Incredible,
Aloïs Alzheimer is talking to you

On 5 October 2016 you received a fascinating letter from your epiphysis, also known as pineal gland. It acts as the genuine leader of the Sleep-Wake regulation and the secretions of all endocrine glands. Everyone over 50 years of age should read this letter to understand what I, Aloïs Alzheimer, am writing this week.

This information is for everyone. The general public, perfectly capable of understanding me, as well as all scientific colleagues, female and male health professionals, regardless of their speciality: researchers, physicians, pharmacists, midwives, nurses, physiotherapists, naturopaths, osteopaths, chiropractors, Chinese medicine, etc.

A little history[1]

My name is Aloïs Alzheimer. I was born more than a century after James Parkinson, in 1864. James was born in 1755. He lived in London all his life, where he died in 1824. He described his condition in 1817. I, Alois Alzheimer, was a physician in Bavaria, a psychiatrist and neurologist, but also a neuropathologist. This means that I knew the brain from within. I was able to scrutinise it after the death of patients and translate their disorders into anatomical and even histological terms. Therefore I learned, using the means available at the time, how to analyse brain tissue under the microscope. I was dubbed the "psychiatrist with the microscope" by my colleagues. In the brain of very old patients, I discovered what I called "miliary sclerosis[2], in reference to the multiple damage to the lungs caused by tuberculosis at the time. The term "senile plaques" only emerged later, in 1898.

Thanks to this three-fold competence I was able to describe the disease named after me. In 1906, I published an initial case typical of this disease during the 37th conference of German psychiatrists.

The history of the first patient I published was presented using her initials, A.D., i.e. Augusta Deter, born in May 1850 and married to Karl Deter, who took his wife to the Frankfurt am Main municipal asylum on 25 November 1901. She died on 8 April 1906. What a joy for me: the medical record was found in the cellar of the clinic in 1995, and the histological preparations of her brain were recovered in Munich in 1997. For the specialists among you, the analysis of Augusta's brain sections helped reconstitute the genotype of apolipoprotein E, and revealed in 2013 that she suffered from a genetic form (presenilin gene, in less than 1% of cases) of Alzheimer's disease linked to a PSEN1 gene mutation on chromosome 14. Of course I could not have known that in my time.

I published the second case in 1911. In the meantime, this type of dementia had already been called "Alzheimer's disease" (Alzheimer Krankheit) in 1910 by my boss at the Munich Chair of psychiatry, Emil Kraepelin, who had taken me under his wing.

This recognition and support allowed me, Alzheimer, to found the Munich school of neuropathology and I was appointed professor of psychiatry in Breslau.

In my time the barrier between "pre-senile" and "senile" dementia was set at 65 years of age, as this was the legal retirement age in the German Empire.

I died very young, aged 51 in 1915 in Prussia, from the renal and cardiac complications of acute rheumatic fever. Nowadays I would have been cured. My body was laid to rest in Frankfurt's principal cemetery, but that does not prevent me from thinking of you and writing to you.

Life goes on in another place that you will all eventually become familiar with, and I am delighted to be given the opportunity to speak by adapting to your era.

An exciting discovery was made by Pr Jean Bernard Fourtillan, in France, in 1994. I really wish to spread this discovery across the entire world, most of all among all those who are at risk for this disease, which is such a burden. We will be able to curtail this disease, even probably avoid it.

Below is the essence of all recent epidemiological knowledge

Women are more affected than men. A British study noted that one extra year of work prior to retirement seems to delay the onset of Alzheimer's disease by 6.8 weeks. Moreover, every additional working year after the age of 60 reduces the risk by 3%. And people who retire at 65 are 15% less at risk than those who retire at 60. Work therefore plays a beneficial role! This is a good reason to finally raise the retirement age.

The disease that bears my name erases memories – we will see which ones – and leads to degeneration which impairs judgement and develops into dementia.

