Geriatrics and Aging-Associated Diseases

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Chapter 1

Geriatrics

Elderly female in residential care home

Geriatrics is a sub-specialty of internal medicine that focuses on health care of elderly people. It aims to promote health by preventing and treating diseases and disabilities in older adults. There is no set age at which patients may be under the care of a **geriatrician**, or physician who specializes in the care of elderly people. Rather, this decision is determined by the individual patient's needs, and the availability of a specialist.

Geriatrics, the care of aged people, differs from gerontology, which is the study of the aging process itself. The term *geriatrics* comes from the Greek *geron* meaning "old man" and *iatros* meaning "healer". However, geriatrics is sometimes called **medical gerontology**.

Scope

Differences between adult and geriatric medicine

Geriatrics differs from standard adult medicine because it focuses on the unique needs of the elderly person. The aged body is different physiologically from the younger adult body, and during old age, the decline of various organ systems becomes manifest. Previous health issues and lifestyle choices produce a different constellation of diseases and symptoms in different people. The appearance of symptoms depends on the remaining healthy reserves in the organs. Smokers, for example, consume their respiratory system reserve early and rapidly.

Geriatricians distinguish between diseases and the effects of normal ageing. For example, renal impairment may be a part of ageing, but renal failure and urinary incontinence are not. Geriatricians aim to treat any diseases that are present and to decrease the effects of aging on the body.

Increased complexity

The decline in physiological reserve in organs makes the elderly develop some kinds of diseases and have more complications from mild problems (such as dehydration from a mild gastroenteritis). Multiple problems may compound: A mild fever in elderly persons may cause confusion, which may lead to a fall and to a fracture of the neck of the femur ("breaking her/his hip").

Elderly people require specific attention to medications. Elderly people particularly are subjected to polypharmacy (taking multiple medications). Some elderly people have multiple medical disorders; some have self-prescribed many herbal medications and over-the-counter drugs; some adult physicians prescribe medications to their specialty without reviewing other medications used by the elder patient. This polypharmacy may result in many drug interactions and may cause some adverse drug reactions. Drugs are excreted mostly by the kidneys or the liver, either of which may be impaired in the elderly, and as a result the medication might need adjustment to avoid overwhelming the kidneys or liver.

The presentation of disease in elderly persons may be vague and non-specific, or it may include delirium or falls. (Pneumonia, for example, may present with low-grade fever, dehydration, confusion or falls, rather than the high fever and cough seen in middle-aged adults.) Some elderly people may find it hard to describe their symptoms in words, especially if the disease is causing confusion, or if they have cognitive impairment. Delirium in the elderly may be caused by a minor problem such as constipation or by

something as serious and life-threatening as a heart attack. Many of these problems are treatable, if the root cause can be discovered.

Geriatric giants

The so-called **geriatric giants** are the major categories of impairment that appear in elderly people, especially as they begin to fail. These include immobility, instability, incontinence and impaired intellect/memory.

Impaired vision and hearing loss are common chronic problems among older people. Hearing problems can lead to social isolation, depression, and dependence as the person is no longer able to talk to other people, receive information over the telephone, or engage in simple transactions, such as talking to a person at a bank or store. Vision problems lead to falls from tripping over unseen objects, medicine being taken incorrectly because the written instructions could not be read, and finances being mismanaged.

Practical concerns

Functional abilities, independence and quality of life issues are of great concern to geriatricians and their patients. Elderly people generally want to live independently as long as possible, which requires them to be able to engage in self-care and other activities of daily living. A geriatrician may be able to provide information about elder care options, and refers people to home care services, skilled nursing facilities, assisted living facilities, and hospice as appropriate.

Frail elderly people may choose to decline some kinds of medical care, because the risk-benefit ratio is different. For example, frail elderly women routinely stop screening mammograms, because breast cancer is typically a slowly growing disease that would cause them no pain, impairment or loss of life before they would die of other causes. Frail people are also at significant risk of post-surgical complications and the need for extended care, and an accurate prediction—based on validated measures, rather than how old the patient's face looks—can help older patients make fully informed choices about their options. Assessment of older patients before elective surgeries can accurately predict the patients' recovery trajectories. One frailty scale uses five items: unintentional weight loss, muscle weakness, exhaustion, low physical activity, and slowed walking speed. A healthy person scores 0; a very frail person scores 5. Compared to non-frail elderly people, people with intermediate frailty scores (2 or 3) are twice as likely to have post-surgical complications, spend 50% more time in the hospital, and are three times as likely to be discharged to a skilled nursing facility instead of to their own homes. Frail elderly patients (score of 4 or 5) who were living at home before the surgery have even worse outcomes, with the risk of being discharged to a nursing home rising to twenty times the rate for non-frail elderly people.

