

The major causes of functional dependency

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■ THE CHALLENGE OF LONGEVITY

First of all, we should remember that the increase in longevity is above all a great privilege of Western nations. Of course, increased length of life can only be considered a privilege if the majority of the elderly population is active and in good health. In contrast to certain statistical interpretations, the figures from the Handicap, Disability, Dependency (HID) study lean towards optimism in this respect. They show that only 7% of those aged over 60 years suffer from a degree of dependency and, therefore, that 93% of the population remains independent.

Of course, dependency increases with age, but it remains remarkably infrequent between 60 and 69 years. I have a particular interest in this age group because I am fundamentally in favour of the promotion of professional activity for seniors and it is remarkable that very few people are dependent at these ages. The increase in dependency with age concerns mainly women and those older than 90 years. But, even at this age, less than half of the population is dependent and men cope remarkably well, with 70% of over 90s remaining independent.

This being the case, the age pyramid of the French population is evolving towards an increase in the proportion over 85 years. Thus, by 2020, this age group will have gone from 1.2 million to 2 million people and there is therefore, a risk that we will see an increase in the number of dependent individuals (figure 1).

■ CAUSES OF DEPENDENCY

■ DISEASES KNOWN TO BE AGE-RELATED

The majority of dependency comes about from age-related diseases. The second cause of dependency is considered to be (though here I place a question mark) “frailty”. The third of these causes is inactivity or, more generally, lifestyle.

All so-called age-related diseases, such as cardiovascular disease, dementia, cancer, osteoarthritis and osteoporosis, and sensory disorders can cause dependency, but they are, in general, linked to risk factors and, therefore, can be prevented. Reduction of these risk factors can, therefore, prevent a large amount of dependency and this prevention should be even more effective in the future thanks to current progress such as cellular therapy, DNA chips, and biotechnology. The inadequacy of prevention in most countries must be brought into question.

■ HEALTH PROMOTION

Health promotion centres primarily on lifestyle improvement. Americans are extremely concerned by the increase in obesity in their country. Some consider that it will be responsible for a considerable decrease in the mean life expectancy in the US. Yet, it is clear that better health promotion of a wide range of lifestyle improvements would probably bring about a decrease in the incidence of a large number of diseases, notably obesity.

The most important factor for the reduction of mortality is certainly education throughout life. There is no doubt that a considerable injustice exists between educated and non-educated individuals. It has been clearly demonstrated that it is primarily the level of education of the mother, but also the father because young men today participate in the education of their children, which determines the health of their children when they become adults.

■ EXAMPLES OF FAILINGS IN PATIENT MANAGEMENT THAT MAY LEAD TO DEPENDENCY

Certain failings in curative or preventive management can lead to avoidable dependency. I will cover congestive heart failure (CHF) and osteoporosis briefly as they have been specifically dealt with elsewhere during this symposium, and discuss Alzheimer's disease in more depth.

■ Congestive heart failure

We know that the incidence of CHF increases dramatically with age, to reach a prevalence of nearly 10% in the 80–89 year age group. However, it has been shown that the majority of patients who are affected are not treated according to the standards derived from evidence-based medicine. More precisely, the elderly are less well treated than younger people. Today it is recommended that CHF be treated by angiotensin-converting enzyme (ACE) inhibitors and beta-blockers. Yet, these two categories of treatments are less often prescribed for people aged over 80 than for those under 80 years [1]. This observation is true for the general population, and even more so in retirement and nursing homes. An ongoing study of 14 000 residents has shown that the prevalence of heart failure is 31% in the over 80s. Ultrasound is far more widely used than was expected (64%), but it is likely that it is carried out before entry into the retirement home. On the other hand, recommended treatment according to evidence-based medicine is not as widely used as it should be; ACE inhibitors are only prescribed in 43% of patients and beta-blockers in 28% [2].

■ Osteoporosis and fractures

Osteoporosis and the fractures it can lead to are a major cause of dependency. The risk increases with age, and the incidence of fractures of the femoral neck increases exponentially in the absence of prevention [3]. We are lucky enough to have access to treatments that are able to effectively prevent fractures: calcium and vitamin D supplementation; bisphosphonates; and strontium ranelate. Yet, a recent study showed that only about a third of patients were receiving

osteoporosis treatment in the period before a fracture [4]. According to British data, the 1 year mortality rate after a hip fracture is 19%; hip fractures also bring about functional decline of 32% at discharge from hospital and 16% after 1 year. In France, osteoporotic fractures are associated with levels of both dependency and mortality of 30%.