It affects more than 3% of the over 60 population[3]. This rate is nearly at 15% in individuals over 90, with women more commonly affected (1.4 women for 1 man).

This disease affects 20% of young octogenarians. One in 4 women and 1 in 5 men from the age of 85. The incidence rate is 1.5% of the population affected between the ages of 60 and 70, 5% between 70 and 80, 15% between 80 and 90, and 40% beyond the age of 90. According to a report published in 2012 by the World Health Organisation and the Federation of Alzheimer associations, the likelihood of contracting the disease doubles every five years after the age of 65.

In 2013, the Alzheimer Disease international association estimated that 44 million people worldwide suffered from Alzheimer's or another form of dementia, and that this figure would rise to 76 million by 2030 and 135 million by 2050. This is huge but luckily solutions are now within your reach.

In France, dementia[4] affects an extra 225,000 people each year, including 150,000 who present with the anomalies I described earlier.

Some people love to scare the population

In 2015 in France alone, nearly one million people are affected, with a vast majority being Alzheimer's patients. Officially we are told that 50% of the patients are not known to health services... We should be wary of this type of extreme and frightening statement...

Nonetheless, the disease is spreading very quickly, too quickly: according to the latest projections, there will be 1.3 million patients in France in 2020, and 2 million in 2040. 24 million people worldwide are

reportedly affected. And it appears that this figure doubles every twenty years. In 2040, a staggering 80 million individuals could be affected[5]. This disease is the number one cause of dependency.

Exorbitant spending for the health service

The monthly treatment of a patient costs anywhere from €1,750 early in the disease to €4,000 at least in its late stages. The France Alzheimer association has worked out that €1,500 to €1,600 per month – after aid has been received – remains payable by the family for patients in medical facilities.

In 2008, the Médéric Alzheimer Foundation already identified 1,533 healthcare facilities with at least one unit dedicated to Alzheimer's patients. The number of beds soared from 22,430 to 28,000 in two years, i.e. a 25% increase. All this comes at a cost, and the health service, with its colossal deficit, is obviously incapable of bearing the costs of the treatments required by these patients. The cost of Alzheimer's disease in your country, France, has nearly reached €10 billion, i.e. €22,099 per patient, 44% of which is borne by the families. The same applies to my country, Germany.

Fear can lead to suicide : 3 to 4 times more in older people[6], because they are misunderstood and lack support

This makes sense when you are poorly prepared to age, when you refuse to grow old, when you are drowning in pessimism, bitterness and the drugs that go with it. Drugs turn individuals into vegetables, as young people say.

In terms of suicide, the elderly are more vulnerable than most. This is true in many countries, including regions of the world (such as Asia) where the cultural context "appreciates old age": even in these lands (China, Korea, Japan, Singapore), the suicide rate in the over 65 population is three to four times higher than in the overall population.

A survey conducted in Taipei City (Taiwan) among more than 100,000 people aged 65 and over notes that certain factors increase the suicide rate in a statistically significant manner: being male; a low income level; the presence of physical afflictions; not living with a partner; a depressive state; anxiety; insomnia; social isolation. Medicine must bear some responsibility when it needlessly stresses old people.

The pharmaceutical industry at the patient’s bedside

It is not uncommon to hear someone saying how surprised they are about the scale of Alzheimer's disease and that they find it odd. We all have great or great-great-grandparents who ended up senile. They were referred to as "dotty".

I cannot help wondering whether I, Alzheimer, have not become the symbol of the ordeal that is old age. The critics of the medicalisation of normal life stages (from ADHD in children to Alzheimer's disease in the elderly, including bipolarity in teenagers, female or male menopause later, etc.) are already convinced of it.

There has been a broadening of diagnosis criteria which actually increases the number of patients. And degenerative diseases, like many chronic diseases that cannot yet be cured, are seen as an opportunity to use treatments which, while they can at best improve the patients' condition (sometimes), essentially maintain a long-term chemical dependence.

