

# HIGHLIGHTS

## *Aging and Chronic Diseases. Intervention Strategies for a Successful Aging*



*L'Aquila (Italy)*  
*September 3-5, 2015*



Fondazione  
Internazionale  
Menarini

# HIGHLIGHTS

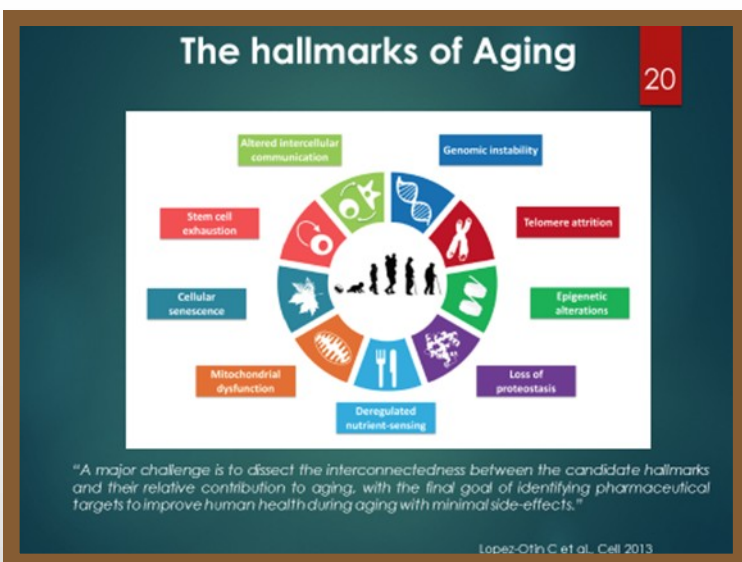
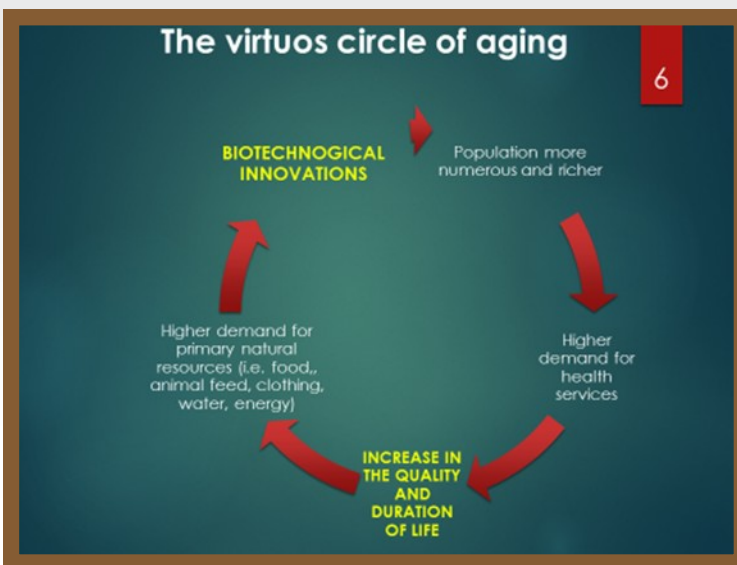
## Jump to the future: from translational medicine to healthy aging

Francesca Zazzeroni (L'Aquila, Italy)

Professor Zazzeroni pointed out that OECD (the Organisation for Economic Cooperation and Development) estimates by 2030 a growth by 28% of the world population and an improvement of the average annual income per person. The result will have to be accompanied by an improvement in the quality of healthcare services to ensure high quality of life during aging. The *red biotechnology*, a branch of biotechnology applied to medicine, plays a very important role in this process.

What is happening is a transition from traditional to translational medicine based on predictive, preventive, participatory and personalized studies, called in Italian *individuocentrica* medicine. It is a shift from illness response to illness prevention, i.e. from illness to wellness.

Personalized medicine allows, for example, to isolate cancer cells in a tumour identifying single



modified signaling of the cells. This technique opens the way to a specific personalized treatment for each single patient and it is called *target therapy*.

Where is red biotechnology mainly applied?

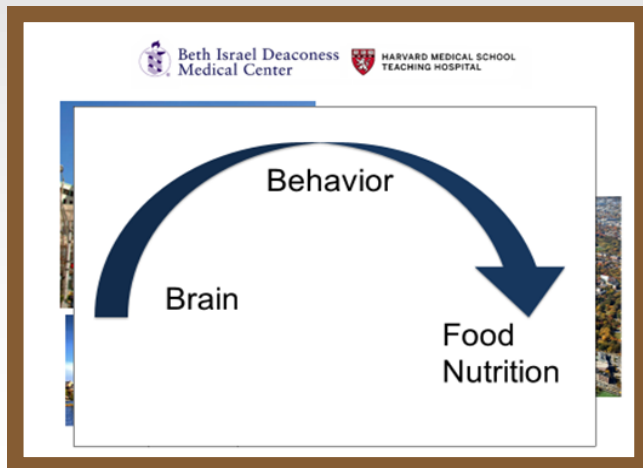
What are the relations between *red biotechnology*, *target therapy* and aging?



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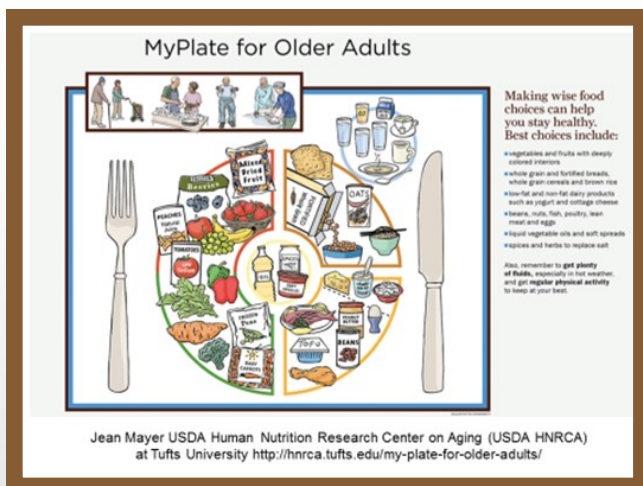
## Eating behavior, physical activity and neurocognition

