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Prevalence of dementia is growing as the overall age of the population rises. This article, the first in a four-part series, differentiates between dementia and normal ageing

DEMENTIA: PART 1 OF 4

How dementia differs from normal ageing

In this article...

- The differences between dementia and 'normal' ageing
- Physiological changes that lead to dementia
- The concept of 'inflammaging'

Author Laura Ginesi is a lecturer in physiology, School of Health Sciences, University of East Anglia;
Catharine Jenkins and Bernie Keenan are senior lecturers, School of Nursing, Midwifery and Social Work, Birmingham City University.

Abstract Ginesi L et al (2016) Dementia 1: How dementia differs from normal ageing. *Nursing Times*; 112: 24, 12-15.
Dementia is a collective name for a set of symptoms that include memory loss, mood changes, confusion and increasing difficulty with everyday tasks. This four-part series provides an overview of dementia and its treatment, from its causes and pathophysiology to diagnosis and the nurse's role in its management. This first article reviews the main forms of dementia and how research is shedding new light on the differences between dementia and normal ageing.

While the speed at which the human brain processes information naturally slows with age, dementia is not an inevitable part of the ageing process. Rather, it involves a progressive impairment of cognitive skills, including memory, awareness of place and time and the ability to learn new information. Each person experiences dementia differently, but in essence it remains an incurable and progressive condition (Alzheimer's Society, 2016; Jenkins et al, 2016).

This four-part series explores the main forms of dementia, highlights the differences between normal ageing and dementia, investigates the pathophysiological neurodegeneration that leads to the impaired thinking, judgment, skills and behaviour seen in the condition, and examines the signs, symptoms and difficulties of those affected. It outlines how dementia can be assessed and diagnosed before focusing on the nurse's role in managing the complex needs of patients while working in partnership with patients, their families and carers, and the multidisciplinary team.

Is dementia a consequence of ageing?

Ageing is an ongoing process and a natural part of living. With passage of time, however, structural, functional, biochemical and psychological changes begin to limit people's ability to adapt to changing circumstances and lead to increased vulnerability and frailty.

The benign memory lapses many experience as they grow older are a common feature of the ageing process. These so-called senior moments affect recent memory and, unlike the more permanent memory loss affecting people with dementia, those who experience them are usually aware they have taken place, as illustrated by participants in a study by De Witt et al (2010).

Similarly, these memory lapses are not usually problematic; only a small proportion of memory complaints are severe enough to interfere with everyday activities (Mitchell et al, 2014). Strategies such as leaving lists or memos in obvious places can help reduce the effects of these lapses. In contrast, people with dementia become increasingly dependent on care from other people and eventually require help with all aspects of daily living (Jenkins et al, 2016).

5 key points

1. Dementia is not an inevitable part of ageing
2. Dementia is a neurodegenerative disorder that leads to cognitive impairment
3. Better understanding of the ageing process is contributing to greater understanding of the brain physiology that results in dementia
4. There is no cure for dementia but greater understanding of its symptoms and causes can help nurses to provide better care
5. Alterations in metabolism, increasing frailty and reduced tolerance to physiological stressors result in 'inflammaging'

Causes of dementia

Dementia is an umbrella term for a number of conditions, and the risk of developing it rises with age but is thought to arise from a diverse range of contributing factors. Alzheimer's disease, vascular dementia, dementia with Lewy bodies and frontotemporal dementia are among the most common neurodegenerative diseases of the brain (Table 1), but HIV/AIDS, Cruetzfeldt-Jakob disease and brain tumours can also cause dementia; types of dementia are discussed in more detail in part 2 of the series.

Similarly, acquired brain injury due to stroke, arrhythmias, trauma, alcohol misuse or exposure to environmental chemicals or pollutants can also contribute to the development of dementia (Jenkins et al, 2016; Blossom and Brayne, 2014).

At a physiological level, dementia generally arises from the impaired ability of neurons in the brain to communicate effectively. The brain communicates and stores information through a process called synaptic plasticity – altering and changing the synaptic connections between neurons (Koeppen and Stanton, 2010).