Even so, we cannot deny the obvious spread of these diseases, or underestimate the physicians' hard work in the field and the research conducted by teams of scientists worldwide for thirty years.

I recommend that collective stress is avoided, and I will help you do so in this letter.

The signs of the disease that bears my name

I would remind you that it is a neurodegenerative affliction of the brain tissue, with a progressive loss of neurons. It results in the irreversible loss of mental faculties, notably the memory. This is the most frequent form of dementia in human beings.
When I performed the histopathological examination of my patient's brain, Augusta Deter, who suffered from dementia, I highlighted the presence of two types of brain lesion: senile plaques, currently known as amyloid-beta aggregates, and neurofibrillary degeneration, abnormal tau protein filaments building up in the neurons, ultimately causing their death.

All this is wonderfully described and illustrated in the video you will find at « Les Causes et le Traitement de la maladie d'Alzheimer enfin découverts ! » (The Causes and Treatment of Alzheimer's disease finally discovered!) on YouTube, co-directed by Professors J B Fourtillan and H Joyeux.

The first symptom is often a loss of memories (amnesia), initially manifesting itself by minor distractions, which grow as the disease progresses. The oldest memories are however relatively preserved.

Neurological damage subsequently spreads to the frontal and temporoparietal association cortices, resulting in more severe cognitive impairments (confusion, irritability, aggressiveness, mood and emotional disorders, executive function and speech disorders) and long-term memory loss. The destruction of the neurons continues, leading to the loss of autonomic functions and death.

The diagnosis of the disease to which I, Aloïs Alzheimer, gave my name, is initially essentially based on questioning, neuropsychological tests and the detection of cortical atrophy which affects the internal temporal lobe first, notably the hippocampus, an important region for the memory. This is apparent on MRI and DAT Scans (DAT scans help differentiate between Lewy body dementia and the disease that bears my name).

It is generally diagnosed from the age of 65. Early and rarer forms (less than 5% of patients) can however appear much earlier. The first signs are often confused with the normal aspects of senescence, depression, stress or other neurological pathologies such as vascular dementia. This is how it was under-diagnosed until the 1960s.

The speed and progress of the disease vary from one subject to another, making it difficult to formulate an accurate prognosis. Life expectancy therefore varies from 3 to 8 years depending on the patient's age at the time of the diagnosis. As the disease progresses, patients sometimes suffer from rejection by society and their family.

In light of the prevalence of the disease, medical research is striving to discover a drug that would help stop the neurodegenerative process. A number of clinical trials designed to eliminate the senile plaques in the brain have failed.

No treatment is currently available to curtail the progress of this disease. The care offered is mostly palliative, and its effect on the symptoms is limited. However, cognitive stimulation, physical exercise

combined with a Mediterranean diet, excellent hydration, etc. could delay the onset of cognitive impairments in old people who are too often dehydrated.

To find a preventive and curative treatment (at least up to a certain stage of the disease), it is imperative to identify the causes

To date, all research avenues consisting of determining the origin of both types of brain lesion have been fruitless. No treatment is currently available to curtail the progress of this disease.

For many years, the main research avenue has focused on the amyloid plaques formed between the neurons during the disease, and on the tau protein aggregates which cause the neurofibrillary degeneration inside the neurons.
This research approach is doomed to fail as it confuses the consequences of the disease, i.e. the senile plaques and neurofibrillary degeneration, with its actual causes.

The accumulation of amyloid-beta proteins (senile plaques) and abnormal tau protein filaments (neurofibrillary degeneration), which ultimately causes the death of neurons, is only protein debris resulting from the destruction of neural protein structures by oxygenated free radicals which are toxic to your neurons.

The solution lies in the extraordinary discovery recently revealed by Pr Jean-Bernard Fourtillan: the identified regulation of the Sleep-Wake system, made up of 3 hormones secreted by the pineal gland at night, between 10pm and 6am. It unveils the causes of the disease that bears my name, which contributes to explaining its symptoms.