Clearly, with respect to both CHF and osteoporosis, we are not treating elderly patients in the optimal manner.

■ **Alzheimer's disease and related illnesses**

A major public health issue

Alzheimer's disease is a considerable public health issue. The prevalence of this disease increases enormously after 80–85 years and the longer an individual is alive, the higher the risk for developing Alzheimer's disease or a related illness [6]. There are currently 20 million patients afflicted by Alzheimer's disease or a related illness across the world and this is projected to increase to 80 million people afflicted in 2040 if there is no progress in this field. Each year there are 4.6 million new cases, equating to 1 new case every 7 seconds [7].

The search for preventive treatments or treatments able to act on the neurodegenerative process must be a priority, but the substitutive symptomatic treatments that we currently have are still under-used. In France, 850 000 people suffer from Alzheimer's disease and related illnesses, of which half are not diagnosed, and only 17 % are treated. Again, there is a lot of work to be done in this disease area.

Causes of intellectual deterioration

Personnes Agées Quid (PAQUID) is an epidemiological study with the objective of studying cerebral and functional aging after 65 years. The patient cohort of just over 4000 elderly persons in the Gironde and Dordogne areas has been followed since 1988. According to data from this study, 72% of potential beneficiaries of personal autonomy allowances have dementia, of which 55% is Alzheimer's disease. Institutionalisation is due, in 70% of cases, to Alzheimer's disease or a related illness [8] (figure 2).

Efficacy of substitutive symptomatic treatments

The efficacy of substitutive symptomatic treatments on cognitive function, activities of daily living, and global judgments of the patient is moderate, but nonetheless significant. This benefit, albeit modest, must be taken into account. I am opposed to the current criticism of these treatments which are considered too costly in comparison with other therapeutic approaches. Indeed, they are expensive, but if we had adopted a step-by-step therapeutic and research approach for Alzheimer's disease, as was done for AIDS, we would probably not be facing the current problems.

Preventive approaches for dementia

What are the preventive approaches for dementia? The effects of various classes of treatments, such as oestrogens, anti-inflammatories, antioxidants, antihypertensive treatments, calcium channel blockers, statins, and anti-amyloids are currently being studied. Epidemiological studies have shown that long-term users of oestrogens, anti-inflammatories, or statins have an incidence of Alzheimer's disease significantly lower than that of the general population. Indeed, treatment with statins could reduce the incidence of Alzheimer's disease by 70%! However, controlled trials, which are the only way of proving the efficacy of these substances, have to date been negative. The epidemiological arguments are very strong, and it is almost certainly too early to state that these products have no use in the prevention of dementia.

Antihypertensive treatment and dementia

Two randomised placebo-controlled trials have demonstrated that treatment of hypertension reduces the risk of dementia:

- The Systolic Hypertension in Europe (Syst-Eur) study, in which subjects aged 60 years or more with isolated systolic hypertension received a calcium channel blocker as first-line therapy [9, 10];
- The Perindopril Protection Against Recurrent Stroke (PROGRESS) study, carried out in subjects with hypertension or normotension and having had a stroke, treated with a ACE inhibitor and a diuretic [11].

Treatments acting on the lesion process

There is much hope in treatments which address the cause of Alzheimer's disease. A number of ongoing studies are assessing the area of anti-amyloids (secretase modulators, beta- and gamma-secretase inhibitors, and alpha-secretase stimulators) which act on amyloidogenesis, one of the two lesions in Alzheimer's disease. Researchers are also interested in the second characteristic lesion of this disease, the aggregation of tau protein in a neurofibrillary form, and are evaluating the anti-tau approach with inhibitors of tau phosphorylation, kinase inhibitors (CDK5, GSK-3 β), and phosphatase activators.

This research is very intensive and 140 pharmaceutical firms around the world are thought to be working on these subjects. We hope to see the arrival, within the next few years, of treatments able to stop the progression of Alzheimer's disease during its early stages though we still need to be able to recognise this moment!