Subspecialties and related services

Some diseases commonly seen in elderly are rare in adults, e.g., dementia, delirium, falls. As societies aged, many specialized geriatric- and geriatrics-related services emerged including:

Medical

- Geriatric psychiatry or **psychogeriatrics** (focus on dementia, delirium, depression and other psychiatric disorders).
- Cardiogeriatrics (focus on cardiac diseases of elderly)
- Geriatric nephrology (focus on kidney diseases of elderly)
- Geriatric dentistry (focus on dental disorders of elderly)
- Geriatric Rehabilitation (focus on physical therapy in elderly)
- Geriatric oncology (focus on tumors in elderly)
- Geriatric rheumatology (focus on joints and soft tissue disorders in elderly)
- Geriatric neurology (focus on neurologic disorders in elderly)
- Geriatric diagnostic imaging
- Geriatrics dermatology (focus on skin disorders in elderly)
- Geriatric subspeciality medical clinics (As Geriatric Anticoagulation Clinic **Geriatric Assessment Clinic**, **Falls and Balance Clinic**, **Continence Clinic**, **Palliative Care Clinic**, **Elderly Pain Clinic**, **Cognition and Memory Disorders Clinic**)
- Geriatric emergency medicine
- Geriatric Physical Examination of interest especially to Physicians & Physician Assistants.
- Geriatric public health or Preventive Geriatrics (focuses on geriatrics public health issues including disease prevention and health promotion in elderly)
- Geriatric pharmacotherapy

Surgical

- Orthogeriatrics (close cooperation with orthopedic surgery and a focus on osteoporosis and rehabilitation).
- Geriatric Cardiothoracic Surgery
- Geriatric urology
- Geriatric otolaryngology
- Geriatric General Surgery
- Geriatric trauma
- Geriatric gynecology
- Geriatric ophthalmology

Other geriatrics subspecialties

- Geriatric anesthesia (focuses on anesthesia & perioperative care of elderly)

- Geriatric intensive-care unit: (a special type of intensive care unit dedicated to critically-ill elderly)
- Geriatric nursing (focuses on nursing of elderly patients and the aged).
- Geriatric nutrition
- Geriatric Occupational Therapy (part of Geriatric Rehabilitation)
- Geriatric Pain Management
- Geriatric Physical Therapy
- Geriatric podiatry
- Geriatric psychology

History

The Canon of Medicine, written by Abu Ali Ibn Sina (Avicenna) in 1025, was the first book to offer instruction in the care of the aged, foreshadowing modern gerontology and geriatrics. In a chapter entitled "Regimen of Old Age", Avicenna was concerned with how "old folk need plenty of sleep" and how their bodies should be anointed with oil, and recommended exercises such as walking or horse-riding. Thesis III of the *Canon* discussed the diet suitable for old people, and dedicated several sections to elderly patients who become constipated.

The famous Arabic physician, Ibn Al-Jazzar Al-Qayrawani (Algizar, circa 898-980), also wrote a special book on the medicine and health of the elderly, entitled *Kitab Tibb al-Machayikh* or *Teb al-Mashaikh wa hefz sehatahom*. He also wrote a book on sleep disorders and another one on forgetfulness and how to strengthen memory, entitled *Kitab al-Nissian wa Toroq Taqwiati Adhakira*, and a treatise on causes of mortality entitled *Rissala Fi Asbab al-Wafah*. Another Arabic physician in the 9th century, Ishaq ibn Hunayn (died 910), the son of Hunayn Ibn Ishaq, wrote a *Treatise on Drugs for Forgetfulness* (*Risalah al-Shafiyah fi adwiyat al-nisyan*).

The first modern geriatric hospital was founded in Belgrade, Serbia in 1881 by doctor Laza Lazarević.

The term geriatrics was proposed in 1909 by Dr. Ignatz Leo Nascher, former Chief of Clinic in the Mount Sinai Hospital Outpatient Department (New York City) and a "Father" of geriatrics in the United States.

Modern geriatrics in the United Kingdom really began with the "Mother" of Geriatrics, Dr. Marjorie Warren. Warren emphasized that rehabilitation was essential to the care of older people. Using her experiences as a physician in a London Workhouse infirmary, she believed that merely keeping older people fed until they died was not enough; they needed diagnosis, treatment, care, and support. She found that patients, some of whom had previously been bedridden, were able to gain some degree of independence with the correct assessment and treatment.

The practice of geriatrics in the UK is also one with a rich multi-disciplinary history. It values all the professions, not just medicine, for their contributions in optimizing the well-being and independence of older people.

Another "hero" of British Geriatrics is Bernard Isaacs, who described the "giants" of geriatrics mentioned above: immobility and instability, incontinence, and impaired intellect. Isaacs asserted that, if examined closely enough, all common problems with older people relate back to one or more of these giants.

The care of older people in the UK has been advanced by the implementation of the National Service Frameworks for Older People, which outlines key areas for attention.

