dot blot procedure.[16] We are now devising a nonradioactive method for labelling the probe. Such improvements should greatly facilitate early antenatal diagnosis of X-linked genetic disorders.

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SUBCUTANEOUS HORMONE IMPLANTS FOR THE CONTROL OF CLIMACTERIC SYMPTOMS

A Prospective Study

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Summary 55 postmenopausal women on established hormone replacement therapy were treated with either oestradiol and testosterone implants or placebo at the time of return of climacteric symptoms. Their response to therapy was assessed prospectively. The statistically highly significant levels of symptom relief that followed an oestradiol and testoserone implant were contrasted sharply with the lack of any significant relief with placebo. Despite the success of oestradiol and testosterone implants in relieving symptoms of the climacteric, symptoms returned once the treatment was stopped. Evidence is presented that it is the fall in hormone levels rather than the level itself that provokes the return of climacteric symptoms.

Introduction

THE use of subcutaneous implants as an alternative route of oestrogen administration in the climacteric was pioneered by Greenblatt.[1] Implants bypass the intestine, avoiding the first-pass effect on liver metabolism of the hormone. This prevents the unphysiological ratio of oestradiol to oestrone found with oral preparations.[2] Oral preparations, unlike implants, also reduce liver metabolism of clotting factors and lipids.[3]

Although interest in implant therapy is increasing, it has still not gained the acceptance of oral therapy and very little prospective work has been done on this route of administration. Implantation is a simple outpatient procedure carried out under local anaesthesia, and it is normally repeated every 6 months.[4] Our policy is to insert a pellet of testosterone 100 mg (T) in addition to a pellet of oestradiol 50 mg (E) in women who complain of coexistent lethargy, depression, and loss of libido.

The few side-effects of E+T implant therapy have been described elsewhere.[5] An unexpected finding was that when the symptoms returned after 4 to 6 months, the oestradiol and testosterone levels had fallen only to within the normal premenopausal range. It was therefore considered necessary to compare the effects of placebo treatment on these patients at the time of return of climacteric symptoms.

Patients and Methods

55 postmenopausal women were recruited from the Dulwich menopause clinic. All were regular attenders at the clinic and had previously received implants that gave them good relief from their climacteric symptoms (table I).

Patients were randomly divided into two groups depending on their hospital number. Those with an even case sheet number were given E+T, and those with an odd number were given placebo. Norethisterone 5 mg daily for 7 days each cycle was given to all patients with a uterus to prevent endometrial hyperplasia.[2,6,7]

There was no significant difference in the average age and weight between the two groups (table II). Patients were not aware of which implant they were receiving. They were asked to score a symptom list using a five-point scale. They were then followed up at 2-month intervals for 8 months. The symptoms assessment sheet was

TABLE I—IMPLANT HISTORY OF STUDY POPULATION

—	Mean±SEM
No of implants per patient	6·0±0·4
Duration of treatment	32·9±2·3 mo
Start of appreciable benefit	2·1±0·1 wk
Maximum benefit	5·2±0·4 wk
Start of decline	2·5±0·3 mo
Implant wore off	6·4±0·2 mo

completed by the patients at each visit. They were not allowed to see their previous assessment sheets. Though a repeat implant was offered at 6 months, the women were encouraged to persist without any additional treatment at any other time. However, if they demanded treatment within 6 months, an implant of E+T was always given. If a patient was satisfied at 6 months and insisted that her previous implant was still giving her adequate relief, she was not given a repeat. For each patient a comparison was made for each individual symptom, and the total sum of all symptoms, between her score at month 0 and month 2, month 0 and month 4, month 0 and month 6, and month 0 and month 8. Patients who required treatment at any stage were not considered in the subsequent analysis.

TABLE II—PATIENT DATA

—	All	E+T	Placebo
No of patients	55	33	22
Mean age (yr)	44·4	43·9	47·8
Mean weight (kg)	62·6	62·5	62·4
Mean no of previous implants	6·0		

Statistical Methods

The significance levels were calculated with the Wilcoxon rank test, a non-parametric test. The results were analysed by the Department of Medical Statistics, King's College Hospital Medical School, with the statistical package for social sciences.

Results

The symptom responses to the active implant and the placebo implant are shown on tables III and IV.

With the active implant there was a statistically significant improvement in all symptoms investigated except "aches and pains", and there was an improvement of only short duration in the urethral syndrome. At 6 months the symptom scores had returned to non-significance in six of the symptoms; a significant improvement was maintained only in flushes, headaches, irritability, insomnia, depression, and lethargy.

None of the 33 patients who had received an implant of E+T requested a repeat implant at 2 months or at 4 months. 24 (72·7%) who were offered one at 6 months accepted, but 9 patients did not need further treatment at that time.

There was no change in symptoms in the patients receiving placebo implants (table IV) at 2, 4, or 6 months. 2 patients insisted on having repeat implants at 2 months and another 5 at 4 months because they were not receiving adequate relief from placebo compared with their previous implants. By 6 months only 15 patients were left in the placebo group. They were then offered a repeat implant, and all but 4 accepted.

