The Climacteric
from the Present into the Future

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by

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CLIMACTERIC (greek KLIMAKTER) means...

a rung of a ladder

or

a crisis
The Future of the Climacteric?

Its future is

Growth in Age
The practice of Medicine

• Gender (female) based
• Chronological
• Holistic, or Integrated
• Organ/System specific
**Chronobiologic Medicine**

*The Time Table of a Woman’s Life Span*

M. Neves-e-Castro, 2008
“The compression of morbidity”

Fries JF et al 1981
Are *Women* in a *crisis*?

YES !

Why?
Because

We have a tendency to accept as valid the headlines that circulate in the media without having critically read the full papers to which they refer.

We are not able to explain to our patients the meaning of those risks and how small they are compared to other risks to which they are expose.
how is Medicine practiced today?
There are two types of medical practice:

– the **Medicine for one individual**, at a time (**Clinical Medicine**)

– the **Medicine for many individuals**, the population, at the same time, (**Public Health Medicine**)
Practioners are guided:

- by the best available information that can be extrapolated with validity to their patients, and

- by their accumulated experience
Public Health doctors are guided by what epidemiologists suggest ...

but ...

Most epidemiologists only establish associations of events and seldom determine cause/effect relationships

MNC/05
Is there a *Menopausal Medicine*?

There is only **ONE** Medicine (*L. Speroff*)

There are only **TWO** Medicines (*M.N.C.*):

a **BAD** Medicine *and*

a **GOOD** Medicine
Therefore, what we must learn, is...

how to practice a GOOD MEDICINE!

mnc/05
The Future of the Climacteric?

Is an inter-relation of the

Aging of a woman

with the

Lowering of her hormones
In the developed world, the percentage of women over 50 years of age has tripled in the last 100 years.
A menopausal woman is a mid-aged woman.
As a *mid-aged* woman:

She will suffer from the process of natural aging, both from a biological and a psychological perspective.

MNC
As a *menopausal* woman:
She is hypoestrogenic and will suffer, at various levels, from its consequences.
A modern gynecologist must ...

know how to **identify** risk factors and to **modify them** in order to **prevent** diseases.
The **climacteric**, is a complex, multifaceted process that responds to the interaction of different biopsychosocial factors.

The future of women in a changing and aging World

Targets:

- The QUALITY OF LIFE
- The preservation of HEALTH
- The prevention of DISEASES
Managing the Climacteric

by

Objectives
Critical Objectives

a) The treatment of symptoms
b) The elimination of risk factors
c) The diagnosis of diseases
d) The treatment of diseases
Aging in the World

The Elderly Health Promotion, is focused on

**Active Aging:**
- physically
- mentally
- socially

Kalache A. The 3rd World Congress of the Aging Male
Determinants of

- Economic determinants
- Social determinants
- Physical environment
- Behavioral determinants
- Personal determinants
- Health and social services

*Kalache A. Gender-specific health care in the 21st century: a focus on developing countries. The Aging Male 2002;5:129-138*
Social Health

a) macrosocial conditioners
b) microsocial environment
A Woman is one cell of the Social Body
Mental Health
Mental Health

a) psychosomatics
b) emotions and feelings
c) behaviour
d) coping
The woman’s perception of her own *existence* and *identity*:
Cogito, ergo sum
I think, therefore I am

António R. Damásio
« Descartes’ Error », 1994

I FEEL therefore I AM
Eu sinto logo existo
Depression and Cancer

Depression also affects components of immune function that may affect cancer surveillance.

Spiegel D. Biol Psychiatry 2003; Vol 54(3):269-82
Effect of a psychosocial treatment on survival of patients with metastatic breast cancer

Survival from time of randomisation and onset of intervention was:

- a mean 36.6 (SD 37.6) months in the intervention group
- compared with 18.9 (10.8) months in the control group.

Spiegel D. Lancet 1989; 2(8668):888-91
Physical Health
Causes of Death Among Women*

*Percentage of total deaths in 1999 among women aged 65 years and older.

Causes of death and trends in female mortality

Across all ages, the most frequent causes of death among women are:

- diseases of the circulatory system (accounting for 43% of all deaths)
- cancer (26%)
- diseases of the respiratory system (6%)
- suicide and accidents (5%).