Geriatricians' training

In the United States, geriatricians are primary-care physicians who are board-certified in either family medicine or internal medicine and who have also acquired the additional training necessary to obtain the Certificate of Added Qualifications (CAQ) in geriatric medicine.

In the United Kingdom, most geriatricians are hospital physicians, whereas some focus on community geriatrics. While originally a distinct clinical specialty, it has been integrated as a specialisation of general medicine since the late 1970s. Most geriatricians are, therefore, accredited for both. In contrast to the United States, geriatric medicine is a major specialty in the United Kingdom; geriatricians are the single most numerous internal medicine specialists.

Minimum Geriatric Competencies

In July 2007, the Association of American Medical Colleges (AAMC) and the John A. Hartford Foundation hosted a National Consensus Conference on Competencies in Geriatric Education where a consensus was reached on minimum competencies (learning outcomes) that graduating medical student needed to assure competent care by new interns to older patients. Twenty-six (26) Minimum Geriatric Competencies in eight content domains were endorsed by the American Geriatrics Society (AGS), the American Medical Association (AMA), and the Association of Directors of Geriatric Academic Programs (ADGAP). The domains are: cognitive and behavioral disorders; medication management; self-care capacity; falls, balance, gait disorders; atypical presentation of disease; palliative care; hospital care for elders, and health care planning and promotion. Each content domain specifies three or more observable, measurable competencies.

Research

Hospital Elder Life Program

Perhaps the most pressing issue facing geriatrics is the treatment and prevention of delirium. This is a condition in which hospitalized elderly patients become confused and

disoriented when confronted with the uncertainty and confusion of a hospital stay. The health of the patient will decline as a result of delirium and can increase the length of hospitalization and lead to other health complications. The treatment of delirium involves keeping the patient mentally stimulated and oriented to reality, as well as providing specialized care in order to ensure that her/his needs are being met.

The Hospital Elder Life Program (HELP) is an innovative model of hospital care created by Sharon Inouye, MD, MPH and her colleagues at the Yale University School of Medicine. It is designed to prevent delirium and functional decline among elderly individuals in the hospital inpatient setting. HELP uses a core team of interdisciplinary staff and targeted intervention protocols to improve patients' outcomes and to provide cost-effective care. Unique to the program is the use of specially trained volunteers who carry out the majority of the non-clinical interventions.

In up to 40% of the cases, incident delirium can be prevented. To that end, HELP promotes interventions designed to maintain cognitive and physical functioning of older adults throughout the hospitalization, maximize patients' independence at discharge, assist with the transition from hospital to home and prevent unplanned hospital readmissions. Customized interventions include daily visitors; therapeutic activities to provide mental stimulation; daily exercise and walking assistance; sleep enhancement; nutritional support and hearing and vision protocols.

HELP has been replicated in over 63 hospitals across the world. Although the majority of the sites are based in the United States located in 25 different states, there is a growing international presence. International sites include: Australia, Canada, the Netherlands, Taiwan and the United Kingdom. HELP is protected by copyright held by Sharon Inouye MD, MPH. The Dissemination Team including Dr. Inouye are located at Hebrew SeniorLife at the Institute for Aging Research in Boston, MA.

Pharmacology

Pharmacological constitution and regimen for older people is an important topic, one that is related to changing and differing physiology and psychology.

Changes in physiology with aging may alter the absorption, the effectiveness and the side effect profile of many drugs. These changes may occur in oral protective reflexes (dryness of the mouth caused by diminished salivary glands), in the gastrointestinal system (such as with delayed emptying of solids and liquids possibly restricting speed of absorption), and in the distribution of drugs with changes in body fat and muscle and drug elimination.

Psychological considerations include the fact that elderly persons (in particular, those experiencing substantial memory loss or other types of cognitive impairment) are unlikely to be able to adequately monitor and adhere to their own scheduled pharmacological administration. One study (Hutchinson et al., 2006) found that 25% of participants studied admitted to skipping doses or cutting them in half. Self-reported

noncompliance with adherence to a medication schedule was reported by a striking one-third of the participants. Further development of methods that might possibly help monitor and regulate dosage administration and scheduling is an area that deserves attention.

Another important area is the potential for improper administration and use of potentially inappropriate medications, and the possibility of errors that could result in dangerous drug interactions. Polypharmacy is often a predictive factor (Cannon et al., 2006). Research done on home/community health care found that "nearly 1 of 3 medical regimens contain a potential medication error" (Choi et al., 2006).

Ethical and medico-legal issues

Elderly persons sometimes cannot make decisions for themselves. They may have previously prepared a power of attorney and advance directives to provide guidance if they are unable to understand what is happening to them, whether this is due to long-term dementia or to a short-term, correctable problem, such as delirium from a fever.