TABLE III—SYMPTOM CHANGES WITH OESTRADIOL 50 mg + TESTOSTERONE 100 mg* (N = 33)

	Month 0	Month 0–2		Month 0–4		Month 0–6	
Symptom	M	M	p	M	p	M	p
Flushes	2·3	1·4	<0·01	1·3	<0·01	1·4	<0·01
Palpitations	2·0	1·5	<0·05	1·5	<0·05	1·5	NS
Headaches	3·4	2·2	<0·001	2·3	<0·01	2·5	<0·05
Irritability	3·7	2·2	<0·001	2·1	<0·001	2·6	<0·01
Lack of concentration	3·1	1·8	<0·001	2·2	<0·01	2·4	NS
Insomnia	3·1	2·0	<0·001	1·7	<0·001	2·3	<0·05
Depression	3·4	2·1	<0·001	2·3	<0·01	2·3	<0·01
Aches	2·5	2·0	NS	2·3	NS	2·2	NS
Dyspareunia	2·5	1·3	<0·01	1·6	<0·05	1·8	NS
Loss of libido	3·3	2·0	<0·001	1·9	<0·01	2·3	NS
Urethral syndrome	1·9	1·3	<0·01	1·7	NS	1·5	NS
Lethargy	4·4	2·6	<0·01	2·4	<0·05	2·5	<0·05
All symptoms	28·8	19·1	<0·001	19·8	<0·01	22·6	NS

M = mean score (5 = maximum severity of symptom).
p = level of significance (Wilcoxon rank test).
NS = not significant.
*Significance levels in improvement of symptoms when compared with scores obtained at month 0.

TABLE IV—SYMPTOM CHANGES WITH PLACEBO*

	Month 0	Month 0–2	Month 0–4	Month 0–6
Symptom	M (n = 22)	M (n = 22)	M (n = 20)	M (n = 15)
Flushes	2·2	2·0	2·1	1·9
Palpitations	1·7	2·1	2·0	1·6
Headaches	3·0	2·7	3·0	3·0
Irritability	3·3	3·3	3·5	3·4
Lack of concentration	2·8	2·6	3·2	3·1
Insomnia	2·4	2·4	2·4	2·5
Depression	3·2	3·1	2·9	3·3
Aches	2·6	2·3	2·6	3·1
Dyspareunia	2·5	2·0	2·0	1·8
Loss of libido	2·5	2·6	3·1	2·7
Urethral syndrome	2·0	1·7	2·1	1·9
Lethargy	3·0	2·0	4·0	2·1
All symptoms	26·9	24·8	27·6	2·6

2 patients dropped out, requesting treatment at 2 months.
5 more dropped out, requesting treatment at 4 months.
M = mean score (5 = maximum severity of symptom).
*None of the changes in symptom score at any time was statistically significant at the 0·05 level.

Discussion

The statistically highly significant levels of symptom relief that followed an oestradiol and testosterone implant contrast sharply with the lack of significant relief obtained with placebo at any of the times studied. The only exception to the significant levels of symptom relief with E+T were the muscular "aches and pains", of which many postmenopausal women complain. This finding suggests that this symptom is probably not due to hypo-oestrogenism.

Our results leave little doubt about the superiority of the E+T implant over placebo. They show the efficacy of this treatment in relieving symptoms of the climacteric, and they demonstrate that symptoms return once the oestrogen is stopped.

Thom et al[8] showed that mean oestradiol, oestrone, and testosterone levels fell between month 4 and month 6 by 32%, 29%, and 39% respectively, in contrast to the rise in these hormone levels between months 0 and 2 and the steady level between months 2 and 4. Cardozo et al[5] showed that 6 months after repeat E+T implants, oestradiol, oestrone, and testosterone levels were still well within the premenopausal range and that symptoms returned when oestrogen levels fell from moderately high levels to within the normal premenopausal range. These symptoms were relieved with active therapy and did not respond to placebo.

This indicates that common climacteric symptoms occur in response to a fall in oestrogen levels rather than actual hypo-oestrogenism and that hormone therapy is effective in the treatment of these real symptoms regardless of the actual blood hormone levels. This probably explains the frequency and severity of the climacteric symptoms in women approaching the menopause[9] despite regular periods and oestrogen levels in the normal range. The failing ovary of these patients is indicated, however, by high levels of follicle-stimulating hormone.[10]

The rate at which an implant wears off can also be deduced. The active period has been described as being 6 months, and this figure corresponds to that given to us retrospectively by our patients (table I). However, prospectively at 4 months, in our series of patients on E+T, the improvement in the urethral syndrome loses its significance. By 6 months, a total of six symptoms lose their statistical significance, when compared to the severity of symptoms at month 0. In addition, the overall improvement of the total sum of all symptoms loses its significance.

On this information, a case could be made for offering a repeat E+T implant every 4 months instead of every 6 months.

