

THE AGEING MALE

B. Lunenfeld

INTRODUCTION – DEMOGRAPHIC TRANSITIONS

In times, when the changes around us are accelerating, but our perceptions of these changes are lacking behind, it becomes of crucial importance to have a vision of the future. I will therefore make an attempt to briefly review in this paper some data from the past and present, and from the lessons learned, attempt to apply these to the most likely projections for the future.

The significant increase of the mean worldwide life expectancy at birth, is a victory of human will, endurance and technology [1]. However at the beginning of a new millenium, new challenges are arising in relation to the lengthening life span. How do we use current and evolving technologies to impart a greater quality of life across that increasing time frame?

The past century has witnessed a transition from a high mortality/high fertility pattern to one of low mortality/

low fertility. This change of pattern resulted in a rapidly growing and rapidly ageing world population. This phenomena is a basically new feature in the history of mankind [2]. The human race entered the 19th century with a global population of 978 million people, the 20th century with 1650 million people and the 21st century with a worldwide population of 6168 million. The estimates and projections of the United Nations indicate that between 1900 and 2100, world population will increase seven-fold, from 1.65 billion to 11.5 billion: an increase of almost 10 billion people. This rapid increase in world population is in spite the fact that effective family planing has significantly reduced fertility rates, and that 10 countries including Italy, France and Germany are today well below the replacement levels (Table 1).

Due to the worldwide prolongation of the mean life expectancy and the drastic reduction of fertility rate it is projected that the elderly (above 65) will increase within the next 25 years by 82 %, whereas the new born only by

Table 1. Total fertility rate and population (million) in the European Union and selected countries of Europe 1995

	Total fertility rate	Population (Mio.)
European union (15 countries)	1.51	370
Other Europe (21 countries)	1.65	355
Italy	1.24	57.2
Spain	1.27	39.6
Germany	1.30	81.6
Austria	1.47	8.0
Russian Federation	1.53	148.5

Table 2. Life expectancy of males in different ages

Year	At birth	Age of 15	Age of 45	Age of 65
1888	43.9	43.9 (58.9)	22.6 (67.6)	10.8 (75.8)
1988	70.5	56.4 (71)	28.2 (73.2)	13.0 (78)

Table 3. Life (LE) and health expectancy (HE) of men (Selected countries).

Country	LE	HE
USA	70.1	55
Canada	73	67
France	70.7	61

3 %. The working age population will increase by only 46 %. The UN projects (in their 1998 revision) that by 2050, the proportion of persons above 60 will exceed for the first time the proportion of children below 15, and 13 countries will have more than 10% of the oldest old > 80 years old, in their population. Italy will be leading with 14 %.

Hence the marked increase of the elderly population in relation to the working age population will be compounded by a simultaneous decrease in the population of children who comprise the working age population of the next generation. Thus a declining labour force will have to support an increasing number of elderly.

The last century has been marked by the triumph of partially preventing the premature termination of life. This was mainly due to the development of antibiotics, vaccines, safer water, better sanitation and personal hygiene. These events were responsible for the decrease of the appearance of epidemics and the control of many infectious diseases. The mean life expectancy at birth has been prolonged by more than 25 years within the last century, how-

ever life expectancy at the age of 65 increased by less than 3 years during the same time frame (table 2). Moreover despite the enormous medical progress during the past few decades, 25 % of life expectancy after age 65 is spent with some disability, and the last years of life are accompanied by a further increase of incapacity and sickness. Life has been prolonged, and acute disease is not any more the major cause of death. Today one dies from chronic illnesses, degenerative diseases, metastatic cancer, immune-deficiencies and other diseases which prolong disability, immobility and dependency, and make dying a long, painful, and expensive procedure (Fig 1).

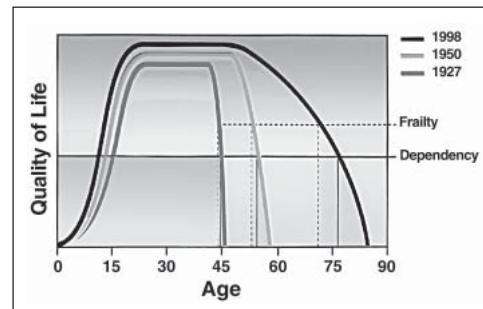


Figure 1. In 1927, the average life span was around 45 years and death resulted usually from acute disease. Hospitalization and/or dependency lasted for only days or at most weeks. In 1950, the average life span was about 58 years and hospitalization or dependency lasted for weeks or month. In 1999, the average life span is about 80 years and death results from cancer, degenerative diseases, organ failure or immune deficiencies and hospitalization or dependency may last months or years.