*Miguel Alonso-Alonso (Boston, USA)*

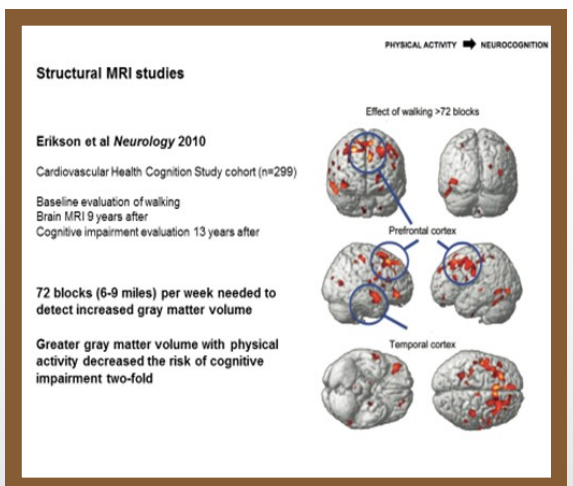


Professor Alonso-Alonso has deeply examined the existing interactions between brain, nutrition habits and physical activity. Life habits influence the food choice, which in turn affects significantly the brain functions. Over time, these close relations have developed new tools with the aim to study the association between nutrition and neurocognition. The two factors are closely related with the aging process. A poor eating habits and the lack of physical activity influence significantly the outcome of elderly people and increase their risk of morbidity and mortality. There is a specific correlation between dietary habits,

memory and attention capacities. At the basis of this phenomena are specific interactions between brain cognitive ability and external stimuli. Some brain functions have been identified as responsible to evaluate the adequate food amount to consume during meals. The obesity, for example, seems to be connected to a reduced attention response of the frontal brain cortex areas and that leads to a late evaluation of the



amount of food and a greater food intake during meals. Another key point is the so-called “satisfaction” for the intake of particular food.



**What are the mechanisms underlying the interaction between eating behaviour and neurocognitive functions? - - What are the main study methods of these mechanisms? - - What is the connection between “Response Inhibition” and obesity? - - What are the main training programs for the so-called “inhibitory control over food intake”? - - What is the association between physical activity and neurocognitive ability?**



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## Science and Healthy Aging

*Gaetano Crepaldi (Padua, Italy)*

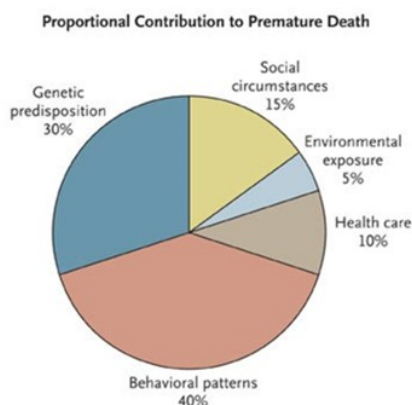
### American Wisdom on Prevention, Circa 1900

▪ "The only way to keep your health is to eat what you don't want, drink what you don't like, and do what you'd rather not."

• Twain M. Pudd'nhead Wilson's new calendar. In: Following th  
• Equator, Vol. II. New York, NY: Harper & Brothers; 1907: 13

The relationship between science and health, or better between scientific findings and their impact on lifestyle habits, is not always free from apparent contradictions. It is generally recognised that healthy lifestyle means healthy eating habits and "inconvenient and obliged" living conditions in order to reduce medium-long term invalidating disease processes. Is it true? Professor Crepaldi tackled this interesting issue presenting data regarding lifestyle, nutrition habits, physical activity, blood pressure and their connection with diseases in elderly patients.

Physical activity is not regular in people over the age of 65 and the majority of them have an unhealthy weight. 33% of elderly people fall at least once a year, 35% avoid influenza vaccine and 20% become unsuitable medication. All this means a significant increase of cardiovascular and total morbidity and mortality.



"What fits your busy schedule better, exercising one hour a day or being dead 24 hours a day?"

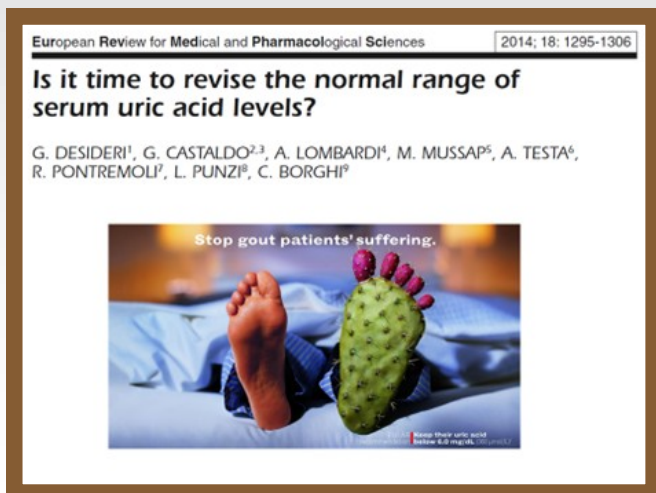
What is the impact of a proper lifestyle on the health? - - What are the benefits of a regular blood pressure control? - - What is the impact of smoke on neoplastic diseases? - - What is the impact of the Mediterranean diet on the incidence of cardiovascular diseases and diabetes?



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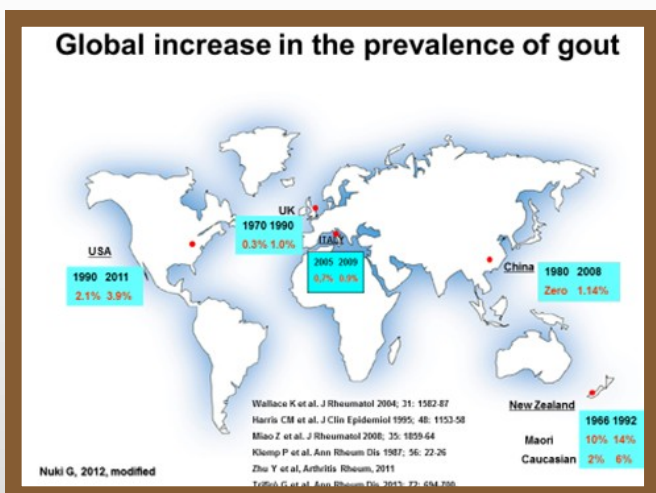
## Urate crystal deposition and gout: epidemiology and clinical evidence

*Leonardo Punzi (Padua, Italy)*



Professor Punzi presented updated data regarding gout from epidemiological and clinical point of view. Gout is a growing health problem; there is a worldwide increase in its prevalence and an incidence especially in people never suffering from this disease before. What are the underlying causes of this nearly exponential rise in gout? In his speech, Professor Punzi examined a series of issues starting from the number of methodological differences to diagnose this disease. Gout is often asymptomatic and it outbreaks in different ways, therefore, it is not always possible to recognized it. In addition, the normal reference ranges of uric acid level are not jet standardised. Most laboratories consider 7mg/dL of uric acid in the blood a normal value, whilst for the scientific societies 6 mg/dL is the regular quantity. Another important issue is the raising levels of the world's middle age population.