Commission Report of 22 May 1997 on the state of women's health in the European Community
and again...

The inevitable *WHI*...

I’m becoming bored to talk about it...
But …

I can’t avoid telling you …

some stories…
about the impact of the WHI...

- on *women*

- on the *medical profession*
There are *controversies* about the present management of the climacterium which are due to:

- a **lack of culture** that prevents a correct criticism of the published results
- a **bad practice of medicine** that ignores the woman in her totality (*holism*)
- **political lobbies** from the *NIH*
- a **lack of scientific accuracy** manifested by many of the WHI writers
- **lobbies from several pharmaceutical industries** through the activities of many well known doctors that “offer” themselves to transmit their “messages”

MNC
Then, why all this noise?...

Mainly because the conclusions of recent trials were severely misinterpreted by the medical professionals, the media and by the women, themselves.
The applicability of the WHI findings to women between age of 51.1 and 56.1 years and younger is unknown...

Ostrzenski A and Ostrzenska KM. Am J Obst Gynecol 2005;193:1599-604
It is not possible to extrapolate conclusions from the study of one compound, dose, and route of administration directly to another.
“...most articles and broadcast segments tended to focus exclusively on either the small absolute risks or the larger relative risks, neglecting the more even-handed picture that presented both.

Since the sharply increased relative risks got the most play, news coverage about the trial’s findings had an alarming cast.”

It takes but a few wrong statements to cause a tsunami of panic.

It takes years to correct the disaster and give back good quality of life to the women of the world.

Neves-e-Castro M. Gynecological Endocrinology, 2007; 23(8): 433–435
New data on hormone therapy must lead to re-evaluation of official guidelines: a plea for health authorities

The results of the WHI trial were wrongly extrapolated to the whole postmenopausal population, which led to a major change in recommendations and guidelines on HT.

IMS Plea, August 20, 2007
WHI ... The Truth!
My dream

I imagined in My Dream that the day would come when the WHI investigators would apologize to women, all over the world, for the damage they had caused with their wrong advice, as follows…

When a dream comes through . . .

It is now my great pleasure to see that it seems that my dream is becoming true. It took 4 years since my own interpretation of the WHI [1] until the WHI was submitted to several re-analyses [4] that confirmed what I had already concluded: women in the early menopause being treated for the relief of their vasomotor symptoms were protected from CVD.

Neves-e-Castro M. Gynecological Endocrinology, 2007;23(8):433-435
An *update* of the *WHI* Study!

**WHI investigators** reported *(Feb 2006)* a statistically significant *(34%) lower risk* for the combined endpoint of myocardial infarction (heart attack), coronary death, coronary revascularization and confirmed angina among **women who were between the ages of 50 and 59 at the start of the study** *(RR 0.66; 95% CI 0.45-0.96).*

BENEFITS OF HORMONE THERAPY

In women less than 60 years old, recently menopausal and without prevalent cardiovascular disease, the initiation of HT does not cause early harm and may reduce cardiovascular morbidity and mortality.

Continuation of HT beyond the age of 60 should be decided as a part of the overall risk–benefit analysis.

IMS press statement, February 2007
“Younger recently menopausal women have very low rates of adverse events related to hormone therapy, so if they’re getting symptom and quality of life benefits, those benefits are still likely to outweigh the risks.”

Manson, JA

cited by Tara Parker-Pope. in “Health” New York Times, 2008, March 4
"We continue to encourage women to use hormones only if needed for menopausal symptoms, and for the shortest time possible, and to adopt and maintain a healthy lifestyle, that is, engage in regular physical activity, maintain a healthy body weight, consume a diet low in saturated fat, and to not smoke, to reduce their risks of cardiovascular and other chronic diseases."

Stefanick M et al. JAMA 2008;299(9):1036-1045
When a dream comes through. . .

It seems that “my dream” was nothing but a premonition...
Is the WHI the only Study of HT?
Menopausal women and their doctors are scared about the side effects of HRT mainly about breast cancer
The danger of cancers is always in the physician’s minds; but they do not know that approximately 10 times more women die of a cardiovascular disease than of cancer.
Conclusion: This study showed no increased incidence of invasive breast cancer among postmenopausal HT users when compared with non-users.