Hence we must take into account both "life expectancy" and "health expectancy" (Table 3). Health authorities should be encouraged to publish both these data, as some already do. The cost of caring for the increasing population of senior citizens will become prohibitive with its attendant socio-economic consequences. To the prudent health care administrators, the establishment of preventive measures, rather than concentration on inter-ventive care is an important strategic thrust in overall management of the ageing population.

Frailty, disability and dependency will increase immensely the demand to the social and health services. The very high cost in relation to these services may strain to the limit of the ability of health, social and even political infra-structures not only of developing but also of the most developed and industrialized nations.

The ability to permit men to age gracefully, maintain independent living, free of disability, for as long as possible is a crucial factor in ageing with dignity and would furthermore reduce health service costs significantly. To achieve this objective, a holistic approach to the management of ageing has to be adopted.

The promotion of healthy ageing and the prevention, or drastic reduction of morbidity and disability of the elderly must assume a central role in the formulation of the health and social policies of many, if not all, countries in the next century. It must emphasize an all encompassing life-long approach to the ageing process beginning with pre-conceptual events and focus on appropriate interventions at all stages of life (Fig. 2). Since the determinants of "ageing" and of "life expectancy" extend from genetic and molecular determinants to the increasingly powerful

forces of environmental, economical, technological and cultural globalization, specific measures should include the promotion of a safe environment, healthy lifestyle including proper nutrition, appropriate exercise, avoidance of smoking, drug and alcohol abuses, social interactions to maintain good mental health, and medical health care including the control of chronic illnesses. If done effectively, it should result in a significant reduction of the health and social costs, reduce pain and suffering, increase the quality of life of the elderly and enable them to remain productive and contribute to the well-being of society.

MEN, AGEING AND HEALTH

In contrast to the recent and much needed attention to the social position and health status in women, men health concerns have been relatively neglected. Men continue to have a higher morbidity and higher mortality rate and life expectancy for men is significant shorter then that for women in

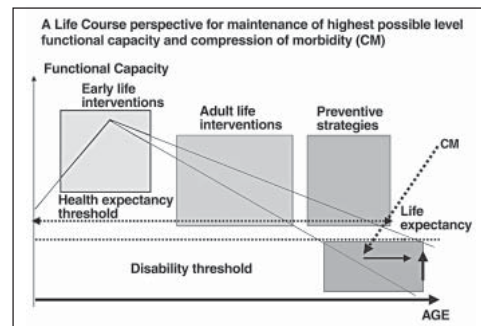


Figure 2. Early life interventions should be aimed at maximizing functional capacity, bone mass and optimal body composition. They must include effective vaccination, promotion of healthy life-style with outdoor activities, healthy nutrition and health and sex education.

most regions of the world [3]. The course of disease, response to disease and societal response to illness exhibit gender differences and often result in different treatments and different access to health care.

The major causes of morbidity and mortality all take effect over extended periods. Therefore, primary prevention strategies will be most effective when initiated at the earliest opportunity. Ischemic heart disease, hypertension and stroke, as well as lung cancer, are diseases which primary prevention needs to be addressed. When problems are more prevalent at older ages, as with prostate and colorectal cancers and osteoporosis, early diagnostic tests, such as appropriate and periodic use of laboratory tests (e.g. PSA), and screening procedures can play an important role in secondary prevention and self care strategies [4].

Significant numbers of male related health problems such as changes in body constitution, fat distribution, muscle weakness, urinary incontinence, loss of cognitive functions, reduction in well being, depression, as well as sexual dysfunction could be detected and treated in their early stage if both physicians and public awareness of these problems were more pervasive. This could effectively decrease morbidity, frailty and dependency, increase quality of life and reduce health service costs.

