ETTORE MAJORANA FOUNDATION AND CENTRE FOR SCIENTIFIC CULTURE

ERICE’S INTERNATIONAL SEMINARS ON PLANETARY EMERGENCIES
NEW MANHATTAN PROJECT: ERICE 2016

Project Proposal: Cancer, Metabolic Disfunctions and Nutrition Issues in Elderly

(Chairmen I.Carreca., C.Caruso., A.Russo)
The 'aging is one of the main characteristics of the end of the last century and of the' beginning of this. unexpected speed phenomenon that has seen the 'life expectancy go from little more than 60 years of the 50's to over 80 oggi. Il quintile of ultra85 y o is the quintile with the highest percentage growth (over 200% in the 2000-projection 2020), are 20,000 centenarians in Italy (by dozens of the first '900), and several hundred thousand in the world. This has repercussions in the life of every day, an average family of north-central Italy is the second 'ISTAT composed of a child, two parents, four grandparents and two great-grandmothers ... but has repercussions especially impacting the health sphere.
Change the 'epidemiology and die single disease, paradigm of' medical approach to health and the still in service studio model. Change the background that supports methodologically modern medicine, the so-called "Evidence-based medicine (EMB)". It does not in fact make more sense to talk about diabetes or hypertension or prostate cancer as a distinct disease entities. This does not happen nearly as: the patient "normal" has diabetes, hypertension and prostate cancer together, perhaps to a cognitive impairment or a principle of incontinence. It takes 4-5-8 drugs together. Nothing can EBM to rationally deal with this patient, yet you do not study the multimorbidity and polypharmacy, no randomized trial can understand these realities.
In addition there are new dimensions as the frailty and disability. Research is thus shifting from single diseases to the overarching reality that characterize the 'aging, the frailty that is still reversible and the disability that is being treated. Fragility understood as the easy disturbance of 'homeostatic balance of' individual and disability as inability to perform normal activities of daily living.

In this scenario, the cancer is one of the key players because it is typical disease of 'age, because it determines disability and frailty before then, because it is often in charge of the transition from multimorbidity to self-sufficiency.
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...dimension of problem....
Elderly people.......... Who are?

Young old: 65-74 years of age

Older old: 75-84 years of age

Oldest old: over 85 years of age
Maps show the % of each area’s total population that will be aged 60+ in 2050. It is divided by region, not country.
76 YEARS
Global life expectancy in 2050, up from 68 years today.  

ONE IN FIVE
By 2050, one in five people will be aged 60+; they will outnumber people under 14.  

4.1 MILLION
Number of people aged 100+ globally in 2050, up from 454,000 in 2009.  

Ratio of Workers to Seniors

<table>
<thead>
<tr>
<th>Year</th>
<th>Workers</th>
<th>Seniors</th>
</tr>
</thead>
<tbody>
<tr>
<td>1950</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>2009</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>2050</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

The chart shows the number of people of working age (15-64) per person aged 65+ globally. In developed countries today, only 24% of men and 14% of women aged 60+ are economically active. The dramatic fall in the ratio of workers to seniors will have major impacts on the solvency of social security and healthcare systems.  

Longer Life, Fewer Babies:
The Causes of Demographic Shift

The aging of the global population is driven by two trends: declining fertility and increasing life expectancy. By 2050, life expectancy (top graph) will have risen by a decade, to hit 76 years. The most dramatic rises will be in the less developed regions. The gap in life expectancy between the developed and developing worlds will narrow to seven years (from 12 years in 2000).

Globally, fertility will decline from five babies per mother in 1950 to the replacement level of 2.1 in 2050 (bottom graph). In developed countries, fertility hit a record low in 2000-2005 of 1.5 children per woman.  


The Built Environment

Driven by growth in African and Asian cities, urbanization will be a major trend of the 21st century. By 2050, up to 70% of the world's population will live in cities. WHO sees making urban environments more friendly to seniors crucial to healthy, active aging. Among its aims: appropriate housing; barrier-free buildings; seating areas; accessible public transit, and enabling participation in community life.  