Physicians are not always prepared to cope with the outbreak of this disease. Finally, a key aspect is the importance of lifestyle changes, especially of dietary habits, to reduce blood uric acid levels



**IN DAILY PRACTICE...a diet must be feasible**

<b>To avoid</b> Beer	Alcohols	Fructose-sweetened beverages
<b>To limit</b> Meat	Fat fish	Seafood
<b>To encourage</b> Milk	Drink water (2L/day)	Game

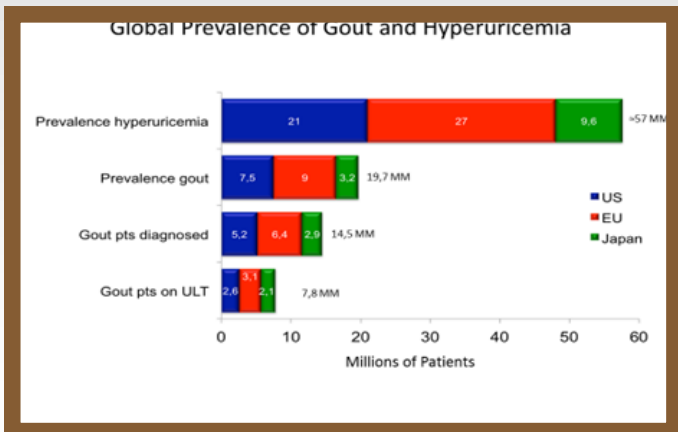
**What is the prevalence of gout in Europe and in the United States? What is the association between gout and hyperuricemia?**



# HIGHLIGHTS

## The challenge of gout management in the elderly

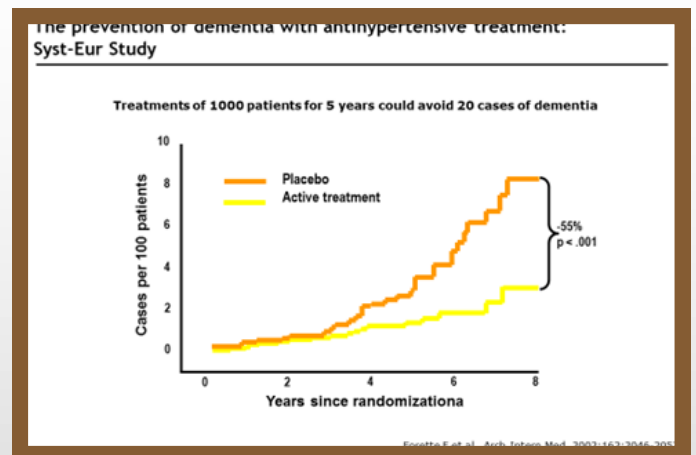
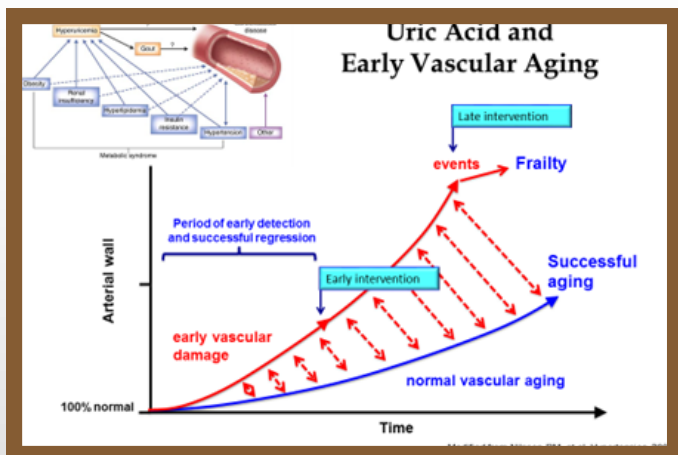
*Giovambattista Desideri (L'Aquila, Italy)*



Gout in the elderly was the topic approached by Professor Desideri. The therapeutic management of this disease is challenging as it presents a series of problems. The first problem is that it is high prevalent and widespread throughout the world. In the elderly, the prevalence of gout is constantly increasing and it is a consequence of the high level of uric acid. Another problem is the difficulty to diagnose the disease in elderly; in those patients, gout often occurs in an unusual way, with a less evident symptomatology. Another problem is the difficulty to diagnose such disease in elderly: gout often occurs in those patients in

an unusual way, with a less evident symptomatology. The usual uric acid deposits in the tissues around joints, the tophi, are often mistaken for osteoarthritis or rheumatoid nodules. Furthermore, we shall not forget also the strong effects of gout and tophi on the quality of life of elderly patients. There are then a series of related comorbidity to gout due to the link of uric acid with cardiovascular disease and cognitive decline.

What are the therapeutic challenges? Is it enough to treat symptomatic gout with classical therapies to solve effectively the problem of its management in elderly patients? Professor Desideri submitted extremely interesting data regarding the new therapeutic strategies.



What is the relationship between uric acid and cardiovascular disease? - - Which is the most sensitive and specific diagnostic test to diagnose gout? - What is the connection between hyperuricemia and vulnerability in elderly patients? - - What are the new treatments to manage the gout/hyperuricemia disease in elderly patient?



# HIGHLIGHTS

## Hypertension management in the oldest old

*Claudio Borghi (Bologna, Italy)*



### Worldwide burden of HBP

- The prevalence of HBP (20-40%) is increasing worldwide in particular for patients uncontrolled
- 54% of Stroke and 47% of CHD worldwide attributed to high blood pressure.
- 7.6 million deaths each year (13.5% of total) are attributable to high blood pressure.
- First co-morbid condition (> 85%) in patients with CVD (CHD, CHF, AF)
- 6.3 millions of years of disability (4.4% of total)

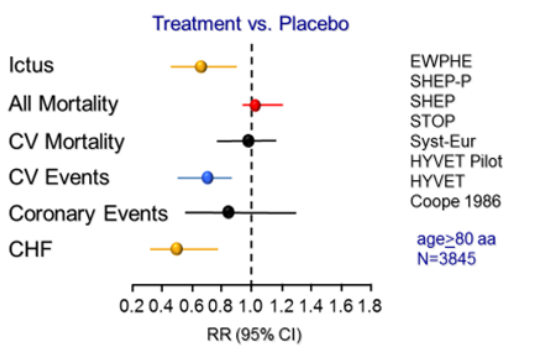
Lawes, Hoon, Rodgers: Lancet 2008; 371: 1513-18  
 Lim SS et al. The Lancet Volume 380, 2013: 2224-2260  
 Arnett KD et al. Circulation 2014; 128:1287-1293

The oldest old is a person who attained the significant age of over 80 years old. How to treat the high blood pressure disease in these type of patients? Professor Borghi addressed this current issue as in our society the prevalence of old elderly and of high blood pressure disease are constantly increasing. A consequence of that are a growing number of cerebrovascular and cardiovascular events. How to treat a patient older than 80 years of age and with elevated blood pressure? The actual scientific literature data are uncertain. The therapy that normalize blood pressure seems not to reach the therapeutic goal in every pathological condition. How to treat, then, an elderly patient with high blood pressure?