Dendritic spines are tiny structures that stick out from the main dendrites of some neurons and form synapses to receive and integrate information (Nimchinsky et al, 2002). They are highly dependent on the proteins of the cytoskeleton for their structure, which can be modulated by sensory experience. Dendritic spine formation, stability, plasticity and maintenance depend on input from excitatory (glutamatergic) synapses. Without these dynamic structures, the synapses would be unable to change that is, they would not be "plastic".

Although there is some loss of dendritic spines through normal ageing processes, they can be severely affected by brain diseases. Alterations in synaptic numbers and the shape of dendritic spines is thought to precede eventual neuronal death in degenerative diseases, including Alzheimer's, Parkinson's and Huntington's diseases.

New information about the molecular mechanisms of synaptic function, along with improved imaging of the brain, are providing evidence of the key role played by neuronal networks in normal cognitive function (Herms and Dorokstkar, 2016; Maiti et al, 2015; Copstead and Banasik, 2013; Koeppen and Stanton, 2010).

Genetic factors have been associated with fewer than 5% of all dementia cases, but in some families genetic mutations may increase risk (Ferencz and Gerritsen, 2015).

The brain contains more lipid (fat) – which is essential to neuronal functioning and integrity of membranes – than any other organ in the body. Oxidative stress produces free radicals (also called reactive oxygen species, or ROS), which leak from mitochondria into the cytoplasm, damaging lipids, DNA and proteins. The end products can be toxic, causing misfolding of proteins and inducing apoptosis (programmed cell death) of neurons (Newton et al, 2015). All the above factors lead to neuronal and synaptic loss, which in turn leads to the degeneration seen in dementia. This will be discussed in part 2 of the series.

TABLE 1 MAIN TYPES OF DEMENTIA

Type	Features
Alzheimer's disease	● Primarily characterised by a build-up of abnormal protein structures in the brain called 'plaques' and 'tangles'. These lead to a breakdown in the connections between nerve cells and death of brain tissue ● Progressive memory loss is the main symptom. Others include reduced ability to make decisions and carry out tasks, poor orientation and visuospatial skills, difficulty with language and mood disturbances
Vascular dementia	● Caused by failure of oxygen supply to the brain due to diseased blood vessels; may also involve transient ischaemic attacks, microbleeds or cerebrovascular incidents (strokes) ● The death of brain cells means it is characterised by problems with cognition, particularly memory and reasoning, which eventually affect daily activities ● Symptoms depend on area of brain affected, but can develop quickly after a stroke, for example, or more slowly in the case of blood vessel disease
Dementia with Lewy bodies	● Lewy bodies are tiny deposits of abnormal protein that collect in the nerve cells, and over time seem to interfere with nerve cells, eventually causing a loss of brain cells ● Lewy bodies are also a factor in Parkinson's disease, and can cause a mix of cognitive symptoms similar to Alzheimer's such as memory loss, and physical symptoms linked to Parkinson's disease such as motor difficulties
Frontotemporal dementia	● This dementia involves a range of conditions that include Pick's disease. Sometimes misdiagnosed as mental health problems and/or associated with neurological problems, it has two subtypes: a behavioural subtype and a language disturbances subtype

Signs and symptoms

As with many other long-term conditions, there is no fixed starting point for the different forms of dementia, which means that the initial clinical picture can be confusing. Different areas of the brain, such as those responsible for language, social inhibition, visuospatial processing, memory and executive functions, are not affected in a uniform way. Dementia does not progress in a linear manner but is characterised by periods of stability followed by decline (Jenkins et al, 2016; Hughes, 2011).

Nurses can look out for a number of initial indicators of dementia. Subtle signs and symptoms that become more apparent over time include a decline in short-term memory, which is often the most obvious early symptom, but the rate of decline depends partly on the type of dementia. The common shared symptom is impairment of higher cognitive skills: memory, cognition, decision-making, comprehension, learning and judgment (National Institute for Health and Care Excellence, 2010; Hughes, 2011).

