Article 1 :

What is dementia? An introduction to changes associated with progression of dementia

The speed of information processing by the human brain changes with age but dementia is not part of the normal ageing process. Dementia is a progressive impairment of cognitive skills – remembering things, awareness of place and passage of time and ability to learn new things. Each person will experience dementia in his or her own way, and it is incurable and unrelenting.

In this series of articles, we explore some of the main forms of dementia, highlighting new understanding of the difference between normal ageing and dementia (article 1) before explaining some of the new findings related to pathophysiological processes that contribute to signs, symptoms and behaviour of those who are affected (article 2 of this series). Risk factors and risk reduction measures associated with the disorder are discussed and evaluated before we describe signs and symptoms and outline how dementia can be recognized, assessed and diagnosed (article 3 of the series). In the final article we consider the experience of the person with dementia and then focus on the nurse's role in responding sensitively to complex needs while working in partnership with people living with dementia, their family carers and the multi-disciplinary team (article 4 of the series).

Ageing is a dynamic, on-going process that happens to us all. To live is to age, but with the passage of time structural, functional biochemical and psychological changes limit people's ability to adapt to changing environments and lead to increased vulnerability and frailty.

Dementia is different from normal aging processes and also from the common, but benign, forgetfulness that is experienced by many people as they get older. Although they can be a source of frustration, "senior moments" affect recent memory and people who are affected are acutely aware of their memory deficits. However, perceived memory complaints may not always be problematic; only a small proportion of memory complaints are severe enough to interfere with everyday tasks and activities and many people with subjective memory complaints do not deteriorate more rapidly than usual (Mitchell et al, 2012). Strategies like making lists, writing memos and leaving them in conspicuous places can be helpful for those who are affected and will help them to remember what they have forgotten.

This article compares some of the physiological features of normal ageing with the pathophysiological progression that appear to be playing a significant role in neurodegeneration and lead to impaired thinking, judgment, skills and behaviour that are characteristic of dementia. People who are affected by the disease will eventually require help with all aspects of daily living and become increasingly dependent on care from other people (Jenkins et al, 2015).

Inflamm-aging – new concepts and insights

Harman's free radical theory of ageing first postulated that old age was the result of accumulated damage to tissues and organs by highly reactive chemical agents called free radicals, Early molecular and cellular approaches to explaining why people age therefore focused on understanding why and how Reactive Oxygen Species (ROS) were formed through normal metabolic reactions within cells and progressively contributed to damaging effects that have the potential to jeopardise the maintenance of cellular integrity (Harman, 2009). Studies at that time tended to focus on the production of peroxide by cells, cancer, atherosclerosis and changes across the lifespan.

Cells, including neurons, rely on homeostatic surveillance mechanisms and clearance of these toxic intracellular components (Martinez-Vincente and Cuervo, 2007). Disturbance of this homeostatic equilibrium leads to activation of a variety of defence mechanisms.

The acute inflammatory response evolved as a beneficial, transient response that facilitates repair, turnover and adaptation to invading pathogens or traumatic injury (Koeppen and Stanton, 2010. Copstead and Banasick, 2013). Electrons that escape from biochemical processes in mitochondria and during the inflammatory response react with water to form ROS including the superoxide radical, the hydroxyl radical or nitric oxide. Such entities are associated with oxidative stress, which is a process that impairs healthy cell function - mostly by altering the structure of proteins or nucleic acids (DNA and RNA).

The production of ROS is now considered to be subject to homeostatic regulation through the action of antioxidants such as the enzyme superoxide dismutase, which can neutralise the free radicals before they can cause any damage to biomolecules. However, an accumulation of oxidative damage in a variety of macromolecules with age resulting in a progressive loss in functional cellular processes, leading to the changes associated with ageing (see table 1).

The expression '*inflamm-aging*" has more recently been coined as a unifying concept that describes how chronic, low-grade, mild yet persistent, systemic inflammation can be a key contributing factor to many common conditions that occur with advancing age (Francheschi et al, 2000. Rodgers, 2000). Progressive accumulation of these diverse changes increases the change of disease and death. Although often asymptomatic, the physiological characteristics of Inflamm-aging are increased circulating levels of inflammatory markers, alterations in immune responses and changes in the way energy is utilized by cells (Frank and Caceres, 2015, Mendenhall et al, 2016 . Vitale et al (2013). T-cell numbers are reduced so it takes longer to recover from trauma and infections leaving more opportunity for chronic disease or secondary infection to develop (Hazeldine et al, 2015).