The work of Schenk and colleagues [12] on a preventive and therapeutic "vaccine" against Alzheimer's disease is also an interesting path with great hope. The abnormal accumulation of beta-amyloid peptides (A β) is responsible for the formation of amyloid plaques. Schenk suggested stimulating the immune system so that it produces anti-A β antibodies. Administration of the antigen in mice completely protected them against the formation of amyloid plaques. Even in mice that were already affected, the plaques had a tendency to disappear. However, a clinical trial carried out in humans to test this vaccine had to be suspended due to the occurrence of

several cases of encephalitis among the volunteers. Other studies are underway with fractions of amyloid protein. A second approach with the injection of anti-A β antibodies instead of the antigen is also currently being studied.

■ **FRAILITY**

■ **A complex syndrome of increased vulnerability**

Does frailty exist? According to the definition currently used by experts, frailty is a state of secondary vulnerability with multiple system impairments which bring about a decrease in physiological reserves. Unfortunately there is no agreement on the phenotype or criteria for frailty, or whether or not it is reversible.

■ **Frailty phenotypes**

The most commonly recognised phenotype of frailty groups together syndromes such as weight loss, anorexia, muscle weakness, fatigue, and slowness. These symptoms are associated with sarcopenia, osteopenia, balance and walking disorders, malnutrition, slow walking speed, and a reduced capacity to respond to stress. The consequence of frailty is an increased risk of falls, injuries, hospitalisation, disability, and dependency.

■ **Two types of criteria: motor frailty versus global frailty**

Fried defined frailty using the following criteria: slow walking speed, poor grip strength, weakness/exhaustion, reduced physical exercise, and weight loss. In addition, Rockwood integrated cognitive deterioration into these criteria. According to Fried, the prevalence of frailty is low in the age group 65–74 years, but it increases rapidly among older age groups. The concept is however extremely vague and these figures therefore vary greatly from one study to another.

■ **Is frailty reversible?**

It is possible to target interventions to a number of signs and symptoms of frailty. Numerous potential treatments for sarcopenia are currently under investigation. We know how to manage under-nutrition and balance and walking disorders. Furthermore, physiological modifications in frail elderly subjects are the subject of important research studies which use substances such as testosterone, growth hormone, cytokine inhibitors, caspase inhibitors, and myostatin inhibitors. Nevertheless, improved social integration remains a vital element in the prevention of dependency.

■ **PROFESSIONAL INACTIVITY**

■ **Risk of mortality according to status**

Professional inactivity is associated with an increased risk of mortality, but it is uncertain whether it also linked to a risk of dependency. If we compare professionally active and inactive and unemployed persons, we see a 5-fold increased risk of dependency among professionally inactive men, regardless of age, and a 3-fold increased risk of dependency in the unemployed. It

must be underlined that people may be professionally inactive due to a number of illnesses and dependency. The increase in the risk of dependency is lower in professionally inactive women, but nonetheless remains increased by a factor of 2 to 2.5.

In France, it is astonishing to note that as life expectancy increases, the level of professional activity decreases. Socio-professional status is particularly important and there is a large gap between the mean life expectancy for professionals or freelancers and that of laborers, who are exposed to physically difficult occupations and who work for a shorter time (figure 3). Having said that, little robust data is available to enable analysis of the impact of professional inactivity on dependency. Personally, I think that the promotion of professional activity for seniors is an absolute priority. This can be achieved by maintaining employment in the over 50s, a change in the mentality of employers and employees, modification of working conditions, a progressive increase in the basic pension above 60 years for those still in professional activity, and by relaxing the laws surrounding the accumulation of employment/retirement.

■ **What are the stages of prevention of dependency?**

Primary prevention of dependency is needed throughout life and must begin well before the age of 20 years. Secondary prevention in autonomous but frail persons requires management by a complete and exemplary geriatric department in case of hospitalisation, familial and social integration, and sufficient income. Tertiary prevention of progression of dependency should be carried out through excellent medical and medico-social management, which is not currently the case, and integrative social innovations.

■ **WHAT ARE THE KEYS TO REDUCING DEPENDENCY?**

We need to intensify research into longevity, and I am delighted that a first “Gerontopole” (geriatric center) has been set up in Toulouse. We also need to widely develop the prevention of “age-related” diseases, encourage family links and exchanges with youngsters, break up rigid structures, and encourage “living together”, with integrated accommodation and medical management. Above all, we must stop thinking that longevity is a burden, because in fact it opens fantastic possibilities for everything, particularly for economic growth and employment.