As the condition progresses it may become more difficult for people with dementia to carry out tasks that were previously easy, such as getting dressed or cooking, and their ability to name familiar objects and people may become impaired.

Similarly, strategies such as making lists or leaving reminders as memory cues become less effective over time and people with dementia increasingly experience severe cognitive and memory problems such as getting lost on familiar routes, confusing night and day, and misplacing possessions. While it is common for anyone to misplace keys or mobile phone, people with dementia will also experience difficulties with keeping track of conversations and managing everyday tasks such as paying bills (Hughes, 2011).

Eventually, family members or carers of people affected by dementia will also begin

TABLE 2 PHYSIOLOGICAL CHANGES CAUSED BY AGEING

Body system	Change	Impact
Respiratory	● Diminished vital capacity and increased physiological dead space (the volume of air inhaled that does not take part in gas exchange)	● Lower vital capacity ● Increased susceptibility to infections, pneumonia, acute respiratory distress syndrome
Cardiovascular	● Arteriosclerosis (hardening of the arteries) ● Maximal heart rate; cardiac output diminishes ● Atheroma may develop; clots may form	● Stiffening of the blood vessels tends to increase blood pressure ● Atheroma may rupture or block arteries causing heart attack, stroke or deep-vein thrombosis
Eyesight	● Reduced tear production ● Ciliary body stiffness ● Long-sightedness and losses in motion perception ● Changes in colour perception	● Blurring of text ● Reduced clarity of colours and impaired hazard perception ● Alterations in gaze patterns – affects everyday activities and mobility
Brain	● Forgetfulness and 'senior moments' ● Slower reaction time	● Need to drive more cautiously, for example leave longer distances to car in front
Hearing	● Difficulty following conversations in noisy environments ● Loss of acuity especially with high-pitched sounds	● Impaired ability to distinguish sound against background noise
Taste, touch and smell	● Reduced sensitivity to touch and smell	● Loss of sense of smell and/or ability to discriminate between smells
Urinary system	● Reduced ability to concentrate urine and deal with fluid stress, for example dehydration ● Increased frequency of urination	● Waking at night to go to the toilet ● Feelings of urgency to urinate ● Stress incontinence
Skin	● Skin may become thinner, lose elasticity and become wrinkled ● Melanocytes lose ability to produce melanin ● Changes to distribution of adipose tissue	● Wound healing is slowed
Musculoskeletal	● Muscle mass may reduce or lose strength and power ● Increased bone resorption and loss of bone density	● Reduced ability to carry out activities of everyday living; impaired mobility and increased risk of falls ● Loss of minerals and increased risk of osteoporosis
Sexual health	● Women experience menopause ● Sperm production may diminish	● Cessation of menstrual cycle ● Prostate may enlarge
Liver	● Some changes in enzyme systems	● Prescription medication may need to be reviewed

to notice changes in their mood or behaviour. For example, they may blame others for their mistakes, be increasingly and uncharacteristically suspicious, depressed, agitated or irritable, and problems with language may mean that they substitute, repeat or forget familiar words, making it harder for relatives and carers to understand what they mean. Everyday self-care tasks such as cooking, choosing clothes or coping with new environments may also become more difficult (Alzheimer's Society UK, 2016; Jenkins et al, 2016).

People with dementia are also at particularly high risk of falls due to disorientation or changes in gait, delirium and/or dehydration, while forgetfulness, poor concentration and confusion may arise if they have to be admitted to hospital, leading to feelings of anxiety, confusion, insecurity, agitation or aggression (Barker and Board, 2012; Toot et al, 2010).

As everyday activities become more difficult, people with dementia may become fearful and insecure, while anger, hallucinations and/or delusions can begin to affect their emotional wellbeing. The emotional lability associated with dementia means that family and carers may eventually need to play a prominent role in support and take control of decisions around medical treatment and care.

There is no cure for dementia. Over time, those affected will lose the capacity for speech and comprehension; they will struggle with basic psychomotor skills such as walking, chewing and swallowing food, and may need help with the basic activities of living such as using the toilet.