When discussing age related problems, it is often difficult to separate and to distinguish between the natural ageing process, primarily genetically determined (which today can not be changed), ageing amplifiers determined by environmental and developmental factors (which can be modified) and an acute or chronic illness or intercurrent diseases (which can be prevented, delayed or cured). It must not be forgot-

ten, that ageing by itself is associated with reduced productivity, decreased general vigor ("Frailty of the aged") as well as with increased incidence of defined diseases. These include: cardiovascular diseases, malignant neoplasms, chronic obstructive pulmonary diseases; degenerative and metabolic diseases (arthritis, arthrosis, diabetes, osteoporosis etc.), visual and hearing loss as well as various dementia (i.e. Alzheimer's disease), anxiety and mood disorders

Depression is the most common functional mental disorder affecting ageing males, it is under-diagnosed and under-treated. It has a high rate of recurrence and is associated with significantly increased mortality. Depression is closely linked in this group with physical illness and altered presentation can make diagnosis difficult. Thorough holistic assessment and good communication skills are of utmost importance. Nurses and medical professionals can improve the mental health of these patients with therapeutic attitudes and actions. It must be remembered that about 90% of older men who attempt or complete suicide have depression either not diagnosed or inadequately treated. If men continue to under-report depression, the morbidity of this condition will continue to increase. Proper identification and treatment of depression will have significant public health implications.

Cognitive decline with age is inevitable but the global impairment of the higher cortical functions can be delayed. In women HRT was shown to delay the onset of Alzheimer's disease. There is an urgent need to obtain such information also in men. Dementia is a major public health issue accounting for significant morbidity, loss of independence, loss of dignity and eventual institutionalization. The prevalence of

severe dementia increases from 1% at age of 65–74, 7% at age of 75–84 and 25% after the age of 85. 37% of patients with Alzheimer's disease lived in institutions compared with 1.7% of subjects without dementia.

PARTIAL ENDOCRINE DEFICIENCY IN AGEING MEN (PEDAM)

The most important and drastic gender differences in ageing are related to the reproductive organs. In distinction to the course of reproductive ageing in women, with the rapid decline in sex hormones and expressed by the cessation of menses, men experience a slow and continuous decline of a large number of hormones but do not show an irreversible arrest of reproductive capacity in old age [5].

In the ageing male, endocrine changes and decline in endocrine function involves:

1) reduced secretory output from peripheral glands due to sclerosis of blood vessels (in the interstitial tissue of Leydig cells, this process contributes for example to a large extent, to the decrease of gonadal androgens),

2) alterations in the central mechanism controlling the temporal organization of hormonal release. The heterogeneity in basal neuroendocrine function in ageing reported in the literature, is compounded by the fact that basal hormone levels are far from constant but fluctuate considerable, due to the interaction of circadian rhythmicity, sleep, and for some of the hormones intermittent pulsatile releases at different intervals. During ageing, a number of morphological and neuro-chemical alterations have been found in the supra-chiasmatic nuclei, (the central circadian

pacemaker) and are likely to be responsible for the dampened circadian hormonal and non hormonal rhythms. These are in part responsible of the age-dependent decrease of the peripheral levels of testosterone, dehydroepiandrosterone (DHEA), growth hormone (GH), IGF1, and melatonin. In addition sex hormone binding globulin (SHBG) increase with age resulting in further lowering the concentrations of free biologically active androgens. Since however some Leydig cell function persists during ageing, *strictu sensu* the andropause does not exist.

However a growing body of literature supports the point of view that a true decrease in gonadal and adrenal bio-available androgens [6, 7] as well as of GH [8] develops in most ageing men and these result in "partial endocrine deficiencies". The partial endocrine deficiency syndrome of the ageing male (PEDAM) may be associated with a broad spectrum of symptoms.

1. A decrease of general well-being
2. A decrease of sexual pilosity
3. A decrease of libido
4. A decrease of cognitive function
5. A decrease of red blood cell volume
6. A decrease in muscle strength
7. Osteoporosis
8. A decrease of immune-competence
9. An increase of fat mass and change in fat contribution and localization
10. An increase in cardiovascular events

Moreover, in ageing men also melatonin secretion decreases, and the circadian periodicity of melatonin is gradually disrupted. Sleep in these older men is shallow and fragmented [9]. These alterations influence particular growth hormone secretion, which occurs with deeper stages of sleep (SWS, slow wave sleep). In men, approximately 70% of the daily GH out-

put occurs during early sleep (SW). During ageing, SW sleep and GH secretion decrease with the same chronology, raising the possibility that the peripheral effects of the hypsomatotropic of the elderly may partially reflect age-related alterations in sleep-wake homeostasis. While the association between sleep and GH release has been well documented, there is also evidence indicating that components of the somatotrophic axis are involved in regulating sleep [10]. It has been shown that in elderly men the decrease in melatonin secretion and the circadian periodicity of melatonin was correlated with:

- 1) mood disorders,
- 2) decay in cognitive functions,
- 3) increase of sleep disorders,
- 4) regulation of platelet production, probably due to an inhibitory effect of melatonin on macrophage-mediated platelet destruction.

