Neurodegenerative diseases affect people of all ages and results from progressive degeneration and/or death of neurons. Nowadays, it is not known the causes of their appearance and how this degradation can affect the movements of the body and brain functioning, causing dementia.

Presently, these diseases are the most important medical and socio-economic problems, but still there is no cure for these pathologies.

This chapter consists in 4 sections that focus in thematic about neurodegenerative disorders: 1 section is about Alzheimer’s disease (cover the following topics: pathology; symptoms, causes and risk factors; incidence (distribution by age and sex, global and regional distribution); diagnosis, treatment), 2 section is about Parkinson’s disease, 3 section is about others Neurodegenerative Diseases (brief considerations), 4 section focus the impact of Neurodegenerative Diseases in society, 5 section is about Neurodegenerative Diseases prevention.
ALZHEIMER DISEASE

Pathology

Alzheimer’s Disease (AD) is a neurodegenerative disorder which is recognized as the most common form of dementia. This is a type of dementia that causes a global, progressive and irreversible deterioration of cognitive functions (memory, attention, concentration, language, thought, spatial orientation...) [1-3]. This deterioration has consequences as changes in behavior, personality, psychosocial performance and functional capacity of the person, making it difficult to carry out their daily routines.

Although not fully understood, the pathophysiology of AD is characterized by sequentially interacting pathological cascades, including the interaction of Amyloid-β (Aβ) aggregation with cytoskeletal abnormalitie, and the hyperphosphorylation and aggregation of tau protein in neurons with formation of tangles [2,4-7]. These processes lead to the formation of neuritic plaques and neurofibrillary tangles, that contributes to synaptic integrity loss and progressive neurodegeneration [2,4,5]. There isn’t communication within the brain and damages the connection between brain cells. These cells die and this is translated into an inability to recall information. Thus, as Alzheimer’s disease will affect the various brain areas, certain functions or abilities will be lost.

There are two different types of Alzheimer’s disease:

a) Sporadic Alzheimer’s disease (can affect adults of any age, but usually occurs after 65 years). This is the most common form of Alzheimer’s disease.

b) Familial Alzheimer’s disease (is transmitted from one generation to another). This type is a less common form and affects a very small number of people [1].

Symptoms

The manifestations worsen as the brain cells are dying and communication between them is changed. Often they begin by memory oversight and difficulty to find the right words for simple everyday objects.

Other symptoms are: persistent and frequent memory difficulties (especially recent events); it is present a gap speech during the conversations; loss of enthusiasm in carrying out activities previously enjoyed; it takes more time to perform daily activities; people or places known are forgotten; inability to understand questions and instructions; deterioration of social skills; emotional unpredictability; depending on the people and the brain areas affected, the symptoms and the diseases progress is different.

People capabilities may be different from day to day or even within the day. These manifestations may worsen during stress times, fatigue and health problems (diabetes, cardiovascular diseases...). The truth is that there will be a deterioration over time and the rate of cognitive decline in AD
patients varies considerably between individuals, some patients shows rapid and substantial
cognitive decline in a relatively short time, and others shows little or no change over years [5].

Alzheimer’s disease is progressive, degenerative and currently irreversible.

**Causes and Risk Factors**

Every day researchers have more discoveries about biochemical changes that causes damage
to brain cells in Alzheimer’s disease.

Familial Alzheimer’s disease is transmitted from one generation to another, by one gene. The ApoE14 is the only gene associated with a slightly increased risk of developing Alzheimer’s disease, late onset [5,7].

However, in sporadic Alzheimer’s disease, people who may have or not a family history of the disease.

Researchers are investigating different suspected causes, including: environmental factors, biochemical disorders (metabolic and vascular parameters, type II diabetes mellitus) and immune processes [1].

The cause may be different from people and may be due to one or more factors.

**Incidence**

Alzheimer’s disease is the leading cause of dementia worldwide. It accounts for more than half of the overall number of demented people. It is estimated to be around 46 million people living with dementia worldwide [8]. This number is expected nearly to increase to 131.5 million in 2050, as a consequence of the steady aging growth population in both developed and developing countries [7,8].

Anybody may develop Alzheimer’s disease. However, the prevalence rate of dementia increases with the age, and it is more often after 65 years. In Europe and the Americas peak incidence is among people aged 80-89 years, in Asia it is among people aged 75-84, and in Africa among people aged 65-74 [8].

**Diagnostic**

Currently, there is no specific test to identify Alzheimer’s disease.

The diagnosis is made after a careful clinical observation (may include: detailed medical history, physical examination and extensive neurological examination of intellectual functioning, psychiatric evaluation, neuro psychological evaluation, and blood and urine laboratory tests) [9,10].