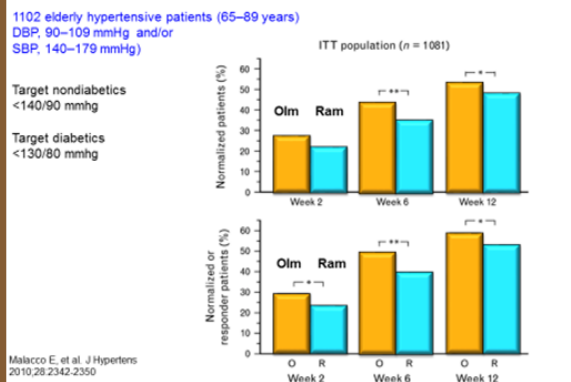
patient with high blood pressure?

Professor Borghi presented some interesting and useful general rules that may be used as an aid in treating this problem. The first point to note is to control the blood pressure level of an oldest old patient considering his general clinical conditions. In the old elderly, it is important to take into high consideration the blood pressure variability due to postural changes, especially at the early stage of an antihypertensive therapy. Furthermore, the presence of any co-morbidities and concomitant drug treatments should be carefully considered.

Treatment of hypertension in patients 80 years and older: the lower the better? A meta-analysis of randomized controlled trials



Antihypertensive efficacy and safety of olmesartan medoxomil and ramipril in elderly patients with mild to moderate essential hypertension: the ESPORT study



Are the published data of large clinical trials always favourable towards pharmacological hypertension treatments in old elderly? The lower the better, is it always true? What is the guidelines approach? How significant are blood pressure variations in older adults consequent to a change in nutritional habits? How to plan a new antihypertensive treatment in an old elderly patient? What are the most appropriate drugs for old elderly patients?



# HIGHLIGHTS

## Vaccines in older individuals: do they really protect?

*Stefania Maggi (Padua, Italy)*

### Vaccine success stories (1)

- 1) **Smallpox: complete eradication achieved**
  - In the 20<sup>th</sup> century, smallpox killed 300–500 million people<sup>1</sup>
  - Since the middle of the 20<sup>th</sup> century, widespread vaccination programmes led to complete eradication of smallpox by 1980<sup>2</sup>
- 2) **Poliomyelitis: worldwide eradication is the aim**
  - Prior to widespread vaccination, almost all children were infected with polio viruses and paralytic poliomyelitis affected worldwide approximately 1 in 200 susceptible individuals<sup>3</sup>
  - Following introduction of the vaccine in the 1950's, Europe has been certified free from wild-strain polio viruses since 2002<sup>4</sup>
- 3) **Diphtheria: no longer a common cause of death**
  - Prior to the availability of a vaccine, approximately 1 million cases and 50,000-60,000 deaths due to diphtheria occurred annually in developing countries<sup>5</sup>
  - A diphtheria vaccination program introduced in the 1970's has led to more than 90% decrease in disease incidence<sup>5</sup>

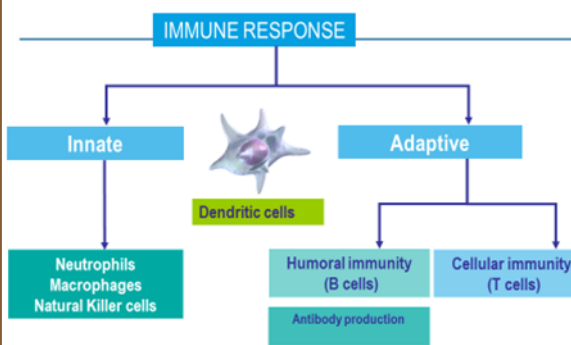
1. PATH. 2009. Available at [http://www.gtrcoalition.org/files/VAC\\_vacc\\_history\\_fr.pdf](http://www.gtrcoalition.org/files/VAC_vacc_history_fr.pdf)  
2. European Federation of Pharmaceutical Industries and Associations: Medicines for Mankind: Better health through vaccination. 2004  
3. World Health Organization. *Wkly Epidemiol Rec* 2010;85:213-28  
4. Unicef. 2002. Available at [http://www.unicef.org/meda/media\\_19193.html](http://www.unicef.org/meda/media_19193.html)

The vaccination for older adults is a current problem as infectious and common diseases may lead to serious complications up to death in elderly population. Professor Maggi addressed this issue presenting some data regarding the effect of vaccination on older adults. The decline in T and B immune functions is a typical factor in old elderly and this can lead to a lower immune response after vaccination. In the history of vaccination several notable successes have been achieved such as the eradication of certain infectious diseases that represented in the past a real health scourge as smallpox and tetanus.

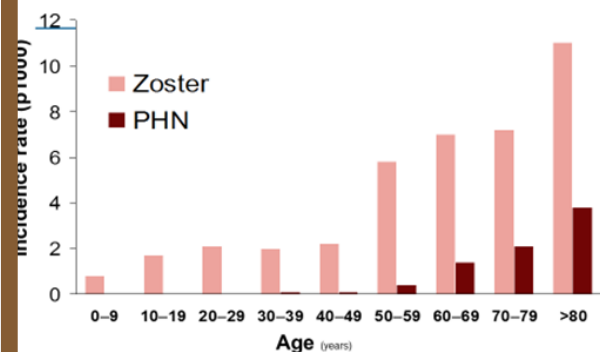
Thanks to vaccination, the disease incidence and mortality of pertussis was dramatically reduced. There is good

evidence to recommend the use of vaccines in older adults, despite the biological age limits, as they reduce morbidity and mortality for infectious diseases and related complications.

### The innate and adaptive immune responses



### PHN: a geriatric condition



What are in older adults the expected benefits to prevent infective diseases by vaccination?

