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Sense an Elusive Threat (Now Old Age has Nowhere to Hide)

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NO CONFLICT OF INTEREST

PREPHASE

The only thing that comes uninvitedly is old age. A life-threatening condition. Sense an elusive threat. A controversial life. Now old age has nowhere to hide.

In fact, advancing age is the major risk factor for a number of chronic diseases in humans. Aging is a major risk factor for most common neurodegenerative diseases, including mild cognitive impairment, dementias including Alzheimer's disease, cerebrovascular disease, Parkinson's disease, and Lou Gehrig's disease. Wear and tear theories of aging suggest that as an individual age, body parts such as cells and organs wear out from continued use. Wearing of the body can be attributable to internal or external causes that eventually lead to an accumulation of insults which surpasses the capacity for repair. Due to these internal and external insults, cells lose their ability to regenerate, which ultimately leads to mechanical and chemical exhaustion.Old age refers to ages nearing or surpassing the life expectancy of human beings, and is thus the end of the human life cycle.

Key Words Alzheimer's disease, cerebrovascular disease, Parkinson's disease, Lou Gehrig's disease. Cytokine dysregulation, Tauopathy, Gerontology,

1 Introduction

Cytokine dysregulation is believed to play a key role in the remodeling of the immune system at older age ,which seems to be a marker of unsuccessful aging.(1)

It is a dynamic network that is continuously remodeling throughout each person's life as a result of the interaction between our genes, lifestyles, and environments (2–3).

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The cytokine network is a highly complex system of immune molecular messengers, with multiple layers of diverse serum mediators, as well as gene polymorphisms (4).

Today there is increasing of diverse human diseases ranging from , cardiovascular pathology, diabetes, metabolic syndrome, neurodegeneration, and cancer, to aging itself (5.6,7).

Aging is a ubiquitous biological phenomena, characterized by ever-increasing susceptibility to diseases - mitochondrial damages, and ultimately death.(8)

Aging is an ubiquitous biological phenomena characterized by ever-increasing susceptibility to diseases due to increased oxidative stress (OS).(9)

Current evidence suggests both resveratrol and pterostilbene may be modulators for aged-related neurodegeneration, obese, diabetes, and cardiovascular diseases.(10)

Brain aging is mainly characterized by a progressive metabolic imbalance, brain vasculature alterations, and a decline in adult neurogenesis, among other signs (11), leading to a cognitive and motor decline, not only in the context of neurodegenerative diseases (12)

The most important risk factor for PD is aging. Alterations in mitochondrial activity are typical of aging.. 13)

Mitochondria are intracellular organelles deriving and storing energy through the respiratory chain by oxidative phosphorylation (14,15)

Aging is a process characterized by the progressive loss of tissue and organ function. 16)

Neurofibrillary tangles (NFTs) correlate more closely with the severity of dementia than plaque counts (17,18). The association of tangles with a variety of brain damage supports the “tauopathy” concept of neurodegeneration (19).

The brain is highly susceptible to an oxidative imbalance due to its high-energy demand, high oxygen consumption, (20).

2 Significant Gap in Research

Brain function declines with age and is associated with diminishing mitochondrial integrity.Mitochondrial dysfunction may be a principal underlying event in aging, (21).

Mitochondrial membrane potential, respiratory control ratios and cellular oxygen consumption decline with age and correlate with increased oxidant production (22,23). Mutations in genes that encode mitochondrial proteins could compromise mitochondria by altering components of the electron transport chain (24)

Neurofibrillary tangles (NFTs) correlate more closely with the severity of dementia than plaque counts (25). The association of tangles with a variety of brain damage supports the “tauopathy” concept of neurodegeneration(26).

The brain is highly susceptible to an oxidative imbalance due to its high-energy demand, high oxygen consumption, (27).

The incidence and severity of cerebrovascular disease (CVD) increase with advancing age, as does the risk of developing Alzheimer's disease (AD). (28)

L-Carnitine and acetyl-L-carnitine (ALC) are both used to improve mitochondrial function..(29)

L-Carnitine facilitates entry of long-chain fatty acids into mitochondria for utilization as fuel (30)

Developing therapeutic interventions for such conditions demands a greater understanding of the processes underlying normal and pathological brain ageing.(31) Alzheimer's disease, which now affects almost 50% of adults over the age of 85 in the United States (32).