The secretion of GH and its tissue mediator IGH-I from the anterior pituitary declines with increasing age (somatopause). This observation, together with the changes in body composition associated with organic GH deficiency in adults, has led to the suggestion that also some elderly without hypothalamic-pituitary disease maybe GH deficient and may benefit from GH therapy. However it must be stressed that the impact of organic disease of the hypothalamic-pituitary axis in the elderly may result in a further reduction in GH secretion of up to 90%. This reduction in GH secretion is sufficient to cause a fall in the serum insulin-like growth factor-1 (IGF-1) concentration, abnormal body composition and abnormal bone turnover, although bone mineral density is unaffected [11]. Older men are more sensitive to infec-

tions, sepsis, and cope more difficult with sepsis. They respond poorly to healing and to repair of bone fractures. The administration of growth hormone can attenuate the catabolic response to injury, surgery, and sepsis.

In cases of endocrine deficiencies, traditional endocrinology aims to replace the missing hormone or hormones with substitutes. It has been demonstrated that interventions, such as hormone replacement therapies and use of anti-oxidant drugs may favorably influence some of the pathological conditions in ageing men, by preventing the preventable and delaying the inevitable [Lunenfeld, 1999].

A comprehensive medical, psychosocial and life-style history, physical examination and laboratory testing are essential for the diagnosis and management of PEDAM. Acute, chronic or intercurrent diseases must be taken into consideration prior to initiating any hormonal substitution therapy. Hormone substitution should only be performed by physicians with basic knowledge and clinical experience in diagnosis, treatment and monitoring of endocrine deficiencies. Evidence is available that hormone replacement therapy (HRT) reduces the risk of cardiovascular disease.

Male osteoporosis has a prevalence of around 5% (vertebral fractures), but with the increase in life span, osteoporotic fractures are becoming more frequent in men. It has been estimated that 19% of men over the age of 50 in the United States will have one or more fragility fractures in their lifetime moreover more than 4 million men in the United States have low bone mass and are at risk for fractures [12]. The sequelae of skeletal fractures diminish quality of life, advance dependency and constitute an important public health problem. Hip fractures in men

result in a higher morbidity and mortality than in women. Secondary causes such as GI-diseases with malabsorption, alcoholism and malignant diseases are common. Hypogonadism and/or decrease of GH is often unfortunately not diagnosed as clinical signs are subtle.

Criteria for the diagnosis of osteoporosis based on bone density were established by the WHO, using the relationship between risk of fracture and bone mineral density (BMD) in caucasian women. For men such criteria have not been defined. Men have larger bones, with thicker corticalis, although their density and trabecular architecture is similar to that of women.

To date diagnosis of osteoporosis in men is made by history (risk factors), clinical examination (e.g. reduction of stature, back pain), X-ray, densitometry and laboratory work-up. Cut-off values for WHO-classification for male osteoporosis and all densitometry techniques such as dual-x-ray-absorptiometry (DXA), quantitative ultrasound (QUS) and quantitative computed tomography (QCT) need to be developed. QUS can be measured at the calcaneus and phalanges. Phalangeal ultrasound is especially useful as being easily accessible, fast, radiation-free, portable and cheap. Preliminary results show that phalangeal ultrasound might detect structural deterioration especially in patients on glucocorticoid treatment earlier than spinal DXA.

The main reason for a gender difference in fracture rates is because men lose less porous (trabecular) bone than women. Many osteoporosis risk factors can be modified without substantially increasing costs for the individual or the health care system. Risk factors for osteoporosis in older men include insufficient calcium intake, cigarette smoking, alcohol abuse, and physical inactivity.

The first sign of osteoporosis is often a spontaneous fracture of the lumbar spine, or a fracture of the proximal femur or distal radius after a fall. Elderly people are at a higher risk of falling, which can be attributed to use of certain medications, alterations in balance, loss of muscle strength, and prolonged reaction times. Preventive measures should target reducing bone loss and factors that contribute to falling. One of the most cost-effective prevention strategies is physical activity [13], an adequate intake of calcium, adequate vit. D and an exercise program which maximizes bone and muscle strength.

HRT together with proper nutrition and targeted physical activity may postpone the appearance of osteoporosis and delay or prevent bone fractures.