Geriatricians must respect the patients' privacy while seeing that they receive appropriate and necessary services. More than most specialties, they must consider whether the patient has the legal responsibility and competence to understand the facts and make decisions. They must support informed consent and resist the temptation manipulate the patient by withholding information, such as the dismal prognosis for a condition or the likelihood of recovering from surgery at home.

Elder abuse is the physical, financial, emotional, sexual, or other type of abuse of an older dependent abuse. Adequate training, services, and support can reduce the likelihood of elder abuse, and proper attention can often identify it. For elderly people who are unable to care for themselves, geriatricians may recommend legal guardianship or conservatorship to care for the person or the estate.

- End of life issues & Do Not Resuscitate (DNR) orders.
- Euthanasia.

Chapter 2

Geriatric Psychiatry, Geriatric Rehabilitation and Geriatric Oncology

Geriatric psychiatry

Geriatric psychiatry, also known as **geropsychiatry**, **psychogeriatrics** or **psychiatry of old age**, is a subspecialty of psychiatry dealing with the study, prevention, and treatment of mental disorders in humans with old age. After a 4 year residency in psychiatry, a psychiatrist can complete a one year fellowship in geriatric psychiatry. As the population ages, particularly in developing countries this field is becoming more needed. The diagnosis, treatment and management of dementia is one area of this field.

The International Psychogeriatric Association is an international community of scientists and healthcare geriatric professionals working for mental health in aging. *Psychogeriatrics* is the official journal of the International Psychogeriatric Association. Many fellowships in geriatric psychaitry exist. *The American Journal of Geriatric Psychiatry* is the official journal of the American Association for Geriatric Psychiatry (AAGP). The American Board of Psychiatry and Neurology issues a certification in geriatric psychaitry.

Geriatric rehabilitation

Geriatric rehabilitation or **Geriatric Physical Therapy** is the branch of medicine that studies rehabilitation and physical therapy issues in elderly.

Origins

Geriatric rehabilitation covers three areas – normal aging due to disuse and deconditioning, cardiovascular problems like vascular disease and stroke, and skeletal problems including osteoporosis and osteoarthritis conditions such as knee and hip replacements. Physical medicine Physicians use rehabilitation to work toward the goal of

returning the patient to a pre-injury quality of life and may use physical, occupational, and speech therapies.

As we age, we face many physical and emotional changes that can affect our level of function and well-being. Rehabilitation maintains functional independence in the elderly. Rehabilitation of geriatric patients is imperative for the patients' well-being and for society, so that we can thrive socially and economically. Essential to geriatric rehabilitation is communication, specifically improving any sensory impairment, including those related to vision and hearing. The prevention of falls and osteoporosis can improve the patient's health and longevity. Addressing malnutrition can promote healing and vitalize the patient to participate in a formal rehabilitation program. Depression is common in the older population if a functional loss of mobility and an inability to perform activities of daily living (ADLs) predominates. Cognitive impairment, such as delirium and dementia, can affect the patient's rehabilitation goals and outcomes. Finally, a driver's evaluation for an appropriate elderly candidate is an underutilized part of rehabilitation that has a considerable impact on society.

Geriatric Rehabilitation also have a role in intermediate care, where patients are referred by a hospital or family doctor, when there is a requirement to provide hospital based short term intensive physical therapy aimed at the recovery of musculoskeletal function, particularly recovery from joint, tendon, or ligament repair and, or, physical medicine and rehabilitation care when elderly patients get out of sync with their medication resulting in a deterioration of their personal health which reduces their ability to live independently.

Geriatric oncology

Geriatric oncology is the branch of medicine that studies benign and malignant tumors in elderly.

Origin

While anyone can develop cancer, the risk of getting the disease increases with age. Certain cancers, in particular, are linked to aging, such as breast, colorectal, prostate, pancreatic, lung, bladder and stomach cancers.

For many reasons, older adults (generally age 70 and higher) with cancer have different needs than younger adults with the disease. Treatment for older adults needs to consider many issues. For example, older adults:

- May be less able to tolerate certain cancer treatments.
- Have a decreased reserve (the capacity to respond to disease and treatment).
- May have other medical problems in addition to cancer.

- May have functional problems, such as the ability to do basic activities (dressing, bathing, eating) or more advanced activities (such as using transportation, going shopping or handling finances).
- May not always have access to transportation, social support or financial resources.

Cancer and other tumors are common among elderly. Elderly have many peculiarities as regard dosing, complications and tolerance of treatment options of cancer. Clinical trials that guidelines for treatment of cancer were based on were mainly applied for young age and rarely in elders, so a lot of research in this area is needed.