Number of Hip Fractures Worldwide (in millions)

<table>
<thead>
<tr>
<th>Year</th>
<th>Fractures</th>
</tr>
</thead>
<tbody>
<tr>
<td>1990</td>
<td>1.7</td>
</tr>
<tr>
<td>2050</td>
<td>6.3</td>
</tr>
</tbody>
</table>

Fractures associated with osteoporosis are a major cause of disability among the elderly. As the world ages, bone fractures are likely to become a greater health burden, especially among the female population, which is at greater risk of osteoporosis. In 2001-2002, the Australian government estimated the average cost of a fall among people aged 65+ to be USD 3,611.  

The Oldest Old

In 2050, six countries will have populations of more than 10 million people aged 80+, accounting for 57% of the world's 'oldest old.'

- China (99 million)
- India (48 million)
- Indonesia (10 million)
- Japan (17 million)
- Brazil (10 million)
- USA (30 million)
AGE RELATED CHANGES IN ELDERLY

• Poor cough/ sneeze reflex
• Stiff respiratory cage
• Poor mucociliary function
• Prostate hypertrophy-urine stagnation
• Replacement of red marrow with fat
• Deteriorating function of multiple organs e.g. kidney, liver
• Poor blood supply to peripheral tissue
<table>
<thead>
<tr>
<th>Test</th>
<th>Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body weight/fat</td>
<td>+ 35%</td>
</tr>
<tr>
<td>Plasmatic volume</td>
<td>- 8%</td>
</tr>
<tr>
<td>Albumine</td>
<td>- 10%</td>
</tr>
<tr>
<td>Globulins</td>
<td>- 10%</td>
</tr>
<tr>
<td>Total body water</td>
<td>- 17%</td>
</tr>
<tr>
<td>Extracellular fluids</td>
<td>- 40%</td>
</tr>
<tr>
<td>Cardiac electric stym/velocity</td>
<td>- 20%</td>
</tr>
<tr>
<td>Cardiac capacity</td>
<td>- 40%</td>
</tr>
<tr>
<td>Ejection fraction</td>
<td>- 35%</td>
</tr>
<tr>
<td>Vital capacity</td>
<td>- 60%</td>
</tr>
<tr>
<td>Glomerular filtration</td>
<td>- 50%</td>
</tr>
<tr>
<td>Renal/GI ematic circulation</td>
<td>- 40%</td>
</tr>
</tbody>
</table>
The big question:

What is ageing?
Aging:
Changes in the cells (cellular senescence), tissues and organs after maturation

Progressive loss of physiological functions of tissues and organs

Reduced ability to respond to environmental stimuli, due to an ineffective homeostatic response

Increased susceptibility to disease

Increased death risk
WHAT IS BIOLOGICAL AGING?

- Ageing is defined as a systemic loss of molecular **FIDELITY** that after reproduction reaches levels that exceed repair, turnover or maintenance capacity.
- This progressive loss of molecular fidelity reduces the homeostasis of the different organs.
Ageing is a complex process, results from a breakdown of the system of organization of self and a reduced ability to adapt to the environment.

Senescence

The process by which a cell loses its function and its ability to divide and grow.
Diagnosis:
Evaluation of Physical Damage

Action
Cure of Disease

Goal
Healthness

Multi Dimensional Evaluation
State of Damage
Residual Capacity

Action
Cure of disease – comorbidity and frailty impact

Goal
Cure of Disease & QoL maintenance or chronicization of disease

Traditional Medicine

Geriatric Approach

Senin, 2011
DISEASE/CURE

Social and Behaviour conditions

Loss of Omeostasis

Comorbidity

Polypharmacy

Senescence

DISEASE/CURE

SENIN, 2010
Impact of Aging on Cancer

TROUBLE IN THERAPY

Comorbidity

Anemia

Body & Metabolism Disfunctions

PolyPharmacy

Frailty

Sarcopenia
Liquid Biopsies
Circulating Tumor Cells

A. Russo
Department of Medical Oncology
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Liquid Biopsy
The concept of Non invasive test....cancer biomarkers as surrogate endpoint

- Targeted therapy
- Response
- Lack of response

Marker lev.