Figueroa Casas, PR; Rinesi L. Centro de Ginecología, Rosario, Santa Fe, Argentina. In IMS World Congress, Madrid 2008
No increase of breast cancer incidence in Japanese women who received hormone replacement therapy: overview of a case-control study of breast cancer risk in Japan.

5861 samples (3434 cases and 2427 controls) were analyzed: there was a significantly negative correlation between HRT use and breast cancer

The **Mission Study**

study of HRT in 2693 exposed women vs 2256 unexposed.

- Breast Cancer: **no difference**
- Miocardial Infarction and Stroke: **no difference**
- VTE: **less in exposed** (0.15% vs 0.57%)

Mares P et al. 2007, NAMS Congress. Abstract S-26
Breast Cancer

Estrogens and Progestagens

The association between HRT use and breast cancer risk most likely varies according to the types of progestagens used.

Risk of breast cancer by time in MWS
Million Women Study

The follow-up for breast cancer diagnosis was just over 2½ years, meaning that these breast cancers were almost certainly pre-existent at the start of the observational period.

Press Release from the British Menopause Society, 2003
Primary prevention of breast cancer:

New approaches
Lifestyle changes, such as exercise, might reduce the risk of breast cancer.

Cummings S. Maturitas 2007;57:39-41
Recreational Physical Activity and the Risk of Breast Cancer in Postmenopausal Women

Women who engaged in the equivalent of 1.25 to 2.5 hours per week of brisk walking had an 18% decreased risk of breast cancer (RR, 0.82; 95% CI, 0.68-0.97) compared with inactive women.

McTiernan A et al. JAMA 2003;290:1331-6
The association between physical activity in leisure time and leukocyte telomere length

A sedentary lifestyle (in addition to smoking, high body mass index, and low socioeconomic status) has an effect on LTL (leukocyte telomere length) and may accelerate the aging process.

Mediterranean Diet, Lifestyle Factors, and 10-Year Mortality in Elderly European Men and Women

Among individuals aged 70 to 90 years, adherence to a mediterranean diet lifestyle is associated with a more than 50% lower rate of all-causes and cause-specific mortality.

Knoops K et al. JAMA 2004;292:1433-9
## RELATIVE RISK OF BREAST CANCER BY BODY WEIGHT

<table>
<thead>
<tr>
<th>Age at Diagnosis</th>
<th>Weight (Kg) &lt;60</th>
<th>60-69</th>
<th>70+</th>
</tr>
</thead>
<tbody>
<tr>
<td>35-49</td>
<td>1.00</td>
<td>0.54</td>
<td>1.16</td>
</tr>
<tr>
<td>50-59</td>
<td>1.00</td>
<td>1.22</td>
<td>1.43</td>
</tr>
<tr>
<td>60-69</td>
<td><strong>1.00</strong></td>
<td><strong>1.61</strong></td>
<td><strong>1.81</strong></td>
</tr>
</tbody>
</table>

from deWaard et al, 1964, 1978
• At present, **the management of symptomatic climacteric women has been the source of a cascade of discussions** since the publication of the WHI Study.

• These discussions became at times very complex, above all due to the influence of Evidence Based Medicine.
Evidence Based Medicine and/or Medicine Based Evidence?

Manuel Neves-e-Castro
Evidence Based Medicine and/or Intelligence Based Medicine?

Lucas Viana Machado
and

the time has come...
New data on hormone therapy must lead to re-evaluation of official guidelines: a plea for health authorities

Hormone therapy (HT) remains the most effective treatment for vasomotor symptoms and estrogen-deficient urogenital symptoms

IMS Plea, August 20, 2007
Recommendations on postmenopausal hormone therapy

There are no reasons to place mandatory limitations on the length of treatment.

IMS press statement, February 2007
Mortality Associated with HRT in younger and older women

Hormone Replacement Therapy reduced total mortality in trials with mean age of participants under 60 years. No change in mortality was seen in trials with mean age over 60 years.