How effective can be in old elderly patients the HZ vaccine to prevent post herpetic neuralgia?

What is the prevalence of FLU vaccination in Europe?

What to do to increase vaccination coverage in Italy?





# HIGHLIGHTS

## The current management of COPD in the elderly

*Raffaele Antonelli Incalzi (Rome, Italy)*

### The dimensions of COPD

- Respiratory: phenotypic variability
- Possible restrictive component
- Cognitive and affective
- Physical
- Sleep troubles
- Social
- Nutritional
- Comorbidity-related
- What age adds to...

The dimension of COPD pathology is very large in elderly patients as it involves their entire health and not only the respiratory tract. Professor Antonelli Incalzi examined this extremely topical subject as the prevalence of this condition is increasing due to the progressive ageing of the population. One of the main problem is the diagnostic and therapeutic limited capacity of the tools, commonly used to cure this disease, both for the patient adherence therapy and for the difficulty of a correct spirometry in elderly patients. Actually, a patient with COPD has a series of comorbidities, not always recognized, that limit a lot the good management of the disease and have a negative

effective on the prognosis. Another extremely important aspect is the interference of drugs used to treat the prognosis of concomitant diseases. A fundamental issue is the improvement of intervention strategies to positively impact on the main outcomes of the disease. So much remains to be done in this area, said Professor Antonelli Incalzi. A key point could be the physician's capacity in elderly patients of an interdisciplinary overall assessment of the disease.

These standards are not for the elderly (SaRA Study, Am J Respir Crit Care Med 2000; 161: 1094-1100)

COMPLIANCE WITH ACCEPTABILITY AND REPRODUCIBILITY CRITERIA*			
	Cases	Controls	p Value
Acceptability, n (%)	508 (83.6)	747 (81.9)	NS
PEFT, n (%)	405 (66.7)	550 (60.3)	< 0.05
BEV, n (%)	526 (86.6)	741 (81.2)	< 0.05
FET, n (%)	526 (86.6)	748 (82)	< 0.05
EFP, n (%)	246 (40.5)	538 (58.9)	< 0.001
FEV <sub>1</sub> reproducibility, n (%)	573 (94.3)	874 (95.8)	NS
FVC reproducibility, n (%)	532 (87.6)	830 (91)	NS
FEV <sub>1</sub> repr + accept, n (%)	487 (80.2)	725 (79.4)	NS

Definition of abbreviations: BEV = back-extrapolated volume (acceptable if less than 150 ml or 5% of FVC); EFP = end-expiratory plateau (acceptable if no change in volume for at least 1 s); FET = forced expiration time (acceptable if longer than 6 s); FEV<sub>1</sub> reproducibility = if the difference between the largest FEV<sub>1</sub> and the second largest FEV<sub>1</sub> was lower than 200 ml; FVC reproducibility = if the difference between the largest FVC and the second largest FVC was lower than 200 ml; PEFT = time-to-PEF (acceptable if less than 120 ms).

\* No. (%) of tests that meet acceptability and reproducibility criteria.

### Pulmonary rehabilitation is beneficial even in severe COPD

The Mageri Study

MRF: Mageri Respiratory Failure Questionnaire

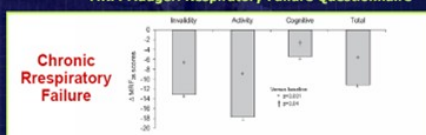


Figure 1 Improvement in MRF scores (patients with CRF) (mean value ± SE) after PR programme.

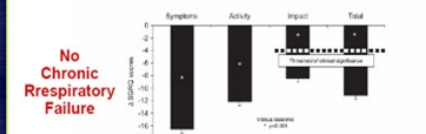


Figure 2 Improvement in SGRQ scores (patients without CRF) (mean value ± SE) after PR programme.

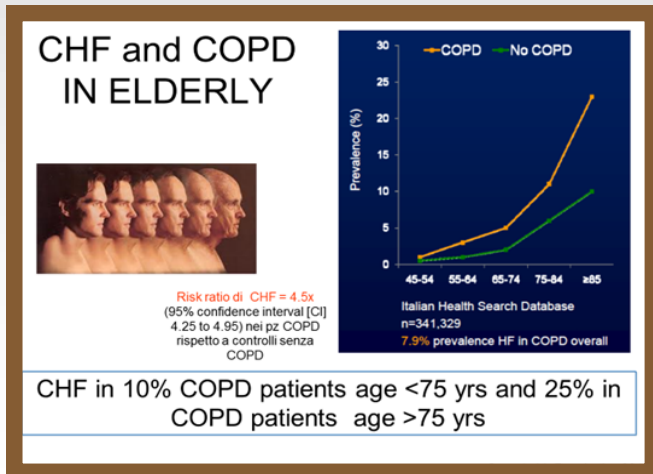
- What are the main diagnostic and therapeutic limits in treating an elderly patient?
- Does respiratory devices affect the efficacy of medicines and how much?
- How important is the rehabilitation for these patients?
- When should it start?
- What are the main therapeutic innovations?



# HIGHLIGHTS

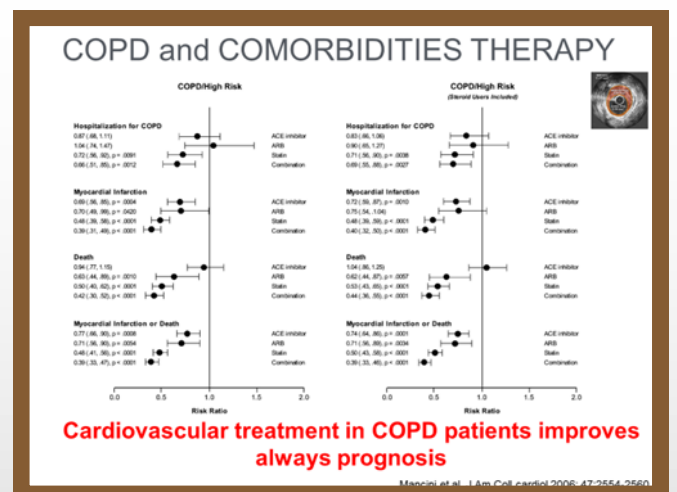
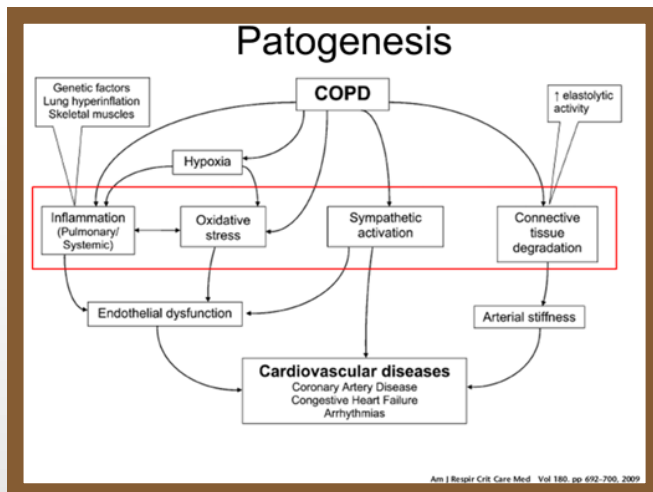
## COPD and cardiovascular diseases: the bad companions