HORMONE REPLACEMENT THERAPY (HRT)

Secondary Leydig cell insufficiency in the ageing man can often be reversed by stimulation with hCG. But this kind of therapy is only recommended if testosterone level doubles within 72 hours following the injection of 5000 IU of hCG. In this situation Leydig cell function can be temporarily restored by weekly injections of 5000 IU hCG. If testosterone levels do not double within 72 hours following injection of hCG, testosterone replacement therapy should be considered (Table 4). Patients with secondary partial androgen deficiency (PADAM) and older than 40 years receiving substitutive testosterone therapy should have a clear indication for this therapy (history, physical examination, and laboratory assessment demonstrating a value of < 13 nm total T, $< 0,30$ nmol / free testosterone/ml).

Testosterone therapy is also to be considered for a trial period of 12 months in men with total T < 15 nm/l or bioavailable T is < 10 nm/l if these levels coincide with complaints or physical evidence of androgen deficiency. Furthermore testosterone replacement may be required in patients with a history of hepatitis, or liver cirrhosis with elevated levels of SHBG and clinical signs of androgen deficiency. Prior to initiation of testosterone therapy all patients should have a digital rectal examination and a serum prostate specific antigen (PSA) level measured, this should be less than 3 ng/ml and should be repeated within 3 months following initiation of therapy.

Table 4. Testosterone supplementation

1. **Testosterone Depot** 250 mg/2–3 weeks (mixtures of testosterone propionate, isocaproate, decanoate or oenanthate)
Under development:
undecanoate 1000 mg / 8–10 weeks
bucilate 1000 mg / 12–16 weeks
MENT 7alpha methyl 19 nortestosterone (sustained release subdermal implants)
2. **Testosterone oral** (undecanoate) (160 mg daily) 1 tab morning and noon and 2 evening (Lymphatic absorption of this product requires it to be taken with meals)
Under development:
Sublingual testosterone cyclodextrin 2.5–5 mg twice daily
3. **Testosterone transdermal** (Testosterone in a proprietary, permeation enhancing vehicle) dermal 2.5 mg or 5 mg patches applied nightly to the back, abdomen, upper arms or thighs. 5 mg daily is comparable to a normal daily production rate.
4. **Testosterone transscrotal** consists of a film containing natural testosterone 1 mg daily
5. **Testosterone Gels**, applicable to the skin

1. If clinical history and physical examination shows improvement (body composition, muscle mass and strength, sense of well being and energy level as well as an improvement of sexual function and libido).

2. If there is no history of adverse effects particularly with regard to urinary obstructive symptoms, polycythemia (Hct > 42% and platelets < 600,000), sleep apnea and if no significant increase in PSA is found, patients should continue with testosterone therapy and have a digital rectal examination and a PSA determination, lipid profile, haemoglobin and serum calcium at yearly intervals.

Testosterone administration should be stopped, if PSA increases by 2.0 ng/ml at any time or if an increase of 0.75 ng/ml occurs over a 2 year period [4].

Replacement therapies for secondary DHEA deficiency are being developed. A 100 mg daily dose of DHEA for 6 months restored serum DHEA levels to those of young adults and serum DHEA sulfate (DS) to levels at or slightly above the young adult range [14]. Serum cortisol levels were unaltered, consequently the DS/cortisol ratio was increased to pubertal (10:1) levels. Relative to baseline, DHEA administration resulted also in an elevation of serum IGF-I levels in men ($16 \pm 6\%$, $P = 0.04$). Serum levels of IGFBP-1 and IGFBP-3 were unaltered, fat body mass decreased with 1.0 ± 0.4 kg ($6.1 \pm 2.6\%$, $P = 0.02$) and knee muscle strength $15.0 \pm 3.3\%$ ($P = 0.02$) as well as lumbar back strength $13.9 \pm 5.4\%$ ($P = 0.01$) increased.

Replacement therapy protocols for GH, and melatonin deficiencies are currently under development. Within the next few years standardized indications, effective products and treatment protocols will become available.

Administration of growth hormone (GH) induces increases in both bone and lean mass and a decrease in fatty tissue in elderly men with GH deficiency [15–17]. The dose of GH required to maintain serum IGF-I levels in the normal range while minimizing side-effects in this group of patients however, has not been fully assessed. Toogood [18] demonstrated that the GH replacement dose in elderly subjects is considerably lower than that required by younger adults with GH deficiency. According to Janssen et al [19] GH therapy at doses of 0.6 and 1.2 IU/day in male and female patients, respectively, is, in general, able to increase serum IGF-I into the normal range after 12 weeks of treatment, without reaching supranormal levels of serum IGF-I. This dose could, therefore, be a starting dose in GH-deficient elderly patients. None of the low dose GH treated patients exhibited a supranormal IGF-I level [18].