Here are the causes of the disease named after me

Professor Jean-Bernard Fourtillan made a tremendous discovery in 1994, with regard to the causes and treatments of what I have described. He is Honorary Professor of Medicinal Chemistry at the Poitiers Faculty of Medicine and Pharmacy[7] in France. Jean-Bernard Fourtillan discovered the formation, within the pineal gland – see the previous letter from this gland - of the 3 hormones which regulate the nycthemeral, sleep-wake cycle.
As the pineal gland has already pointed out, I must also praise his remarkable humility. Far from introducing himself as a great inventor: Jean Bernard Fourtillan claims he was spiritually driven expressing this in his excellent publication « La Glande Pinéale et le Système Veille-Sommeil – Applications thérapeutiques » (The Pineal Gland and the Sleep-Wake System - Therapeutic application), available for sale on Amazon.

I highly recommend it to physicians, specialists, researchers and even the general public, as it is accessible to everyone: "the miraculous concordances in the structure and functioning of this sleep-wake system".
This disease named after me is characterised by a genuine collapse in the secretions of the 3 hormones simultaneously produced by the pineal gland between 10pm and 6am:
- collapse in Melatonin (MLT) content, a hormone which protects the neurons. Its absence causes the progressive degeneration of neurons.
- simultaneous collapse in the secretion of Valentonin (VLT) which results in sleep disorders.
- simultaneous collapse in the secretion of 6-Methoxyharmalan (6-MH), the wake and cognition hormone, resulting in cognitive impairments during the day.

The results of Melatonin dosage studies in biological fluids in patients suffering from the disease that bears my name, published in scientific literature by a number of researchers, are unanimous: they all show a substantial decrease in the secretion of Melatonin, and consequently the other 2 pineal hormones, 6-MH and Valentonin, when compared with normal subject of the same age.

It is therefore possible to accurately correlate the symptoms with the collapse in the pineal gland's secretions of the 3 hormones of the Sleep-Wake system.

At the final stage of the disease, the pineal gland no longer functions.

It was already known that the decrease in Melatonin content in the cerebrospinal fluid is one of the first signs. It even precedes clinical signs. MLT content in the cerebrospinal fluid continues to decrease as the disease progresses.

The 3 consequences of pineal gland deficiency

1. The lack of Melatonin is directly responsible for the progressive destruction of neurons by oxygenated free radicals.

A great deal of experimental research has shown that Melatonin is a powerful endogenous antioxidant, which reduces the amount of free radicals and therefore protects your neurons.
Due to its reducing properties, Melatonin is the most powerful antioxidant known in biological environments; superior to vitamin E, β-carotene, ascorbic acid (Vitamin C), glutathione, etc.
By reducing oxygenated free radicals, Melatonin therefore prevents the degeneration of the neurons by immunising them from the oxidative stress which corrodes and damages your neurons.
For specialists, the presence of vast amounts of 2-oxo-melatonin in the brain, highlighted by Pr Fourtillan and his team using the mass spectrometry technique, is the in vivo demonstration of the antioxidant properties of Melatonin, described by many authors.
This hormone easily passes through the cell membranes and is concentrated in the mitochondria[8] of the cells. Under these conditions, in healthy subjects, Melatonin concentration in neuronal tissue, in contact with the ventricular system which produces the CSF (Cerebrospinal Fluid), is high.
In this disease, insufficient Melatonin content is responsible for the oxidative damage caused by free radicals. The decrease in Melatonin content is directly related to the appearance of amyloids observed in the disease.

For specialists, we should mention the most abundant oxygenated free radicals which possess a single electron (•): superoxide radical anion O_2•- hydroxyl radical HO•, hydrogen peroxide radical HO_2•, peroxide radical ROO• and alkoxyl radical RO• where R is a carbon chain, nitrogen monoxide NO• peroxynitrite ONOO•, singlet oxygen •O-O• and oxygenated free radicals derived from a fatty acid. Free radicals also damage body fat and proteins, more specifically the myelin that surrounds the nerve fibres (axons) and enables the passage of nerve impulses.