Just as a child would see a pediatrician for medical care, an older patient should go to a geriatrician. And an older patient with cancer will benefit from the combined expertise of the Geriatric Oncology Program's physician experts. Older patients have unique needs because of their often complex medical histories, numerous drugs they are taking, their social situations, possible problems with cognitive dysfunction related to age, and general diminution of organ function that occurs naturally in the older population. An expert in geriatrics, working in conjunction with a medical oncologist sensitive to these problems, can decide on the appropriate treatment for any elderly cancer patient.

One of a handful of people around the world who created the field of geriatric oncology during the 1980's was Lodovico Balducci. He was co-editor of the first major medial textbook on the subject, *Geriatric Oncology*, published in 1982, and has been honored with the B.J. Kennedy Award for Scientific Excellence in Geriatric Oncology from the American Society of Clinical Oncology.

Training & education programs

These Programs aims at providing optimal cancer care for senior adults aged 70 and older, and helps patients overcome the special challenges this population faces in battling the disease. Separate fellowships for training in geriatric oncology subspeciality is now established. Books and curriculum are available for training.

All new patients meet with a medical oncologist, a geriatrician, a psychosocial professional, and a nutritionist, all of whom work together to provide a comprehensive assessment of the patient's fitness to withstand the therapy necessary to treat his or her cancer. Patients spend approximately three hours with the Geriatric Oncology Program team. Following the initial assessment, the team meets to evaluate the patient's fitness for therapy. The team's decisions and recommendations are then presented to the patient and his or her family as well as to the patient's primary physician when appropriate. After these discussions, treatment for the patient's cancer is initiated.

Organisation & societies

Geriatric Oncology Consortium is a non-profit organization dedicated to addressing the age based disparities in research, education and treatment in the older adult cancer

population. It is leader in developing and conducting research in older adults and providing older adult cancer education to medical professionals, patients, caregivers and the general public.

The American Society of Clinical Oncology (ASCO) has started a geriatric oncology subspeciality. A webpage didicated to article and resources about geriatric oncology is available.

World oncology network has established a directory for geriatric oncology to promote this subspeciality.

International Society of Geriatric Oncology purpose is to advance the art, science and practice of oncology in elderly patients and disseminate knowledge in order to maintain a high common standard of healthcare in elderly cancer patients. The special aims of the Association are to improve research in the field of geriatric oncology. promote education in geriatric oncology, in order to ensure a high standard of qualification for health professionals, maintain liaison with other medical and health professionals associations, cancer leagues, universities and, where appropriate, the pharmaceutical industry.

Chapter 3

Geriatric Rheumatology and Geriatric Neurology

Geriatric rheumatology

Geriatric rheumatology is the branch of medicine that studies rheumatologic disorders in elderly (joints, muscles & other structures around the joints). Sometimes it is called **Gerontorheumatology**.

Origin

The geriatric rheumatology clinic provides evaluation and management services to patients with various musculoskeletal and soft tissue disorders. Evaluation of the elderly patient is often complex due to the many comorbid conditions encountered in this population often compounded by cognitive disorders, functional decline, polypharmacy and limited social supports.

Training & education programs

During training doctors observe and participate in the diagnosis and management of various rheumatologic conditions which contribute to elderly functional decline including connective tissue disorders, crystal diseases, osteoarthritis and other soft tissue disorders. They also learn to differentiate these various clinical conditions, gain an understanding of the various treatment options available, as well as learn how to work with a multidisciplinary team of health professionals.

Some Departments of Medicine offer a three-year combined Geriatric-Rheumatology Fellowship, which is composed of a year of clinical geriatrics and training in clinical epidemiology and health services research, a year of clinical rheumatology and an opportunity to explore scholarly geriatric-rheumatology research projects in the third year.

Many books and resources are available dedicated to geriatric rheumatology

Many geriatricians and rheumatologists are dedicated to this new subspeciality. Some internal medicine departments have established a separate geriatric rheumatology clinics]

Organisation & societies

International Society of Geriatric Rheumatology was established to help advancing research in the area of geriatric rheumatology and improve the quality of management of rheumatologic disorders in elderly.

Geriatric neurology

Geriatric neurology is the branch of medicine that studies neurologic disorders in elderly.

Origin

In 1991 Advanced Fellowship Program in Geriatric Neurology was started by the Department of Veterans Affairs. Many veterans suffered from neurodegenerative changes such as Alzheimer's disease, Lewy Body dementia, Parkinson's disease, vascular dementia, and other age related central nervous system changes. The implications for family caregivers and the healthcare system were enormous. So the Geriatric Neurology Fellowship Program developed a cadre of physicians for academic leadership in this complex, interdisciplinary field.

The subspecialty of Geriatric neurology is defined by its expertise in the diagnosis, treatment, and care of neurological conditions that affect elderly and by its unique body of knowledge regarding the aging nervous system, its vulnerability to specific neurological disorders, and its influence on the prevalence and expression of neurological disease. Neurologists are called with increasing frequency to provide care for older adults. As the number of elderly in the population increases, there will be a concomitant increase in the prevalence of acute and chronic neurological disorders associated with advancing age. Through training fellowships, the neurological community will endeavor to master, codify and transfer the knowledge and skills to effectively care for the elderly with neurological disorders. Behavioral Neurology Clinic at the Perlman Ambulatory Care Center.