Hormone replacement therapy alone will not suffice to increase muscle strength, decrease fat mass and change in fat contribution and localization in ageing men. Proper nutrition and physical exercise targeted at specific muscle groups is mandatory in order to obtain satisfactory results. Moreover some authors suggest that resistance exercise training improved muscle strength and anabolism in older men, and these improvements were not enhanced when exercise was combined with daily GH administration [20].

The decision to start Hormone Replacement Therapy in men should only be taken after obtaining objective evidence of hormone deficiencies, after exclusion of secondary causes of endocrine dysfunction and after making the balance of risks and expected benefits of the replacement therapy. When data of long-term well-controlled studies will

have become available, long-term substitution therapy with one or more hormonal preparations will most probably, if used correctly improve the quality of life of ageing men and may even delay the ageing process.

Although, it is probably not unrealistic that in the future HRT in men will become as common as in women today, but it goes without saying that even today there is strong evidence that a healthy lifestyle with regular physical activity has significant physiological, psychological and social benefits for older persons.

IMPROVING THE HEALTH OF OLDER MEN

Although it is now well established that significant physiological, psychological, social, and societal benefits accrue from participation in physical activity, the proportion of older individuals who participate regularly in physical activity is generally low. For example, the United States Surgeon General's Report on Physical Activity and Health [21] estimates that only about 17 percent of older persons exercises at or above recommended levels of physical activity. A significant problem is motivating individuals of all ages to begin and to continue to participate in regular exercise [22].

Appropriate nutrition and a healthy and safe environment are critically important in preventing or reducing morbidity and disability. An ageing male counselling session will not be complete, before detailed information is obtained on nutritional habits and daily food consumption. Individualized supplementation of antioxidants and vitamins will often be required in men over fifty.

The impact of diet and specific food groups on ageing and age-associated degenerative diseases has been widely recognized in recent years (Table 5). The modern concept of the free radical theory of ageing takes as its basis a shift in the antioxidant/pro-oxidant balance that leads to increased oxidative stress, impaired regulation of cellular function, and ageing. In the context of this theory, antioxidants can influence the primary "intrinsic" ageing process as well as several secondary age-associated pathological processes. For the latter, several epidemiological and clinical studies have revealed potential roles for dietary antioxidants in the age-associated decline of immune function and the reduction of risk of morbidity and mortality from cancer and heart disease. Meydani [23] reported that long-term supplementation with vitamin E enhances immune function in aged animals and elderly subjects. The addition of the trace element selenium (60–200 micrograms/day) to Vitamin E is recommended since this will significantly increase the anti-oxidant properties. Larry Clark from the University of Arizona claimed significant reduction of prostate, colo-rectal and lung cancer [24]. These and other observations indicate that, at present, the effects of dietary antioxidants are mainly demonstrated in connection with age-associated diseases in which oxidative stress appears to be intimately involved.

Table 5. Nutrition: low calorie, low fat, high fiber, and vitamin- and mineral rich diet

- Drink at least 2 liters of water per day.
- Eat lots of fruit and vegetables
- Be sure that you consume sufficient vitamins, especially C 500 mg, D 400 IU, E 200–600 IU, B complex, folic acid 2.5 mg (Vitamins C and E act as antioxidants)

Patients can be counselled to start their "own anti-ageing program" in getting more active, start to exercise, and loose weight if obese. This will quite physiologically lead to tiredness, better sleep, and consequently higher GH levels. Melatonin secretion will also rise, provided the patient does not sleep in front of the TV or with full lights. Eating only small portions or nothing at all before going to bed (dinner cancelling) can also increase GH secretion.

SEXUAL DYSFUNCTION AND SEXUALITY

Health professionals, educators and elderly men are becoming increasingly aware that libido, interest, capacity and sexual pleasure can remain throughout a lifetime. It was found that persistent interest in sexual activity results in positive mental and physical healthy benefits. Some men may become less sexually active with age. Reasons for decreased sexual activities include loss of libido (partially due to decreased androgen production), lack of partner, chronic illness and or various social and environmental factors, as well as erectile dysfunction (ED). Worldwide more than a 100 million men are estimated to have some degree of ED. The Massachusetts Male Ageing Study reported a combined prevalence of 52 % for minimal, moderate and complete impotence in non-institutionalized 40–70 years old men in the Boston area [25]. Erection is a neurovascular phenomenon under hormonal control and includes arterial dilatation, trabecular smooth muscle relaxation and activation of the corporeal occlusive vein mechanism. Some of the major aetiologies are hypertension, diabetes and