The sequence of the human genome represents our genetic blueprint, and accumulating evidence suggests that loss of genomic maintenance may causally contribute to aging.(33)

Aging is a major risk factor for neurodegeneration, cancer, and other chronic diseases (34)

3 History

In the medieval Islamic world, several physicians wrote on issues related to Gerontology. Avicenna's *The Canon of Medicine* (1025) offered instruction for the care of the aged, including diet and remedies for problems including constipation (35) Arabic physician Ibn Al-Jazzar Al-Qayrawani (Algizar, c. 898–980) wrote on the aches and conditions of the elderly (Ammar 1998, p. 4) (36) His scholarly work covers sleep disorders, forgetfulness, how to strengthen memory (37,38)and causes of mortality (39) Ishaq ibn Hunayn (died 910) also wrote works on the treatments for forgetfulness (U.S. National Library of Medicine, 1994)(40)

Some early pioneers, such as Michel Eugène Chevreul, who himself lived to be 102, believed that aging itself should be a science to be studied. Élie Metchnikoff coined the term "gerontology" 1903 (41)

Modern pioneers like James Birren began organizing gerontology as its own field in the 1940s, later being involved in starting a US government agency on aging – the National Institute on Aging. (42)– programs in gerontology at the University of Southern California and University of California, Los Angeles, and as past president of the Gerontological Society of America (founded in 1945) (43)

With the population of people over 60 years old expected to be some 22% of the world's population by 2050, assessment and treatment methods for age-related disease burden. (44,45,46)

4 Where the Research Go Next?

Many disorders are multifactorial in origin and are best managed by multifactorial interventions. Diseases often present atypically.Not all abnormalities require evaluation and treatment.Complex medication regimens, adhered problems, and polypharmacy are common challenges.Functional screening should include assessment of ADL and IADL and questions to a detect weight loss, falls, incontinence, depressed mood, self neglect, fear for personal safety, and common serious impairments (e.g. hearing, vision, cognition, and mobility).. it may indicate early impairment, such as dementia, incontinence, or worsening hearing loss, which additional gentle questioning or assessment may uncover.Choice of antidepressant agent in elders is usually based on side effect profile and cost. Citralopram and sertraline are often used as first-line agents because of their low side-effect profiles.(47)

Neuronal loss, cochlear degeneration, increased lens rigidity, lens opacification, anterior horn cell loss, dorsal column loss and slowed reaction time. Clinical consequence of age related CNS abnormalities which includes, increased risk of delirium, presbyacusis/high-tone hearing loss, cataract, muscle weakness and wasting, reduced position and vibration sense and increased risk of falls.Reduced lung elasticity and alveolar support, increased chest wall rigidity, increased V/Q mismatch, reduced cough and ciliary action. Clinical consequence of age related respiratory system abnormalities which includes, reduced vital capacity and peak expiration flow, increased residual volume, reduced inspiratory reserve volume, reduced arterial oxygen saturation and increased risk of infection.Reduced maximum heart rate, dilation of aorta, reduced elasticity of conduit/capacitance vessels and reduced number of pacing myocytes in sinoarterial node.

Clinical consequence of age related cardiovascular system abnormalities which includes, reduced exercise intolerance, widened aortic arch on X-ray, widened pulse pressure, increased risk of postural hypotension and increased risk of arterial fibrillation.Deterioration in pancreatic β-cell function.

Clinical consequence of age related endocrine system abnormalities which includes, increased risk of impaired glucose tolerance.Loss of nephrons, reduced glomerular filtration rate and reduced tubular function.