Baseline
Months

Pre-treatment*
Targeted therapy
Response
Lack of response
Tissue biopsy vs Liquid biopsy

Tissue biopsy:
- Often difficult and invasive
- Histological diagnosis
- Not always representative for the all tumor (especially for FNB): TUMOR HETEROGENEITY
- Not always feasible (multiple sampling?)
- Re-biopsy?

Liquid biopsy:
- Minimally invasive, reproducible, reliable, cost-effective
- Molecular characterization of the tumor
- Representative of the tumor TUMOR HETEROGENEITY
- Easily repeatable procedure
- Real-time monitoring of disease (MRD and PD)

Why the need of a liquid biopsy?
**AIM OF PMP**

- **To investigate** new methods to predict define determine risk of frailty in elderly, even if apparently in good health and as possible fight against it.

- **To prevent** cancer in elderly or at least to limit the damages linked to.

- **To make diagnosis of** dismetabolic diseases with a correct nutrition: we will promote educational programs for healthy foods.

- **To identify** new therapeutic strategy devoted to elderly population.

- **To promote** educational programs to improve quality of life for a better aging around in the world.

- **To consider** nutrition care as efficient terapeutical tool.
PERSONS OF HIGH SCIENTIFIC RELEVANCE INVOLVED IN PMP

- R. Bernabei – Catholic University – Rome (Department of Geriatrics and Neuroscience)
- C. Caruso – National University – Palermo – Department of General Pathology
- F. Di Raimondo – National University – Catania (Department of Emathology)
- D. Cova – National University – Milan (Department of Pharmacology)
- G. Lelli – National University – Bologna (Department of Oncology)
- F. Pacini – National University – Siena (Department of Endocrinology)
- A. Russo – National University – Palermo – Department of Oncology (co-chairman)
- A. Puca – National University – Salerno (Department of Medicine)
- G. Scapagnini – National University of Molise (Biochemical Research Institute)
What is The Endocrine System?

● The endocrine system is a system of glands that produce chemical messengers (hormones) and the receptors in tissues that respond to them.

◆ Examples include the thyroid, pituitary and adrenal glands plus the male and female reproductive systems.
Endocrine Disruptors

The prevention of occupational and environmental risks associated with the exposure to endocrine disruptors (EDC) represents a true challenge for experts worldwide.
What are Endocrine Disrupting Chemicals (EDCs)

They are synthetic and naturally occurring chemicals that affect the balance of normal hormone functions in animals (including humans).

- They may be estrogen or androgen modulators.

- These could unbalance sex hormones! As “modulators” EDCs may either mimic these sex hormones or else block their activities (blocking chemicals are called anti-estrogens and anti-androgens). Either way, the effects are very bad.
More Characteristics of Endocrine Disruptors

- The endocrine system appears to be similar in most animals, which means that endocrine disruptors are expected to have similar effects in most animals also in mankind and elderly specifically.

Suspect Endocrine Disruptors Cover Many Different Kinds of Chemicals

The following list illustrates the wide variety of chemicals that may need to be monitored in the environment and food:

- **Biocides** - chemicals that kill animals like barnacles and snails
- **Insecticides** - chemicals that kill mosquitoes and other bugs
- **Herbicides** - chemicals that kill weeds
- **Fungicides** - chemicals that kill fungus
- **Industrial Organic Chemicals** - solvents, plastics, paints, etc.
- **Metals** - mercury, arsenic, tin, and chromium
- **PCBs** - now are banned from commercial use
- **Chemicals with no commercial use** - chlorinated dioxins and furans (these were impurities in Agent Orange used in the Vietnam War to defoliate the forests and they are also produced naturally in forest fires).

Source: Dr. L. H. Keith at the Waste Testing and Quality Assurance Symposium, July 1997, Washington, DC
ACADEMIC PROGRAM

Nutrition & Biology of Aging

New Nutritional Treatments for Slowing Effects of Aging

Functional Foods, Nutraceuticals, and Food Supplements

Maintain Function, Delay Disease & Disability

Healthy Aging and Optimal Longevity

Courtesy of G. Scapagnini
Proposal Translating centenarian genetic studies into medical practice

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THANK YOU FOR YOUR ATTENTION!