heart disease (table 6). Also, genitourinary and colon surgery, as well as many drugs, particularly antihypertensive and psychotropic drugs may cause various degrees of erectile dysfunction. When focusing on the maintenance of quality of life among ageing men, efforts to maintain, restore or improve sexual function should not be neglected. Recent advances of basic and clinical research has led to the development of new treatment options for ED, including new pharmacological agents for intra-cavernosal, intra-urethral and oral use (Table 7). The management of ED should only be performed following proper evaluation of the patient and only by physicians with basic knowledge and clinical experience in diagnosis and treatment of ED.

STRATEGIES TO IMPROVE AND MAINTAIN THE AGEING MAN'S HEALTH

Men who are educated about the value that preventative health care can play in prolonging their life span, quality of life and their role as productive family members, will be more likely to participate in health screening. To obtain this goal it will be necessary to make a group

Table 6. Erectile dysfunction: Incidence (MMAS) [Johannes CB, et al. *Int J Impotence Res* 1998; 10: 414]

	Population (new cases/1000 men per year)
General	26.0
Hypertension	42.5
Diabetes	50.7
Heart disease	58.3

of trained medical professionals available who can understand, guide, educate and manage the problems of the ageing male.

The International Society for the Study of the Ageing Male (ISSAM), has delegated Parthenon Press to publish its official journal (*The Ageing Male*), ISSAM Operations to assist in the standardization of protocols, and products to be used in the quality of life management of ageing men, and the ISSAM academy A) to prepare, provide and assess training curriculum specially tailored for different medical specialties, B) to assist in the organization of training courses for "Men's Health Physician", C) to certify such courses and finally D) to accredit those specialists who have qualified as Men's Health Physician. E) ISSAM operations will assist, and collaborate in the formation and medical management of clinics and/or health institutions who wish to include a men's health management program. F) ISSAM operations

Table 7. Medical management of ED: the revolution!

1982 Virag, the first injection
 1986 use of prostagladin E1
 1995 Caverject in the market
 1996 MUSE in the market
 1998 Sildenafil in the market
 1999 Vasomax
 2001 Spontane Oral Apomorphine
 2001 New phosphodiesterase inhibitors of isoenzymes

In development:

Oral Phentolamine
 Prostaglandine creams
 New drug acting on different level of the erectile mechanism
 Topical treatment
 Gene (cell) therapy

will assist and collaborate with pension funds, insurance companies and social and welfare institutions to help men to age in health and dignity.

Furthermore there is a need to obtain the essential epidemiological data, to intensify basic and clinical research and to develop new and improved drugs for prevention and treatment of the pathological changes related to ageing. A holistic approach to this new challenge of the 21st century will necessitate a quantum leap in multidisciplinary and internationally coordinated research efforts, supported by a new partnership between industry and governments, philanthropic and international organizations. ISSAM in collaboration with the World Health Organization, will attempt to coordinate such efforts.

ISSAM in collaboration with the World Health Organization (WHO) periodically organizes a World Congress on the Ageing Male which unites interesting practitioners, experts and researchers of medical behavioural and social sciences as well as providers of services and technologies for the ageing population. This forum provides an opportunity to exchange information, plan research activities, obtain funding and assist in the formulation of national health and social policies. ISSAM in collaboration with its national affiliates will periodically organize national and regional meetings and facilitate training courses. Information on such meetings is continuously updated (<http://www.kenes.com/aging/>).

It is my sincere hope that the next few years will enrich us with facts and clarify the state of our present knowledge permit us to recognize some of the missing links and give us the tools and methodology to design and plan ways to understand ageing of men, permit us to help to improve the quality of life, prevent the preventable, and

postpone and decrease the pain and suffering of the inevitable.