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Figure 1. Evolution of the proportions of different age groups in France

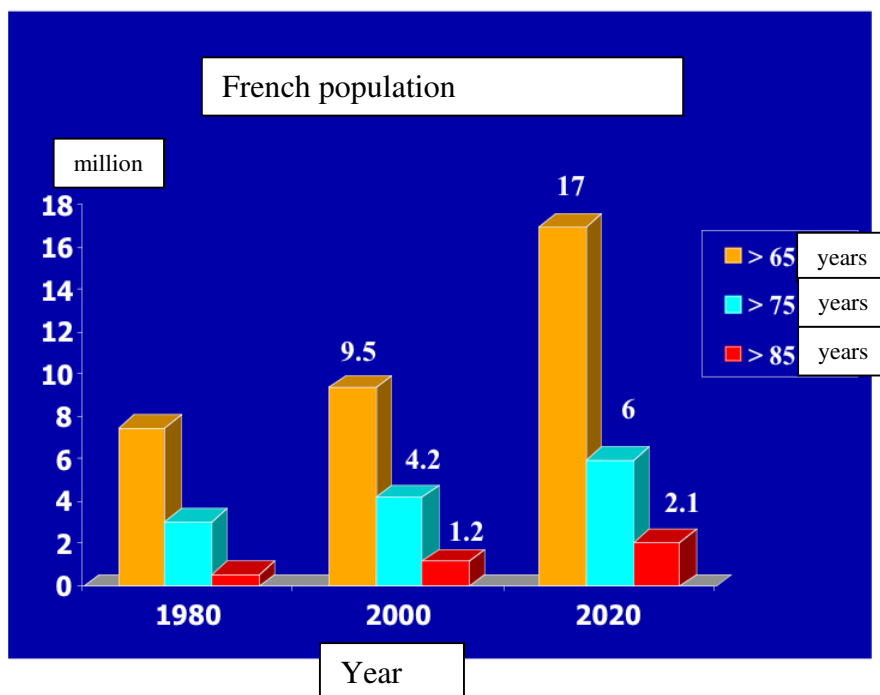


Figure 2. APA: dependency and prospective follow-up at 10 years in the PAQUID cohort (GIR 1 to 4). AD = Alzheimer’s disease.

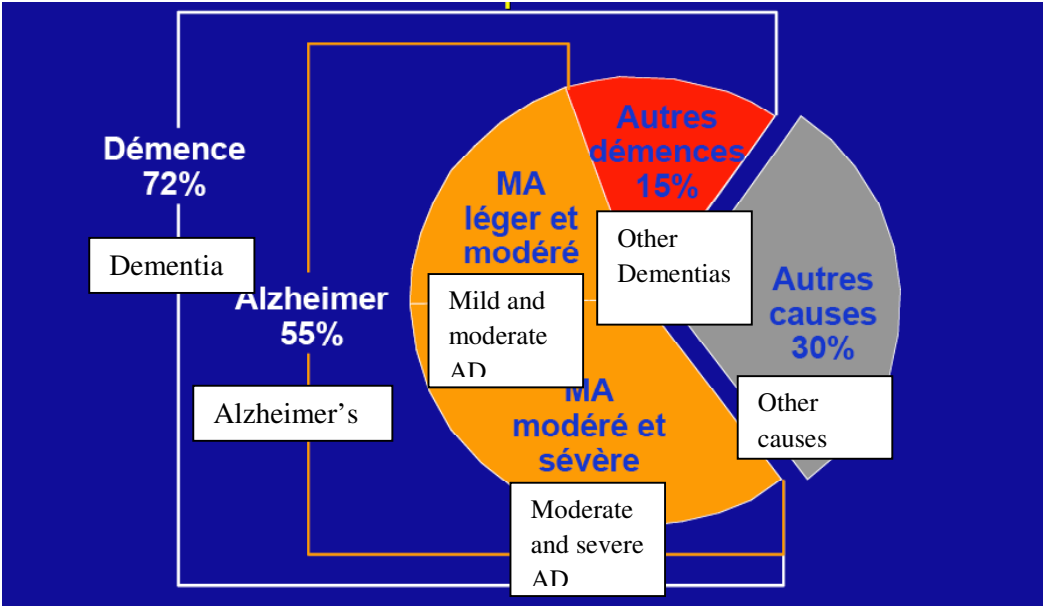


Figure 3. Evolution of life expectancy at birth and age of suspension of professional activity in France between 1960 and 2000.