The Geriatric Neurology Section of the American Academy of Neurology increases awareness of, and fosters interest and expertise in, issues of geriatric neurology in the areas of patient care, research, education, and public policy, and enhances the role of neurologists in geriatric training programs.

Geriatric neurology clinics are starting to appear under different names like Geriatric neurology and dementia clinic, Also Geriatric neurology and psychaitry clinc at Rochester , Behavioral Neurology Clerckship at Mayo Clinic, Cognitive and Behavioral Neurology Clinic at Emory University, Behavioral Neurology Clinic at Oregon health & science university.

Training & education programs

Fellowships for training on geriatric neurology were established.

The Veterans Affair Geriatric Neurology Fellowship Program provides two years of post-residency research, education, and clinical learning opportunities to eligible physician neurologists. Graduates are expected to be role models in leading, developing, conducting, and evaluating innovative research, education, and clinical care in the field of geriatric neurology.

The American Academy of Neurology (AAN) Foundation and the Alzheimer's Association established a two-year Clinical Research Training Fellowship in Alzheimer's disease research. The fellowship is supported by the AAN Foundation and the Alzheimer's Association.

The American Academy of Neurology offers a prize for Research in Pick's, Alzheimer's, and Related Diseases. The American Academy of Neurology offers an award for research in Geriatric Neurology.

Clinical courses and books on geriatric neurology are available.

A journal dedicated to geriatric neurology & psychiatry was issued.

Organisation & societies

The Geriatric Neurology Section of the American Academy of Neurology was organized in 1989 to increase awareness of and foster interest and expertise in issues of geriatric neurology in the areas of patient care, research, education, and public policy, and to enhance the role of neurologists in geriatric training programs.

The United Council for Neurologic Subspecialties (UCNS) has approved geriatric neurology as its seventh subspecialty in May 2007.

Chapter 4

Geriatric Trauma and Geriatric Anesthesia

Geriatric trauma

Geriatric trauma

A woman who suffered blast trauma after a rocket exploded nearby

Geriatric trauma refers to a traumatic injury that occurs to an elderly person. The three prevailing causes of traumatic death in the elderly are falls (which account for 40% of traumatic death in this age group), traffic collisions and burns.

Biomechanics of injury

A progressive decline in central nervous system function leads to a loss of proprioception, balance and overall motor coordination, as well as a reduction in eye–hand coordination, reaction time and an unsteady gait. These degenerative changes are often accompanied by osteoarthritis (degenerative joint disease), which leads to a reduction in the range of motion of the head, neck and extremities. Furthermore, elderly people frequently take multiple medications for control of various diseases and conditions. The side effects of some of these medications may either predispose to injury, or may cause a minor trauma to result in a much more severe condition. For example, a person taking warfarin (Coumadin) and/or clopidogrel (Plavix) may experience a life-threatening intracranial hemorrhage after sustaining a relatively minor closed head injury, as a result of the defect in the hemostatic mechanism caused by such medications. The combined effects of these changes greatly predisposes elderly people to traumatic injury. Both the incidence of falls and the severity of associated complications increase with advancing age.

Physiologic differences in the elderly

Virtually all organ systems experience a progressive decline in function as a result of the aging process. One example is a decline in circulatory system function caused in part by thickening of the cardiac muscle. This can lead to congestive heart failure or pulmonary edema.

Atrophy of the brain begins to accelerate at around seventy years of age, which leads to a significant reduction in brain mass. Since the skull does not decrease in size with the brain, there is significant space between the two when this occurs which puts the elderly at a higher risk of a subdural hematoma after sustaining a closed head injury. The reduction of brain size can lead to issues with eyesight, cognition and hearing.

Epidemiology

Elderly people are the most rapidly growing demographic in developed nations. Although they sustain traumatic injury less commonly than children and young adults, the mortality rate for trauma in the elderly is higher than in younger people.

Geriatric anesthesia

Geriatric anesthesia (or **geriatric anaesthesia**) is the branch of medicine that studies anesthesia approach in elderly.

Origin

The perioperative care of elderly patients differs from that of younger patients for a number of reasons. Some of these can be attributed to the changes that occur in the process of aging, but many are also caused by diseases that accompany seniority. The distinction between so-called normal aging and pathological changes is critical to the care of elderly people. Anesthesia and surgery has become more common as the population survives longer. Preoperative management of the geriatric patients requires knowledges about changes associated with aging physiology and its relation to surgery and anesthesia. Only experienced anesthetists can evaluate patients effectively and plan for their perioperative care to minimize complications. Comprehensive preoperative evaluation of an elderly individual's health status can be a very challenging aspect, especially for the young anesthetist. Sir William Osler's aphorism "Listen to the patient, he'll give you the diagnosis" is as true in the elderly patient as it is in the young. But in the elderly several factors makes taking history more difficult and time-consuming.