Inflamm-aging thus provides health professionals with a useful concept which explains why older people become less resilient in the face of everyday stressors, are

increasingly frail and more likely to develop the many conditions that become more common with advancing age (Franchesi and Campisi, 2014).

At the level of cells, normal cognitive function and memory depend on the function of networks of neurons within the brain but dementia is a syndrome caused by neurodegenerative processes. Detailed descriptions of the processes are beyond the remit of this article but alterations in inflammatory processes and oxidative stress leading to accumulation of abnormal, misfolded proteins including amyloid-beta, tau and alpha-synuclein will be explored in greater detail in article 2 of this series.

It is important that people with concerns about dementia feel supported. Better understanding of dementia and the pathophysiological mechanisms that lead to death of neuronal networks of the brain can give nurses insight into the development of disease and knowledge which can be shared with colleagues, people with dementia and their family members.

Causes of dementia

Most cases of dementia arise from impaired ability of neurons within the brain to communicate effectively with each other. Dendritic spines are microscopic connections between neurons which encode changing levels of activity at synapses, so understanding their structure and function has been key to understanding memory and learning (Kandel et al, 2012, Nicholls et al, 2012). New information about molecular mechanisms of synaptic function along with improved functional imaging of the brain are providing evidence of the key role of neuronal networks for normal cognitive function.

The best correlate for dementia is synaptic loss and key circuits in the hippocampus. The risk of dementia increases as people get older and it is thought to arise from a range of diverse contributing factors. Alzheimer's disease, vascular dementia, Lewy Body dementia and fronto-temporal dementia are amongst the most common neurodegenerative diseases of the brain but HIV/AIDS, Cruetzfeldt-Jacob disease and brain tumours can also cause dementia. Acquired brain injury, for example the result of stroke, arrhythmias, trauma, alcohol misuse or exposure to other environmental chemicals or pollutants may also contribute.

Genetic factors have been associated with fewer than 5% of all cases of dementia but in some families, mutations in genes for the amyloid precursor protein (APP), presenilins or Apolipoprotein E4 (ApoE4) may increase risk. The brain contains more lipid (fat) than any other organ in the human body. Although they are essential to both cell processes and the integrity of plasma membranes, oxidation products from lipids have the potential to cause injury, misfolding of cell proteins and induce apoptosis (programmed cell death) of neurons.

Neuronal and synaptic loss are thought to be the final common pathway mediating the effects of all of these factors and will be explained in article 2.

Signs and Symptoms of dementia

As with many other chronic diseases, there is no fixed staring point for the many forms of dementia which means that the initial clinical picture can be confusing. Different areas of the brain e.g., those responsible for language, social inhibition, visuo-spatial processing, working memory and executive functions do not change in a uniform way. Dementia does not progress in a linear manner, but can be accompanied by periods of stability followed by accelerated decline.

Triggers for suspecting dementia are subtle signs and symptoms that are noticed over a period of time. Decline in short-term memory may be the most apparent early symptom of some forms of dementia but the rate of decline partly depends on the type of dementia that is affecting the person. There are many forms of dementia (see articles 2 and 3 of the series) and the main symptom is impairment of higher cognitive skills – memory, thinking, decision-making, comprehension, learning and judgment.

It may become more difficult for people with dementia to carry out tasks that were previously easy, or the ability to name familiar objects and people becomes impaired. Strategies like making lists or leaving reminders as memory cues become less effective over time. Getting lost on familiar routes, confusing night-time with day-time and misplacing items may happen with increasing frequency as the disease progresses. Anyone can forget where we put our keys, wallets, handbags or mobile phones, but people with dementia may experience difficulties with keeping track of conversations, their finances or bills.