2. The collapse in the secretion of 6-MH disturbing cognition is responsible for memory loss.

Therefore the progressive destruction of the neurons, combined with a reduction in the brain volume by up to 30%, results in the progressive and irreversible loss of mental faculties, notably short-term memory initially, which is normally stored in the Hippocampi.
In patients suffering from the disease named after me, the residual neurons are no longer sufficient to guarantee the transmission of information in the brain. In addition, the two day hormones, the 6-MH and the night hormone, Valentonin, which regulate psychic and vegetative life by modulating the responses

of the receptors specific to the 7 major neurotransmitters and by altering the secretions of the 7 endocrine glands, are no longer secreted.
At the final stage of the disease, nothing is going right. The pineal gland has ceased to function, which explains the clinical signs and the symptoms which worsen until the final stage of senile dementia.

3. Consequences of the discovery of the Sleep-Wake system for the prevention and treatment of the disease named after me

I had already observed that the risk of exposure to the disease that bears my name varies a great deal depending on the individual.
As Pr Fourtillan's team studied the secretion of melatonin in young and old healthy subjects, they clearly observed significant variations in melatonin secretions, with a factor of 13 between extreme pineal secretions. We are therefore not all equal when it comes to the secretion of the 3 hormones by the pineal gland. This is brilliantly demonstrated in the book and video.
Given their serial biosynthesis via acetylation chemical reactions, these three hormones are produced and secreted by the pineal gland in the same proportions, which means that any quantitative variation, either too little or too much, in the pineal secretion will affect the three hormones in the same way.
This results in two logical consequences:
- Melatonin will be used as a secretion marker of the three hormones; measuring its concentration in blood plasma (in pictograms)[9] in the middle of the night provides information on the status of the Sleep-Wake system in patients.
- The three hormones must be jointly administered for all neurological disorders due to the hypofunction of the pineal gland, to avoid any imbalance of the Sleep-Wake system and maintain the harmonious regulation of the body.

For future prevention
The Melatonin content measured in blood plasma in the middle of the night will help assess the scale of the secretions of the 3 pineal hormones, and the condition of the Sleep-Wake system.

Current treatments are ineffective

Four drugs are prescribed for patients suffering from the disease.
- Memantine: Ebixa® and generic drugs. Its chemical structure is similar to that of amantadine (Mantadix®), an anti-Parkinson medication. Unfortunately this drug has adverse effects such as vertigo, headaches and even hallucinations. Although Memantine has been approved for the treatment of moderate to severe forms of Alzheimer's disease, its use was recommended against the advice of the National Institute for Clinical Excellence in the UK, who feels that the high cost of this treatment is not worth the medical benefits observed in most patients. Suffice to say these benefits are non-existent or extremely limited, and insignificant.

- Donezepil: Aricept® inhibits the acetylcholinesterase enzyme[10]**,** which as a result prevents the degradation of acetylcholine, which plays a role in memory.
- Galantamine: Réminyl® and generic drugs. Galantamine inhibits the acetylcholinesterase enzyme. It enhances the action of acetylcholine by preventing its degradation in the synaptic cleft of the connection between neurons.
- Rivastigmine: Exelon® and generic drugs. Rivastigmine is an acetylcholinesterase inhibitor. By inhibiting these enzymes, rivastigmine enhances the action of acetylcholine in the synaptic cleft by preventing its degradation. Its action is referred to as indirect parasympathomimetic. This mechanism helps enhance cholinergic transmissions.

The effectiveness of these drugs on cognitive (thoughts and memory), functional (daily activities) and behavioural disorders, which are commonly associated with the disease, remains very moderate. We already know they are unable to significantly slow down the progress of the disease.

The new treatment with the 3 pineal hormones

They are produced simultaneously in obviously different concentrations :

- Melatonin (MLT) which, by reducing oxygenated free radicals, protects the neurons.