*Stefano Marinari (L'Aquila, Italy)*



Cardiovascular disease often coexist with COPD (chronic obstructive pulmonary disease) and this association dramatically compromises the prognosis of patients, particularly of elderly or even oldest old. Professor Marinari tackled this very topical issue frequently observed in elderly population. The coexistence of these two diseases leads to a significant increase in cardiovascular mortality, which in turn is related to FEV1 levels. The two diseases can trigger pathogenic mechanisms that will reinforce and worsen the illness in elderly patients. The prevalence in the population of persistent inflammation phenotype subjects is 16%; they have higher mortality in comparison to those who do

not have this phenotype status. Should we add to these patients the inflammatory consequences of smoking and the COPD, we would understand how devastating the outcome of the disease results in these subjects.



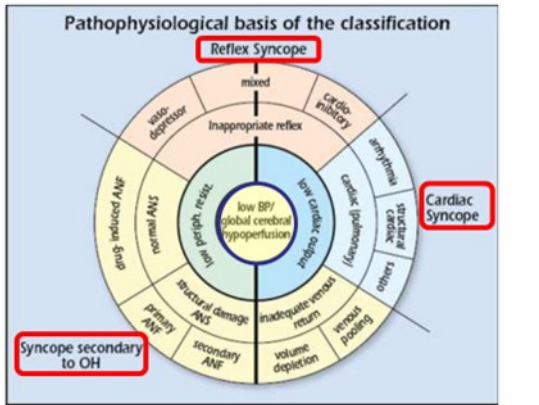
- What are the prognostic factors resulting when the two diseases occur together?
- What are the main common pathophysiologic mechanisms of these two diseases?
- What are the pathogenic theories supporting this comorbidity?
- What are the main therapeutic protocols?



# HIGHLIGHTS

## Syncope and falls in the elderly

*Andrea Ungar (Florence, Italy)*



How frequent are the falls in older or oldest old persons? These are certainly not accidental events, what causes them? In other words, how to distinguish, in older adults, syncope as a cause of falls from other types of recurring falls? In his speech, Professor Ungar replied to these questions. He first started giving the definition of syncope, which is far from being a trivial disease. In addition, pathophysiological basis identify specific types of syncope as the cardiac syncope, whose aetiology differs from the reflex syncope and from many others of unknown genesis. Pharmacological treatments, like diuretics and nitrates,

are seriously considered among the causes of syncope. Carotid sinus massage and glyceryl trinitrate test are essential to be performed but, are they safe in the oldest old? On the other hand, there are also the unexplained falls due to transitory loss of consciousness. They are difficult to identify and so common in older people. Very often falls are unexplained in older patients i.e. it is difficult to understand the

the cause.

### TLOC - suspected syncope

#### Initial evaluation

**History, physical examination, orthostatic BP measurements, ECG**

**And**

**Carotid sinus massage (CSM) in patients > 40 years**



Can we perform **carotid sinus massage** also in the elderly?  
...Is it safe?

- What are the main causes of syncope in older people?
- How to distinguish syncope from loss of transient consciousness?
- What are the main complications during carotid sinus massage?
- What are the devices to implant in the older patients to diagnose syncope?
- What are the main causes for the falls of older patients?



# HIGHLIGHTS

## Erectile dysfunction and cardiovascular risk

*Andrea Isidori (Rome, Italy)*

ANDROLOGY IS AT THE «HEART OF MEDICINE»



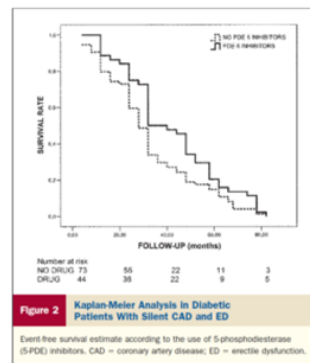
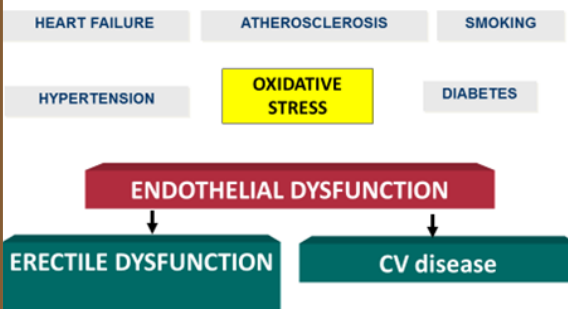
In his speech, Professor Isidori outlined that there is an association between cardiovascular risks and erectile dysfunction. Hypertension, hypogonadism, increasing age, obesity, diabetes mellitus, dyslipidaemia, inflammation are all conditions increasing cardiovascular risk and favouring erectile dysfunction. These two pathological conditions develop in response to endothelial dysfunction.

Although the close correlation between erectile dysfunction and cardiovascular risk, DE disease is rarely treated in the male elderly population. Physicians underestimate the significance of this disease and treat the elderly patient in order to cure other cardiovascular risks. They usually ignore the erectile dysfunction despite the high cardiovascular risk level in this kind of patients.

Pharmacological treatment for DE is based on hormone therapies and 5-phosphodiesterase inhibitors that significantly reduce the cardiovascular risk.

In elderly male, the erectile dysfunction is often related to a significant reduction in sexual activity and this condition leads to a significant increase of CV risk. Erectile dysfunction should therefore be considered a warning sign for future cardiovascular events as it is an early marker of endothelial dysfunction.