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Methods and Devices

PORTABLE CHAIR FOR TESTING ISOMETRIC MUSCLE STRENGTH

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Introduction

TESTING of voluntary muscle strength has long been part of routine physical examination. Clinicians still have to rely, however, on subjective assessment of skeletal muscle power, since no generally accepted method for quantifying muscle strength is presently available for clinical use. Hand-held dynamometers for measurement of grip strength are of limited value, since many muscle disorders disproportionately affect proximal muscles.[1,2] We have developed a portable chair which is especially suited to testing muscle strength in clinical practice. The chair is based on experimental equipment designed to test quadriceps muscle function,[2] but it incorporates several modifications and improvements. It is portable and, using a single load cell, allows measurement of three muscle functions, including both proximal and distal muscle groups. All the components used are readily available.

Materials and Methods

The chair was designed to meet the following requirements:
1. A choice of two separate load ranges (0–10 kg and 0–100 kg) each with an overall accuracy of measurement to within ±2% and a negligible temperature coefficient.
2. Readily changeable between mains and battery operation (with an indication of state of charge of the internal battery).
3. Digital readout of force, with retention of peak force reading and manual reset of peak reading.
4. Facility to drive an analogue meter (with retention of peak reading) to assist patient motivation, and an analogue pen recorder to give the profile of the force/time curve.
5. Built-in calibration checks of system sensitivity.

These requirements were met by the digital strain gauge monitor 'SGA 800 Mk2' (CIL Electronics, Worthing) modified by the manufacturers so that the load range could be selected by a switch. Additional circuitry was provided to protect the analogue meter in case the operator inadvertently changed to the more sensitive scale while the meter was under full deflection on the upper range. The load cell used was model F241 A2T (Novatech Measurements Ltd, St Leonards on Sea) with a range 0–200 kg. The basic chair frame was an adapted physiotherapy quadriceps exercise chair (model Z1079, Nomeq Medical Equipment, Nottingham). The weights were discarded, and arm rests, lockable wheels, and a standard car-type lap seat belt attached (fig 1).

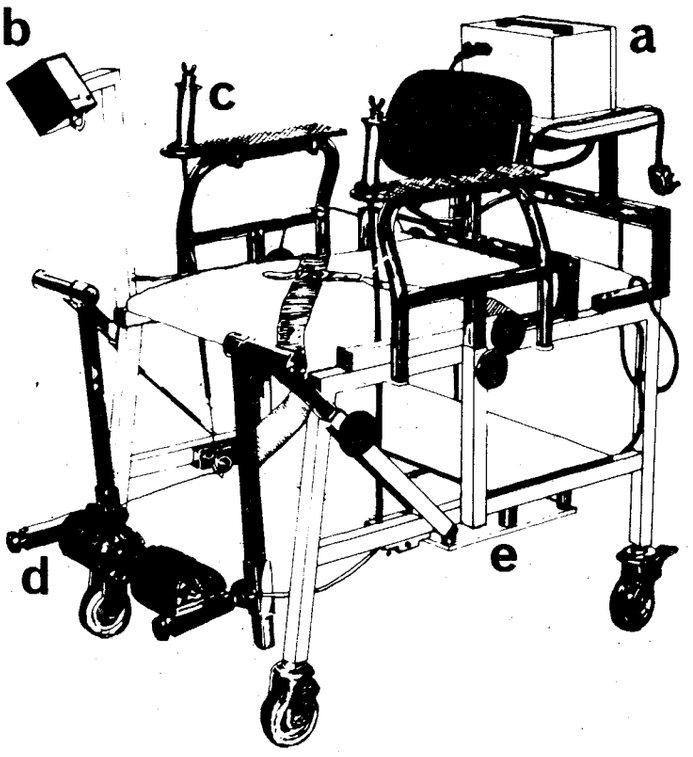

Fig 1—The portable chair.

a = digital monitor; b = patient visual display meter; c = handgrip; d = ankle pad; e = load cell.

The maximum load expected from the quadriceps in healthy adult subjects was under 100 kg.[1] To make full use of the range of the load cell (0–200 kg) it was stressed by way of a 2/1 lever system which enabled both left and right limbs to be tested. The load cell was positioned centrally to the force lever, which was contained by an open pivot at each end. Both were mounted on a ¼ inch Duval plate fixed to the chair frame. For measurement of quadriceps strength, thrust transmitted from the ankle pads is carried by a $\frac{1}{16}$ inch Bowden cable to the force lever. To measure upper arm and hand grip strength, a second cable was fixed on each side to the original cable and connected by way of a pulley to the handgrips. These were constructed with two pins passing through the base (so that they pressed directly on the arm rests) and were mounted in a floating ball joint to counter any side flexing in use.

The unit was calibrated by means of a high-quality spring balance connected directly to the ankle pad or handgrip, and the bridge balance unit was adjusted to ensure that the digital meter reading was within 2% of that of the spring balance. The calibration was checked initially once a month.