Many differences can be seen in geriatric anesthesia. First, the preoperative evaluation of the geriatric patient is typically more complex than that of the younger patient because of the heterogeneity of this patient group and the greater number and complexity of comorbid conditions that usually accumulate with age. Perioperative functional status can be difficult to predict because many elderly patients have reduced preoperative function as a consequence of deconditioning, age-related disease, or cognitive impairment. This makes it difficult to adequately assess the patient’s ability to respond to the specific stresses associated with surgery. A common example is trying to determine cardiopulmonary reserve in a patient very limited by osteoarthritis. Physiologic heterogeneity and decreased functional reserve are also manifested perioperatively. Normal aging results in changes in cardiac, respiratory, and renal physiology, and the response of the elderly patient to surgical stress is often unpredictable. The pharmacokinetics and pharmacodynamics of elderly and younger patients also differ; moreover, the elderly patient’s use of multiple medications may alter homeostatic mechanisms.

Training and education programs

A Syllabus on Geriatric Anesthesiology is available from the American Society of Anesthesiologists

Online resources are also available as the Geriatric Anesthesiology Curriculum.

Graduate medical education in the United States is regulated by the Accreditation Council for Graduate Medical Education (ACGME). Each accredited specialty appoints members to an ACGME residency review committee (RRC) that is responsible for establishing and monitoring education requirements. The Anesthesiology RRC includes a requirement for instruction in geriatric care. Each program must provide "appropriate didactic instruction and sufficient clinical experience in managing problems of the geriatric population." The published joint ASA/American Board of Anesthesiology content outline for in-training examinations also includes a section on "Geriatric Anesthesia/Aging: The Pharmacological Implications, MAC Changes and the Physiological Implications on Major Organ Systems." These mandates make geriatric education a requirement for any program in anesthesiology. Surprisingly this is not the rule in all graduate medical education programs. A recent survey by the Association of Directors of Geriatric Academic Programs2 reviewed ACGME policies required by 100 nonpediatric RRCs. They found that only 27 of these programs had specific requirements for geriatric training; anesthesiology and pain management were two of these.

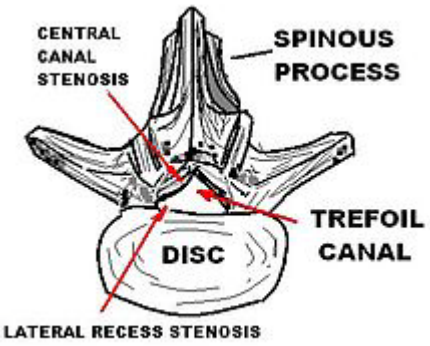
Organization and societies

The Society for the Advancement of Geriatric Anesthesia (SAGA) is dedicated to improving the care of the older patient coming to surgery. It offers educational programs at its annual meeting as well as at meetings of other anesthesia societies. It also offer educational support for anesthesia training programs. The Age Anaesthesia Society is the UK equivalent of SAGA.

Chapter 5

Lumbar Spinal Stenosis

Lumbar spinal stenosis



Lumbar vertebra showing central stenosis and lateral recess stenosis.

ICD-10	M48.0
ICD-9	723.0-724.0
DiseasesDB	31116
MeSH	D013130

Lumbar spinal stenosis (**LSS**) is a medical condition in which the spinal canal narrows and compresses the spinal cord and nerves at the level of the lumbar vertebra. This is usually due to the common occurrence of spinal degeneration that occurs with aging. It can also sometimes be caused by spinal disc herniation, osteoporosis or a tumor. In the cervical (neck) and lumbar (low back) region it can be a congenital condition to varying degrees.

Spinal stenosis may affect the cervical or thoracic region in which case it is known as cervical spinal stenosis or thoracic spinal stenosis. In some cases, it may be present in all three places in the same patient. Lumbar spinal stenosis results in low back pain as well as pain or abnormal sensations in the legs, thighs, feet or buttocks, or loss of bladder and bowel control.

Signs and symptoms

Understanding the meaning of signs and symptoms for the clinical syndrome of lumbar stenosis requires an understanding of what the syndrome is, and the prevalence of the condition. A recent review on lumbar stenosis in the Journal of the American Medical Association's "Rational Clinical Examination Series" emphasized that the syndrome can be considered when lower extremity pain occurs in combination with back pain. This syndrome occurs in 12% of older community dwelling men and up to 21% of those in retirement communities

The leg symptoms in lumbar spinal stenosis (LSS) are similar to those found with vascular claudication giving rise to the term pseudoclaudication. These symptoms include pain, weakness, and tingling of the legs, and "radiation down the posterior part of the leg to the feet". Additional symptoms in the legs may be fatigue, heaviness, weakness, a sensation of tingling, pricking, or numbness and leg cramps, as well as bladder symptoms. Symptoms are most commonly bilateral and symmetrical, but they may be unilateral; leg pain is usually more troubling than back pain.