- 6-methoxyharmalan (6-MH), the wake and cognition hormone which maintains the body in wake mode from 6am to 10pm.

- Valentonin (VLT), the sleep and night hormone which keeps the body in sleep mode for 8 hours, from 10pm to 6am.

Polysomnographic sleep recordings have revealed a decrease in REM sleep in patients suffering from the disease, proportional to their dementia, which can be correlated with memory loss. This is correlated with the collapse in the pineal secretions of Valentonin and 6- Methoxyharmalan.

The decrease in Melatonin content is directly related to the appearance of amyloid plaques observed in the disease I described. By protecting neurons from oxidative damage, this hormone, inhibits the in vitro formation of amyloid fibrils.
Excess free radicals also have a visible effect on the ageing of the skin. They are involved in numerous pathologies such as cancer and other neurodegenerative diseases.
This is why, next week, I will give the floor to my colleague James Parkinson, who will explain the signs of the disease he described, its causes and new therapeutic prospects.
I am delighted with all these discoveries which are explained and presented in a graphic manner in the book and document « Les Causes et le Traitement de la maladie d'Alzheimer enfin découverts ! » + Video on YouTube, co-directed by the two aforementioned friends and colleagues.

Alois Alzheimer, delighted to have updated you.

Good luck to you all and good health.

Pr. Henri Joyeux

Post-scriptum

On website fonds-josefa.org:

- Book and Brochure:
“The pineal gland and the Sleep-Wake system. Therapeutic applications” by Pr J.B. Fourtillan, for sale on Amazon. To order from web site fonds-josefa.org

- The Videos You Tube:
« Pr J B Fourtillan answers questions from Pr H Joyeux », Pr J.B. Fourtillan & Pr H. Joyeux (You Tube : duration: 1 h)
« The pineal gland and the sleep-wake system. Therapeutic applications », Pr J.B. Fourtillan (YouTube : duration: 37 min)
« The Sleep-Wake system in Creation »,
Pr J.B. Fourtillan (You-Tube, duration : 14min 35 s + 2 min 13)
« The causes and the treatment of Alzheimer's disease have finally been discovered ! », Pr J.B. Fourtillan & Pr H. Joyeux (You Tube : duration 13 min 30)
- Donations will help us independently finance the development of the pharmaceutical forms of the patches, see **Make a donation on website** fonds-josefa.org

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Sources :

[1] The source of this information can be found in the book I co-wrote with Dominique Vialard, an international science journalist: « Tout savoir pour éviter sur Alzheimer et Parkinson » (All you need to know to avoid Alzheimer's and Parkinson's); Rocher pub.
[2] Millet seed aspect
[3] In 2008, the Health Insurance Fund already indicated that nearly 3% of the over 60 population suffered from Alzheimer's.
[4] Lewy body dementia, also known as dementia with Lewy bodies, represents 20% of neurodegenerative diseases. It generally progresses rapidly and essentially affects the elderly. Lewy bodies were described by my colleague, neuropathologist Friedrich Heinrich Lewy, in 1912, who worked in my own laboratory, Aloïs Alzheimer.
[5] See "Alzheimer's Disease International", The Lancet, 16 December 2005.
[6] Galen Chin-Lun Hung et al., « Predicting suicide in older adults – a community-based cohort study in Taipei City », Journal of Affective Disord, Taiwan, 2015 ; 172 : 165-170.
[7] Poitiers is famous as on 25 October 732, not far from Poitiers, Frankish leader Charles Martel repelled a Muslim raid from Spain, 80 years only after the death of Prophet Muhammad (circa 570- 632). In 853, the city defeated the Normans. More recently, the city created the Futuroscope, France's 3rd largest amusement park.
[8] This is the cell's power station.
[9] Technique developed by Pr Fourtillan's team.
[10] Technique developed by Pr Fourtillan's team.