Family members or caregivers may notice changes in mood or behaviour e.g. the person may become more likely to blame other people for his or her mistakes. The person who is affected by dementia my become increasingly suspicious, depressed, agitated or irritable than is usual for her or him. Problems with language may mean that the person with dementia substitutes repeats or forgets familiar words which means that heir loved ones and carers can find that communication becomes increasingly difficult because it is harder to understand what they mean. Tasks required for self-care may become more difficult for people with dementia e.g. ability to prepare food, choose clothing or cope with changing circumstances (Alzheimer's Society UK. Jenkins et al, 2015).

There is no cure for dementia. Over time, the person who is affected will lose capacity for speech and comprehension and struggle with basic psychomotor skills e.g. ability to walk, to chew food and to swallow so they will need help with things like eating and using the toilet .

People with dementia are at particularly high risk of falls, delirium (see article 3 of this series) and/or dehydration. Forgetfulness, poor concentration and confusion may arise when someone with dementia is admitted to a hospital ward, leading to feelings of anxiety, confusion, insecurity, agitation or aggression.

Difficulty with everyday activities including hygiene and nutrition or inability to cope with the environment can make people with dementia feel fearful and insecure while tearfulness, anger, hallucinations and/or delusions can pose potential threats to the person's well-being. Emotional lability means that family carers may need to play a more prominent role in support and decision-making related to medical treatment and care.

Improving understanding of pathophysiological processes

Across the globe, the transition to an aging society has been taking place in a relatively short period of time. Since the prevalence of cognitive impairment and dementia increases dramatically in people aged 85 years old or more, with several important factors such as gender, educational attainment, lifestyle choices and financial hardship significantly modulating development and maintenance of cognitive ability and skills.

The bulk of care for people who have dementia is still provided by family members and carers, but the disease is expected to present many financial and healthcare challenges in the future. Discovering and validating accurate, sensitive biomarkers for dementia is an urgent priority (Ahmed et al, 2014), which new and emerging avenues of research into the principles that regulate homeostasis at the cellular and molecular level are addressing.

In the next article of this series, we highlight powerful new hypotheses that have the potential to guide future research into dementia care, facilitate management strategies and provide hope for all those affected by dementia.

Key points

1. The hallmark characteristics of normal ageing include low-grade inflammatory responses.
2. The combination of alterations in metabolic processes, increasing frailty and reduced tolerance to physiological stressors are sometimes called inflamm-aging
3. Better understanding of physiology of the ageing process is contributing to better understanding of alterations in brain structure and function that cause dementia.
4. Dementia is an age-dependent neurodegenerative disorder that impairs the ability of neuron networks to communicate with each other, in turn leading to cognitive impairment.
5. There is no cure for dementia but better understanding of signs, symptoms and causes can help nurses to provide better care and support and offer hope for new therapeutic targets.

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Table 1: changes to body systems with ageing.

Body system	Change to physiology with ageing	Impact for individual(s)
Respiratory system	Diminished vital capacity and increased physiological dead space.	Lower vital capacity Increased susceptibility to viral and bacteria infections, pneumonia, acute respiratory distress syndrome
Cardiovascular system	Arteriosclerosis (hardening of the arteries) Maximal heart rate and hence cardiac output diminishes Atheroma may form; 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.
Visual system	Reduced tear production Ciliary body stiffness Presbyopia and losses in motion perception Changes in colour perception	Blurring of text e.g. signs and menus; Reduced clarity of colours and impaired hazard perception; Alterations in gaze patterns which have effects on everyday activities and mobility
Brain	More forgetfulness and “senior moments” Reaction time gets slower	Need to drive more cautiously e.g. longer distance between self and car in front.
Hearing system	Difficulty following conversations in noisy environment(s) Loss of acuity especially with high pitched sounds (presbycusis) Improving vocabulary	Impaired ability to distinguish sounds when there is 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	Lesser ability to concentrate urine and to deal with fluid stress e.g. dehydration. Increased frequency of urination.	Waking at night to go to the toilet Feelings of urgency to urinate Stress incontinence

Integument	Skin may become thinner, lose elasticity and become wrinkled. Melanocytes lose ability to make melanin Changes to distribution of adipose tissue	Healing of wounds takes place more slowly
Musculo-skeletal	Muscle mass may reduce or lose strength and power. Increased bone resorption and loss of bone density	Reduced ability to carry out the 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 cycles in women Prostate may enlarge in men.
Liver	Some changes in enzyme systems	Prescription medication may need to be reviewed.