However, the exact diagnosis can only be confirmed after the patient’s death, through the observation of brain tissue.
There are three main stages of pathological progression of AD: namely preclinical AD, Mild Cognitive Impairment (MCI) and dementia [7]. It is important to have an accurate diagnosis as early as possible to determine if the clinical condition of the patient is due to Alzheimer’s disease or if the symptoms are being caused by another disease.

Nowadays researchers have been investigating new biomarkers to prevent Alzheimer’s disease. A diagnosis of preclinical AD requires the presence of a biomarker (presence of a genetic risk factor like the ApoE4 gene, an imaging marker, ...) [7].

MCI is diagnosed once cognitive disturbances become noticeable and demonstrable on cognitive testing, but who shows a preserved general cognitive functions and not severe enough to significantly interfere with activities of daily living [7,9]. Dementia diagnosis requires significant functional and cognitive impairment [4,7]. For example, the current diagnostic criteria are: DSM-IV, ICD-10 and NINCDS-ADRDA [4,8,10].

The progression of the disease varies from person to person. But, these diseases lead to a complete state of dependency and, finally, death. A person with this disease can live between seven to ten years (average).

Treatment

Until this date there is no cure for Alzheimer’s disease, no treatments are currently available to cure or even alter the progressive course of this disease. However, there are a few drugs (cholinesterase inhibitors, donepezil, galantamine or rivastigmine; and memantine) that appears to allow some stabilization, limited to a temporary and symptomatic support of cognitive functioning (in mild and moderate stages) in these patients [2,7].

But, numerous new therapies are being investigated in various stages of clinical trials [11]. It is urgent to develop new drugs with disease-modifying properties for AD, to slow the progression of the neurodegenerative process by inhibiting critical events in the pathophysiology of the disease [2,7]. The pathogenesis of AD entails multiple factors such as Aβ, tau, inflammation, oxidative stress, apoE, multi-targeted drugs and therapeutic combination therapies and the specific biomarkers development may lead to the treatment for AD in the future [3,7].

Is important too, to support and improve the lives of people with dementia and their caregivers and families [11].

PARKINSON DISEASE

Pathology

Parkinson’s Disease (PD) is the second most common neurodegenerative disease. It is a chronic and progressive neurodegenerative disease, which affects motor system because of progressive neuronal loss in the brain [12-15]. This disease is a neurodegenerative disorder of the dopaminergic neurons in the substantia nigra (brain region) [12,13]. When the cells of
the substantia nigra die, dopamine levels become abnormally low, which leads to difficulties in controlling the muscle tone and movements.

**Symptoms**

Parkinson’s disease is characterized by motor and non-motor deficits. Motor deficits are: tremor (resting tremor), muscular rigidity, bradykinesia (slowed movement), postural instability, and gait impairment because of progressive neuronal loss in the brain [12-16]. These symptoms usually begin asymmetrically but gradually spread to the body [12]. Asymmetric rest tremor is a common initial symptom (70%-90% of patients). This may be the most visible sign of PD, but it rarely is the major cause of disability [12].

This pathology is also accompanied by a host of non-motor manifestations, including constipation, sensory symptoms (pain and tingling), autonomic dysfunction, urinary symptoms, sleep disorder, olfactory dysfunction, cognitive impairment, loss memory, and neuropsychiatric manifestations (depression, anxiety, apathy, hallucinations and dementia) [13,15-18].

**Causes and Risk Factors**

So far, has not been determined why some people develop the disease and others do not. Some researchers report that the disease is due to the toxic effect of certain drugs. For example, secondary or symptomatic forms include drug-induced parkinsonism, most commonly related to anti-psychotics and anti-emetic agents; post-infectious parkinsonism; structural lesions (stroke); vascular lesions; metabolic conditions; trauma and toxic insults (carbon monoxide,…). Prescribed medications frequently implicated in the development of parkinsonism are haloperidol, risperidone, metoclopramide, and prochlorperazine [12].

Others researchers report that the disease might have a genetic basis. Some genes, including SNCA and LRRK2, PINK1 and DJ-1, have a more modest effect on disease susceptibility. Genetic advances in PD and related disorders have spurred the development of mechanisms underlying the disease [13].

**Incidence**

PD is a chronic and slowly progressive disorder with a mean duration of 15 years from disease recognition until death, although affected individuals can frequently survive longer, but, patients with PD had a short life expectancy compared with the general population [13,19]. This disease is a leading cause of neurological disability among the adult population, affecting 1.5 to 26 per 100,000 [20]. Arises, usually in late middle age, with its beginning, and the estimated number of patients with this disease, around aged >50 years is “between 8.7 and 9.3 million worldwide by year 2030” [20].