CVD and ED develop in response to endothelial dysfunction



*Gazzaruso et al.*

**Among patients with CAD and ED, 5-phosphodiesterase (5-PDE) inhibitor use were associated with a lower rate of MACE (Mantel log-rank test: 4.608; p 0.032)**

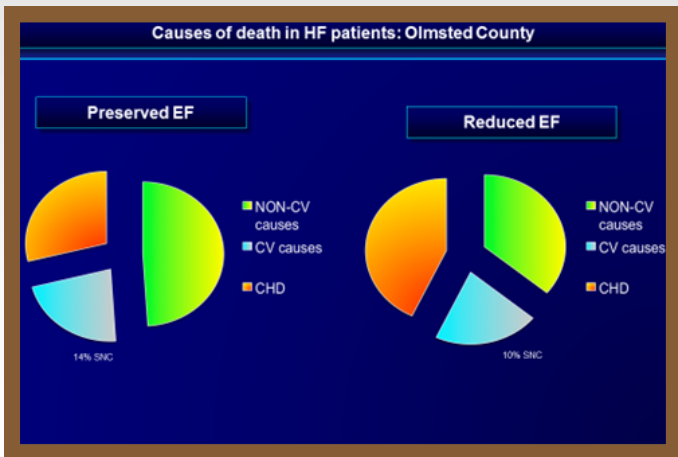
Why the erectile dysfunction occurs before the cardiovascular disease?  
What is the incidence of secondary cardiovascular events due to erectile dysfunction? - - - Are patients affected by erectile dysfunction be protected from CV when treated with 5-phosphodiesterase inhibitors?  
What is the effect of a long lasting treatment with 5-phosphodiesterase inhibitors?



# HIGHLIGHTS

## Clinical use of phosphodiesterase-5 inhibitors in chronic heart failure

*Claudio Ferri (L'Aquila, Italy)*

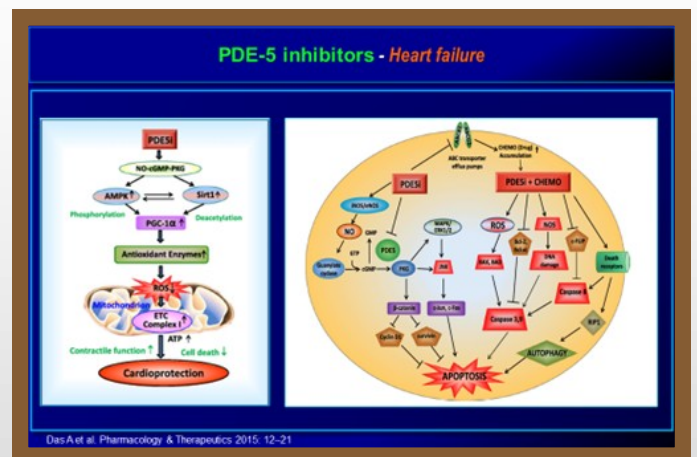
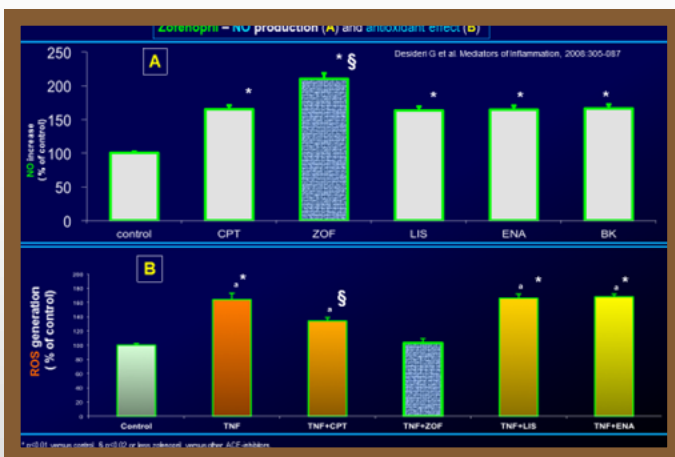


The treatment of the endothelial dysfunction reduces the incidence of major cardiovascular events. What occurs in heart failure patients treated with the 5-phosphodiesterase inhibitors?

Professor Ferri addressed this very important issue starting from the pharmacological treatment of heart failure. The patients affected today by heart failure also present a number of comorbidities as COPD, depression, gastrointestinal diseases, cancer, etc... that cause their death not for cardiovascular events. Heart failure is a complex pathology and its therapy requires today the use of a series of drugs.

A key point of the therapy is the use of medications

inducing in the heart an increase of nitrogen monoxide (NO). Professor Ferri announced in advance that innovative drugs for the treatment of heart failure would be soon introduced. They will radically change the current treatment but they still need to be approved by the European Agency for the Evaluation of Medicinal Products (EMA). What are the effects of 5-phosphodiesterase inhibitors on the heart contractile function in patients suffering from heart failure? The collected results in human being seem to be positive; therefore, the inhibitors have a protective effect, except for patients with hypertrophic cardiomyopathy and/or using nitrates.



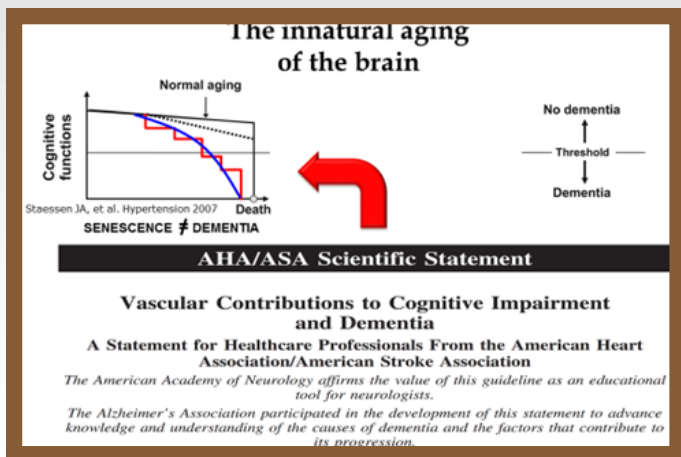
**What is the future of heart failure treatments? - - How act 5-phosphodiesterase inhibitors on the heart? - - Are there possible contraindications in using 5-phosphodiesterase inhibitors in patients with heart failure?**