The concept of 'inflammaging'

The expression 'inflammaging' has been coined as an innovative, unifying concept that describes how low-grade, persistent and systemic inflammation can be a key contributing factor in many common conditions, including dementia, that occur with advancing age (Table 2) (Francheschi et al, 2000; Rodgers, 2000). Progressive accumulation of these changes increase frailty, the chance of disease and death.

Free radicals, also known as reactive oxygen species (ROS), are highly reactive chemical agents formed through metabolic reactions. In excess, they can damage essential molecules, including proteins, lipids and DNA.

One concept that was posited, known as the free radical theory of ageing, suggested that age-related physiological changes were the result of accumulated damage to tissues and organs from ROS found in cells (Harman, 2009). Early molecular and cellular theories that sought to explain why people age focused on understanding why and how ROS are formed through

normal metabolic reactions within cells but then begin to progressively damage cell integrity. According to Harman (2009), studies focused on the production of superoxide and other ROS and changes across a person's lifespan.

Cells, including neurons, normally rely on antioxidant mechanisms to detect and neutralise these toxic intracellular components to maintain homoeostasis (Martinez-Vincente and Cuervo, 2007). Disturbance of this homoeostatic equilibrium resulting from failure of these mechanism leads to activation of a variety of defence mechanisms discussed below.

A balance between production of ROS and antioxidant processes is essential for normal physiological function; if excess ROS are produced, they can overwhelm the body's ability to neutralise them. The resultant disturbance of homoeostasis is called oxidative stress and, in turn, damages lipids, proteins and DNA.

The acute inflammatory response evolved as a beneficial response, enabling the body to repair damage, reproduce and replace cells and adapt to invading pathogens or traumatic injury (Copstead and Banasick, 2013; Koeppen and Stanton, 2010). However, it can also result in the formation of excess ROS that impair healthy cell function, leading to many of the physical changes associated with ageing (Table 2).

Although often asymptomatic, the physiological characteristics of inflammaging include increased circulating levels of inflammatory markers, alterations in immune responses and changes in the way energy is used by cells (Mendenhall et al, 2016; Frank and Caceres, 2015; Vitale et al, 2013). T-cell (or T lymphocyte) numbers are also reduced, meaning the body takes longer to recover from trauma and infections, leaving more opportunity for chronic disease or secondary infection to develop (Hazeldine et al, 2015). Inflammaging is therefore a useful concept to explain why older people become less resilient to everyday stressors, are increasingly frail and more likely to develop conditions such as dementia with advancing age (Franchesi and Campisi, 2014).

At a cellular level, normal cognitive function and memory depend on a network of neurons within the brain, and dementia is a syndrome caused by neurodegenerative processes. Part 2 of this series discusses the role of alterations in inflammatory processes and oxidative stress (essentially an imbalance in the production of free radicals and the body's ability to prevent their harmful effects) in the accumulation of abnormal, misfolded proteins.

Conclusion

Across the globe the average age of populations has risen over a relatively short time. The prevalence of cognitive impairment and dementia increases dramatically in people aged 85 years or over, with several factors such as gender, educational attainment, lifestyle choices and financial hardship significantly affecting the development and maintenance of cognitive ability and skills.

The bulk of care for people with dementia is still provided by family members and carers, but the disease will present many financial and healthcare challenges in future. Discovering accurate biomarkers for dementia is a priority (Ahmed et al, 2014), and new and emerging avenues of research into the principles that regulate homeostasis at the cellular and molecular level are beginning to address this. It is important that people with concerns about dementia feel supported. Better understanding of the disease and the pathophysiological mechanisms that lead to the death of neuronal networks in the brain will provide nurses with insight into the development of disease – knowledge that can be shared with colleagues, people with dementia and their family members.

This article has examined the possible causes of dementia, as well as looking at the concept of inflammaging and the differences between dementia and 'normal' ageing. In the next article in this series, as well as looking in more detail at the different types of dementia, we investigate new theories about the pathophysiology of the condition that have the potential to guide research into management strategies. **NT**

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