What about the **best treatments** during the climacterium and beyond?
There are no really “safe” biological active drugs...

There are only “safe” physicians!

Kaminetzky HA 1993
little attention is paid to other pharmacological interventions (non hormonal) and strategies that have been shown to be important for the prevention of such diseases and to maintain or improve health.
Okinawa Island: A model of “healthy” aging

The exceptional longevity of the Okinawa population may result from a combination of favorable factors and not only genetic determinants. The association of a protective environment with a way of life which combines specific food habits, low energy intake, physical activities, stress reduction, good familial support and rich social relations could explain this exception despite the low income in this population.

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McTiernan A et al. JAMA 2003;290:1331-6
Diet, Physical Activity, Weight Control

Over 40% of breast and bowel cancer cases in rich countries are preventable through diet, physical activity and weight control alone.

Sir Michael Marmot, Chairman of the American Institute of Cancer Research and World Cancer Research Fund, 2009
• Sleep disturbances can lead to immune suppression and a shift to the predominance in cancer stimulatory cytokines,

• Some studies suggest that a shortened duration of nocturnal sleep is associated with a higher risk of breast cancer development

Blask DE-Sleep Medicine Reviews, 2008
Vitamin D plays an important role in controlling cell growth and thus may help reduce risk of deadly malignancies.

Taking at least 1,000 units (preferably 2,000 units/day) of Vitamin D may reduce risk of developing colorectal and breast cancer by as much as 50%.
HEALTH PLAN for the ADULT WOMAN

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TODAY’S WORLD, TODAY’S MEDICINE, TODAY’S HARRISON’S
In my opinion, *in the future, there is only a need to practice Good Medicine.*

*Gynaecologists can no longer be confined to the pathology of the reproductive system.*
Overall they must acquire good knowledge of Internal Medicine, Psychology, Cardiology, Bone Diseases, Metabolic Diseases, Oncology, Sexology, Dermatology, etc.
Whether they want it or not...

**most climacteric women will consider them as their own “family doctors”**...

the ones that can help them to solve so many different complains.
It is also the **responsibility of the attending physician** to be concerned with **cardiovascular** and **osteoporotic risks**, that he must correct.
Progesterone (micronized) has the best profile and can be given intravaginally or orally. Its only function is endometrial protection.

Alternatively, a medicated IUD (Mirena) with a progestagen could be applied to protect the endometrium.
Could transdermal estradiol + progesterone be a safer postmenopausal HRT?

The choice of the transdermal route of administration of estrogens and the use of natural progesterone might offer significant benefits and added safety.

L’Hermite M et al. Maturitas. 2008 Jul-Aug;60(3-4):185-201
Hysterectomized women should never be given progestational steroids.
Sexual dysfunctions are frequent and very important for a woman’s life. Testosterone (gel, patch or implants) may offer good results.
Hormonal treatments should only be prescribed to symptomatic climacteric women, preferably before 60 years of age.

*On and off* treatment should be tried after 3 to 5 years on medication.
In conclusion ...

and to make a long story short...
The World Health Organization

Definition of HEALTH:

“a state of complete physical, mental, and social well being and not merely the absence of disease or infirmity”

This definition not only expresses the interrelatedness of mind, body, and social context but also stresses the positive meanings of health.
To know

the disease that a woman has

is as important as
to know

the woman who has the disease

William Osler
Let us not *medicalize* the Menopause..

instead...

Let us *holistically* approach the Climacteric and the Aging Women.
“He who learns, but does not think is lost. He who thinks, but does not learn is dangerous”.

Confucius
If we both learn and think
we will
neither be lost
nor dangerous
to our postmenopausal women patients”

Wenger NK. Am J Geriatr Cardiol 2000;9:204-9
Preventing a woman from the benefits of a sound postmenopausal hormone therapy because of the fear of rare side effects does not seem to be satisfactory Medicine...

M. Neves-e-Castro, 2000
and now...

this is not the end...
nor even the beginning of the end.
It is perhaps, the end of the beginning!

Winston Churchill
A WOMAN in the autumn of her life deserves an Indian summer rather than a winter of discontent ...

Robert B Greenblatt