# HIGHLIGHTS

## Crossing the border from normal cognitive aging to dementia

*Giovambattista Desideri (L'Aquila, Italy)*

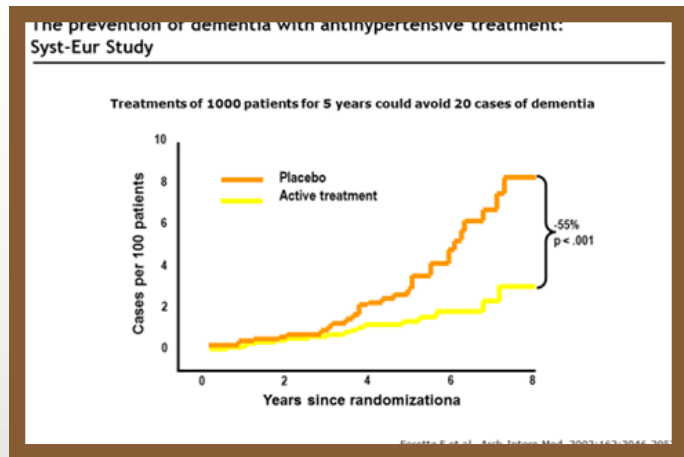
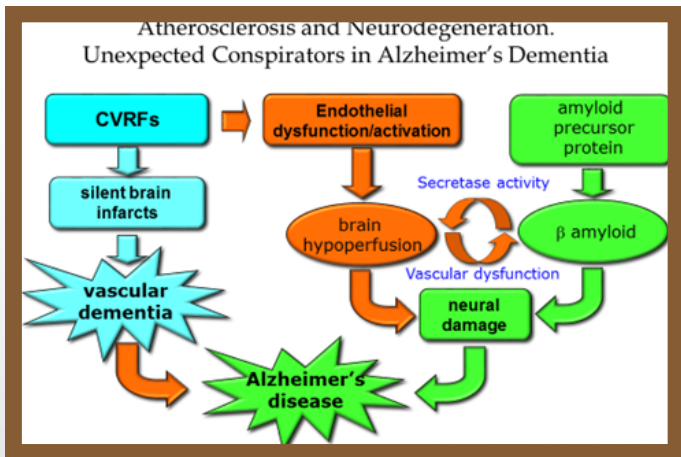


Dementia is a disease exponentially increasing in western world due to the progressive ageing of the population. Is that the only reason for its prevalence? Which are the pathophysiological basis conditions for this disease? With his speech, Professor Desideri tackled this extremely current subject in our society. From pathophysiological point of view, there is a clear association between hypertension and cognitive decline.

The link between hypertension, other cardiovascular risk factors and dementia are based on the atherosclerotic vascular alterations. Such lesions could not only reduce the blood pressure in the brain and therefore

contribute to the outbreaks of the cognitive deficiency, but they are also a direct neurodegenerative risk factor evolving clinically in the Alzheimer's disease.

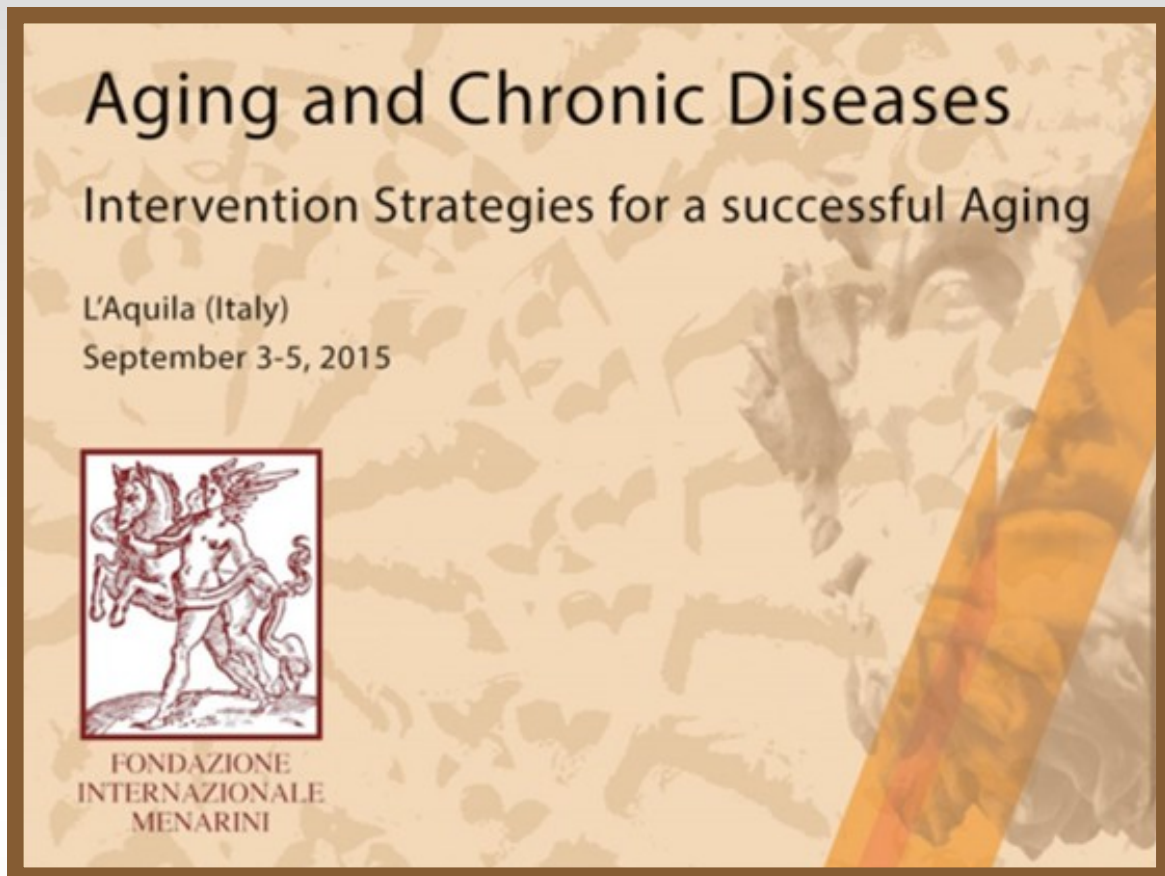
The endothelial dysfunction seems to be a common pathogenic factor. High blood pressure and other cardiovascular risk factors lead to an increase of the accumulation of  $\beta$ -amyloid in the brain. Anti-hypertensive treatment reduces the occurrence of cognitive decline in old hypertensive patients.



**What are the pathophysiological mechanisms associating hypertension to cognitive decline? - - How much does the hypertensive treatment protect the patient from the incidence of a cognitive deficit? - - Are there classes of antihypertensive drugs having a more protective effect against cognitive decline? - - How to modulate the antihypertensive treatment in older fragile patients at risk for dementia?**



# HIGHLIGHTS



These are just some of the topics addressed during the congress. For further details please consult the website of the Fondazione Internazionale Menarini that contains the full version of the congress talk.

Visit the link: [www.fondazione-menarini.it/](http://www.fondazione-menarini.it/)... and, after logging in, enter Multi-media Contents.



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