BIBLIOGRAPHY

1. Lunenfeld B. Hormone replacement therapy in the aging male. *The Aging Male* 1999; 2: 1–6.
2. Diczfalusy E. An aging humankind: is our future behind us. *The Aging Male* 1998; 1: 8–19.
3. Lunenfeld B. Aging Male. *The Aging Male* 1998; 1: 1–7.
4. Tremblay RR, Morales AJ. Canadian practice recommendations for screening monitoring and treating men affected by andropause or partial androgen deficiency. *The Aging Male* 1998; 1: 213–8.
5. Kaufman JM, Vermeulen A. Declining gonadal function in elderly men. *Baillieres Clin Endocrinol Metab* 1997; 11: 289–309.
6. Deuschle M, Gotthardt U, Schweiger U, Weber B, Korner A, Schmider J, Standhardt H, Lammers CH, Heuser I. With aging in humans the activity of the hypothalamus-pituitary-adrenal system increases and its diurnal amplitude flattens. *Life Sci* 1997; 61: 2239–46.
7. Gooren LJG. Endocrine aspects of aging in the male. *Mol Cell Endocrinol* 1998; 145: 153–9.
8. Holl R, Hartman M, Veldhuis J, Taylor W, Thorner M. Thirty-second sampling of plasma growth hormone in man. Correlation with sleep stages. *J Clin Endocrinol Metab* 1991; 72: 854–61.
9. Copinschi G, Van Cauter E. Effects of ageing on modulation of hormonal secretion by sleep and circadian rhythmicity. *Horm Res* 1995; 43: 20–4.
10. Van Cauter E, Plat L, Copinschi G. Interrelations between sleep and the somatotrophic axis. *Sleep* 1998; 21: 553–66.
11. Toogood AA, Shalet SM. Ageing and growth hormone status. *Baillieres Clin Endocrinol Metab* 1998; 12: 281–96.
12. Melton LJ 3rd, Atkinson EJ, O'Connor MK, O'Fallon WM, Riggs BL. Bone density and fracture risk in men. *J Bone Miner Res* 1998; 13: 1915–23.
13. Nordin C. Scope for the prevention and treatment of osteoporosis in improving the health of older people: a world view, Oxford University Press 1990; 160.
14. Morales AJ, Haubrich RH, Hwang JY, Asakura H, Yen SS. The effect of six months treatment with a 100 mg daily dose of dehydroepiandrosterone (DHEA) on circulating sex steroids, body composition and muscle strength in age-advanced men and women. *Clin Endocrinol (Oxf.)* 1998; 49: 421–32.

15. Casanueva FF, Dieguez C. Interaction between body composition, leptin and growth hormone status. *Baillières Clin Endocrinol Metab* 1998; 12: 297–314.
16. Rudman D, Feller AG, Cohn L, Shetty KR, Rudman IW, Draper MW. Effects of human growth hormone on body composition in elderly men. *Horm Res* 1999; 36 (Suppl. 1): 73–81.
17. Goh VHH, Mu SC, Gao F, Lim LC. Changes in body composition and endocrine and metabolic functions in healthy elderly Chinese men, following growth hormone therapy. *The Aging Male* 1998; 1: 264–9.
18. Toogood AA, Shalet SM. Growth hormone replacement therapy in the elderly with hypothalamic-pituitary disease: a dose-finding study. *J Clin Endocrinol Metab* 1999; 84: 131–6.
19. Janssen YJ, Frolich M, Roelfsema F. A low starting dose of genotropin in growth hormone-deficient adults. *J Clin Endocrinol Metab* 1997; 82: 129–35.
20. Yarasheski KE, Zachwieja JJ, Campbell JA, Bier DM. Effect of growth hormone and resistance exercise on muscle growth and strength in older men. *Am J Physiol* 1995; 268: E268–E276.
21. United States Surgeons' General Report on Physical Activity and Health 1996.
22. van der Beld AW et al. Muscle strength as a determinant of quality of life, physical performance and bone mineral density in elderly men. *The Ageing Male* 1998; 1 (Suppl 1): abstr. 119.
23. Meydani M, Lipman RD, Han SN, Wu D, Beharka A, Martin KR, Bronson R, Cao G, Smith D, Meydani SN. The effect of long-term dietary supplementation with antioxidants. *Ann NY Acad Sci* 1998; 854: 352–60.
24. Clark Larry, Arizona, personal communication, 1999.
25. Feldman HA, Goldstein I, Hatzichristou DG, Krane RJ, McKinlay JB. Impotence and its medical psychological correlates; results of the Massachusetts Male aging Study. *J Urol* 1994; 151: 54–61.

Editor:
Franz H. Fischl



MENOPAUSE ***ANDROPAUSE***

Hormone replacement therapy through the ages
New cognition and therapy concepts

[**http://www.kup.at/cd-buch/8-inhalt.html**](http://www.kup.at/cd-buch/8-inhalt.html)

Krause & Pachernegg GmbH
VERLAG für MEDIZIN und WIRTSCHAFT