**Diagnostic**

The diagnosis of PD in living patients is a clinical diagnosis, based on these criteria and in the presence of motor features [13,15]. But, waiting until the motor symptoms develop to make
a diagnosis may be too late, especially if we want to intervene early in the course of the disease with disease-modifying interventions [15]. It is important to analyse non-motor symptoms, are now believed to presage the clinical recognition of bradykinesia, tremor, or gait impairment by as much as 20 years [13].

The diagnosis of PD is adapted from established criteria by the UK Parkinson’s Disease Society Brain Bank, but, clinical presentation may vary from patient to patient [12].

Treatment

Parkinson's disease is a non-reversible condition, extending throughout life, is no cure for this disease. However, quality of life of patients can be significantly improved with the use of medication which can reduce symptoms [17,20].

Research shows that one can resort to the use of several drugs with specific active ingredients, especially in the early stages of the disease [20]. Current pharmacological treatment is focused in dopamine to alleviate the PD symptoms and rivastigmine is the approved drug of choice for dementia treatments associated with PD [16,20]. In more advanced stages of the disease, can also be effective, direct modulation of basal ganglia activity via deep brain stimulators implanted in the subthalamic nucleus [13].

OTHERS NEURODEGENERATIVE DISEASES

There are more neurodegenerative diseases that affect people: Sclerosis Lateral Amyotrophic, Multiple Sclerosis disease, Huntington disease, Familial amyloid polyneuropathies, Machado-Joseph disease.

- Amyotrophic lateral sclerosis is the major neurodegenerative diseases alongside Alzheimer's disease and Parkinson’s disease [21]. It is a progressive disorder, muscular paralysis reflecting degeneration of the motor system at all levels [21-24].

- Multiple sclerosis is a chronic autoimmune, inflammatory neurological disease of the central nervous system [25].

- Huntington disease, Familial amyloid polyneuropathies, Machado-Joseph disease are a neurodegenerative genetic disorders [26-28].

Neurodegenerative diseases are different depending on where neurons degenerate or die (brain and / or spinal cord).

In Alzheimer’s and Parkinson’s diseases, the neurons dying in the brain, whereas in Amyotrophic Lateral Sclerosis death of motor neurons occurs in the spinal cord. And, in Multiple Sclerosis, dying neurons in the brain and spinal cord disease.

Familial amyloid polyneuropathies. Huntington’s and Machado-Joseph diseases are the most common autosomal dominant neurological disorders.

It is important we approach these diseases in another chapter.
IMPACT OF NEURODEGENERATIVE DISEASES IN SOCIETY

These pathologies have impact in society. Nowadays, as a result of increased life expectancy and changing population demographics, neurodegenerative diseases are becoming more common [12,29]. Neurodegenerative disorders, such as Alzheimer’s and Parkinson’s diseases (more common neurodegenerative disorders), account for a significant and increasing proportion of morbidity and mortality in the world and high economic burden [12,15,29].

The diagnosis of these diseases are not easy and healthcare costs related to diseases are projected to rise dramatically in the near future [12]. Accurate diagnosis increases the chance of effective treatment and reduced disability over time, which reduces direct and indirect healthcare costs [12].

These pathologies are progressive degenerative processes that are becoming more serious over the years and have a major impact on professional, social and family of patients, leading to a total inability to exercise any type of everyday activity.

At the professional level these diseases affects physical and mental activity, hindering the development of the proposed tasks and compromising their professional performance.

Several studies have reported executive function deficits in patients with neurodegenerative diseases, such as: cognitive functions like planning, monitoring, cognitive flexibility, inhibition of automated responses, retrieval from declarative memory and the maintenance and manipulation of information in working memory. Impairment in memory depends on many factors like the age of onset of the disease, disease duration and severity of clinical symptoms [16].

Thus, these pathologies have a big impact in quality of life. Limitations in functional ability and nonmotor symptoms have severely impact in quality of life. However, the most adverse impact arises from neuropsychiatric nonmotor symptoms (especially depression and cognitive dysfunction). All these limitations have earnestly impact in quality of life and it decreases when the disease progresses [12].

The quality of life and psychosocial issues can adversely affect adherence to treatment, symptom management, and course of the disease.

Low levels of understanding about these pathologies contribute to perpetuation of stigma and discrimination. Stigma and discrimination extend to family caregivers.

The caregivers and family members of these patients, can be physically and mentally exhausting, leading to enormous stress, fatigue, anxiety, and ultimately depression and a financial burden [12]. It is easy to imagine the strong negative impact that such a disease has on a family.