Clinical consequence of age related renal system abnormalities which includes, impaired fluid balance, increased risk of dehydration/overload, impaired drug metabolism and excretion.Clinical consequence of age related gastrointestinal system abnormalities which includes, constipation and risk of colon cancer.Reduced bone mineral density. In ageing increased risk of osteoporosis and fractures.(48)

5 Major Advances and Discoveries

Age has important influence on the likelihood of being afflicted with cancer..Tragically, children are not spared; cancer accounts for slightly more than 10% of all deaths in the Unites States, second only to accidents. However the types of cancers that predominate in children are significantly different from those seen in adults. Canomas, the most common general category of tumors in adults, are extraordinarily rare among children.The common neoplasms of infancy and childhood include the so-called small round blue cell tumors such as neuroblastoma, Wilms tumor, retinoblastoma, acute leukaemias, and rhabdomyosarcomas. (49)

Just a few years ago, researchers believed that low levels of zinc in the body might contribute to the development of Alzheimer's. However, when scientists at the University of Melbourne in Australia tested the zinc theory, they got disastrous and totally unexpected results.(50)

While some researchers found excessive aluminum in the brain tissues of Alzheimer's sufferers, other scientists said the aluminum came from chemical agents the researchers used to analyze the brain tissue.

Animal studies seem to show an aluminum / Alzheimer's link. When researchers injected aluminum into the brains of rabbits and cats, changes in their behavior and their brain mimicked changes in Alzheimer's victims.

People with kidney failure who have undergone dialysis fluid is made from water containing large amounts of aluminum. This condition is called dialysis dementia.

An experimental drug that draws aluminum out of the body seems to slow down the progression of Alzheimer's disease.

You may have heard that taking an aspirin every day can ward off stroke and heart disease, but now there may be another unexpected benefit.

Some Alzheimer's experts believe that aspirin, ibuprofen, naproxen and other nonsteroidal anti-inflammatory drug (NSAIDs) commonly recommended for arthritis can prevent Alzheimer's disease.

That's the finding of a recent study of 50 pairs of elderly twins. Only one of each set of twins had used NSAIDs. That twin was less likely to develop Alzheimer's disease or developed it years later than the other twin.

You need to talk to your doctor before you begin taking an aspirin a day, though. NSAIDs can cause ulcers and bleeding in your stomach, so you have to weigh your individual risk of heart disease, stroke and Alzheimer's against your risk of stomach problems and bleeding.(51)

Alzheimer's disease (AD) is the most common cause of dementia in older adults, with an increasing incidence as a function of age. The disease usually becomes clinically apparent as insidious impairment of higher cognitive functions. As the disease progresses, deficits in memory, visuo-spatial orientation, judgement, personality and language emerge. Typically over a course of 5 to 10 years, the affected individuals becomes profoundly disabled, mute, and immobile. Patients rarely become symptomatic before 50 years of age; the incidence of the disease increases with age, and the prevalence roughly doubles every 5 years, starting from a level of 1% for the 60- to-64-year-old cohort. His progressive increase in the incidence with increasing age has given rise to major medical, social, and economic concerns in countries with aging populations. About 5% to 10% of cases are familial forms of AD; these have provided important insight into the pathogenesis of the more common sporadic form of the disease. While pathologic examinations of brain tissue remains necessary for the definitive diagnosis of AD, the combination of clinical assessment and modern radiologic methods allows accurate diagnosis in 80% to 90% of cases as confirmed at autopsy.(52)

6 Current Debate

Supported by Hanover, Independent Age, British Red Cross and PA Consulting Group, the big aging population debate includes three fringe events at the party conferences, as well as two seminars at the Guardian's London HQ. An online series of live discussions, features and debate will explore the issues facing older people, their families and those running the services that support them. (53) In the future, the escalation in human lifespan will depend on healthier lifestyles and the availability of improved biomedical advances and biotechnologies. With scientific interventions and environmental improvements, we may be confident that aging will slow down over the course of the current century.(54)Experiments conducted in old mice, have shown that age-related DNA damage diminishes when the cellular level of NAD+ is increased.(55) Another study just published in Nature,demonstrates the role of renewed neuro-stem cells (NSCs) in the hypothalamic region of the mouse brain.(56)Human life expectancy has steadily increased since the nineteenth century. Reports of

supercentenarians — people such as Clement who live to older than 110 — together with observations of model animals whose lifespans can be extended through genetic or dietary modifications, have prompted some to suggest that there is no upper limit on human lifespan. Others say that the steady increase in life expectancy and maximum human lifespan seen during the last century will eventually stop (57)

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