Unlike Alzheimer’s disease, where physical disability is not a factor until later in the disease, in Parkinson’s disease is needed care for physical limitations of the patient and cognitive and
psychiatric complications (which can begin early in the disease), therefore these pathologies have more impact in the caregiver life’s quality [12].

These pathologies have an economic impact in society, too. Economic burden is particularly evident in more advanced pathologies with more severe symptoms, where poorer quality of life, reduced productivity, drug therapy increase and even greater need for healthcare services increase direct and indirect costs. But, it is very difficult to make confident projections of future economic costs. Future costs could be influenced by macroeconomic factors and by diseases specific factors [11].

The reported projections for future growth in numbers of people with Alzheimer’s and Parkinson’s diseases should be analyzed with caution. It is important known the demographic projections, risk factors, diagnosis, treatments. New therapies, development of drugs that can slow disease progression, and better social and medical care may reduce mortality cases and promote quality of life [11,12].

**NEURODEGENERATIVE DISEASES PREVENTION**

Nowadays, because of population aging, neurodegenerative diseases are increased and have seen a growing recognition of the scale of the problem and the need for action [13].

Some countries have developed strategies, policies, plans or guidelines to support these pathologies and to improve the quality of life of patients and their caregivers.

It is important to pay more attention, commitment and resources are required for raising awareness and improving knowledge about these diseases. Raising awareness is an important strategy for reducing the disorders treatment gap. Different media channels (film, television, internet and social media) are an important role to raise awareness about these diseases. There is an urgent need for improving awareness and understanding of neurodegenerative diseases in order to improve the quality of life for people with dementia and their caregivers. Awareness-raising and improved understanding can reduce the stigma associated with these diseases and reduce the fear of the disease itself.

Governments should develop sustainable, integrate programs and support structures to improve the quality of life of people with dementia and their families. Governments have a role to play in resourcing public awareness campaigns and it is a new challenge to governments should underpin policies, plans, legislation and practice guidelines.

Neurodegenerative diseases are a global public health challenge and that urgent action is required to support country preparedness for the increasing burden and cost of dementia. Therefore, it is important to promote healthy lifestyle and raising public awareness and understanding these diseases. Because, neurodegenerative disease can be associated with risk factors, for example, vascular risk factors (including hypertension and high cholesterol).
Therefore it is important to understand the associated risk factors, and healthy lifestyles. It is important the promotion of health behaviors, serious physical and mental activities on a daily basis that contribute to cognitive ability and the maintenance of healthy mental functioning, such as: exercise (activity), exercising the mind, be social, healthy eating, stress and sleep.

In the future, the huge cost of the disease will challenge health systems to deal with the predicted future increase of prevalence. It is needed, to promote and improve public attitudes to and understanding neurodegenerative diseases, investing in health and social systems to improve care and services for people with diseases and their caregivers.

Today, other big task is the development and implementation of neuroprotective therapies, it will be important to have biomarkers that can aid in early diagnosis, identify patients and monitor progression and response to treatment.

There is very important scientific research, improve early diagnosis and development technology, therapies, drugs and to know the neurodegenerative diseases. In these pathologies diagnosis are commonly given in a relatively late stage of the disease process, and the early diagnosis will at least assist in the better management of patient care, improve quality of life and decrease the economic costs.

Although many neurodegenerative diseases cannot be cured at the present time, there are often symptomatic treatments available and new drugs and therapies are emerging to prevent and/or reverse the beginning of the diseases or their progression, and it is important to promote quality of life [12,30].

Biomarkers for neurodegenerative pathologies are essential to facilitate disease diagnosis, ideally at early stages, monitor disease progression, and assess response to existing and future treatments. Neurodegenerative biomarkers with higher sensitivity and specificity can be applied at preclinical stages [2,30]. Research into biomarkers for neurodegenerative diseases has been made in neuroimaging techniques (assess regional structure, function and biochemistry of the brain), in identifying biochemical indices of brain dysfunction (measured by body fluids), and proteomic technologies [9,30].

There is an urgent need for biomarkers to diagnose neurodegenerative diseases early in their course, to differentiate them from other related diseases, and to monitor patients and their responses in to new therapies. To increase the accuracy of a biomarker-based diagnosis, biomarkers in body-fluids have been combined with other biological markers such as structural and functional neuroimaging and neuropsychological testing, will likely lead to understanding of the disease and progression [9,15].

It is very important, the development of drugs, too [12]. More effective management of these diseases, is the development of drugs that can slow disease progression, could potentially reduce healthcare resource utilization and associated costs.
References