Pseudoclaudication, now referred to as neurogenic claudication, typically worsen with standing or walking and improve with sitting. The occurrence is often related to posture and lumbar extension. Lying on the side is often more comfortable than lying flat, since it permits greater lumbar flexion. Vascular claudication "can mimic spinal stenosis" and some individuals experience unilateral or bilateral symptoms radiating down the legs "rather than true claudication". "In contrast to those with vascular claudication, sitting but not standing will relieve symptoms; walking uphill will be better tolerated than downhill walking; and exercise on a stationary bicycle in a seated flexed position will be better tolerated than walking in the erect position."

The first symptoms of stenosis are bouts of low back or neck pain. After a few months or years, this may progress to claudication. The pain may be radicular, following the classic neurologic pathways. This occurs as the spinal nerves or spinal cord become increasingly trapped in a smaller space within the canal. It can be difficult to determine whether pain in the elderly is caused by lack of blood supply or stenosis; testing can usually differentiate between them but patients can have both vascular disease in the legs and spinal stenosis.

Among people with lower extremity pain in combination with back pain, lumbar stenosis as the cause is 2 times more likely in those older than 70 years of age while those younger than 60 years it is 0.40 as likely. The character of the pain is also useful. When the discomfort does not occur while seated, the likelihood of LSS increases considerably around 7.4 times. Other features increasing the likelihood of lumbar stenosis are improvement in symptoms on bending forward 6.4 times, pain that occurs in both buttocks or legs 6.3 times, and the presence of neurogenic claudication 3.7 times. In contradistinction, the absence of neurogenic claudication makes lumbar stenosis much less likely as the explanation for the pain 0.23 times. A clinical scoring system that includes combinations of findings has been reported.

Causes

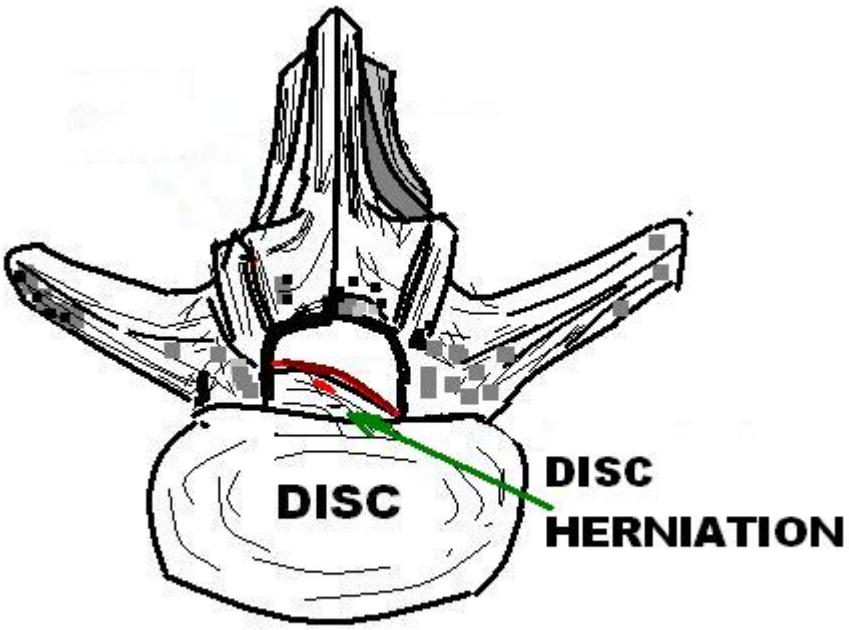
Spinal stenosis may be rarely congenital or acquired (degenerative), overlapping changes normally seen in the aging spine, "resulting from degenerative changes or as consequences of local infection, trauma or surgery". "Degeneration is believed to begin in the intervertebral disk where biochemical changes such as cell death and loss of proteoglycan and water content lead to progressive disk bulging and collapse. This process leads to an increased stress transfer to the posterior facet joints, which accelerates cartilaginous degeneration, hypertrophy, and osteophyte formation; this is associated with thickening and buckling of the ligamentum flavum. The combination of the ventral disk bulging and osteophyte formation and the dorsal facet and ligamentum flavum hyptertrophy combine to circumferentially narrow the spinal canal and the space available for the neural elements. This compression of the nerve roots of the cauda equina leads to the characteristic clinical signs and symptoms of lumbar spinal stenosis."

Degenerative spondylolisthesis

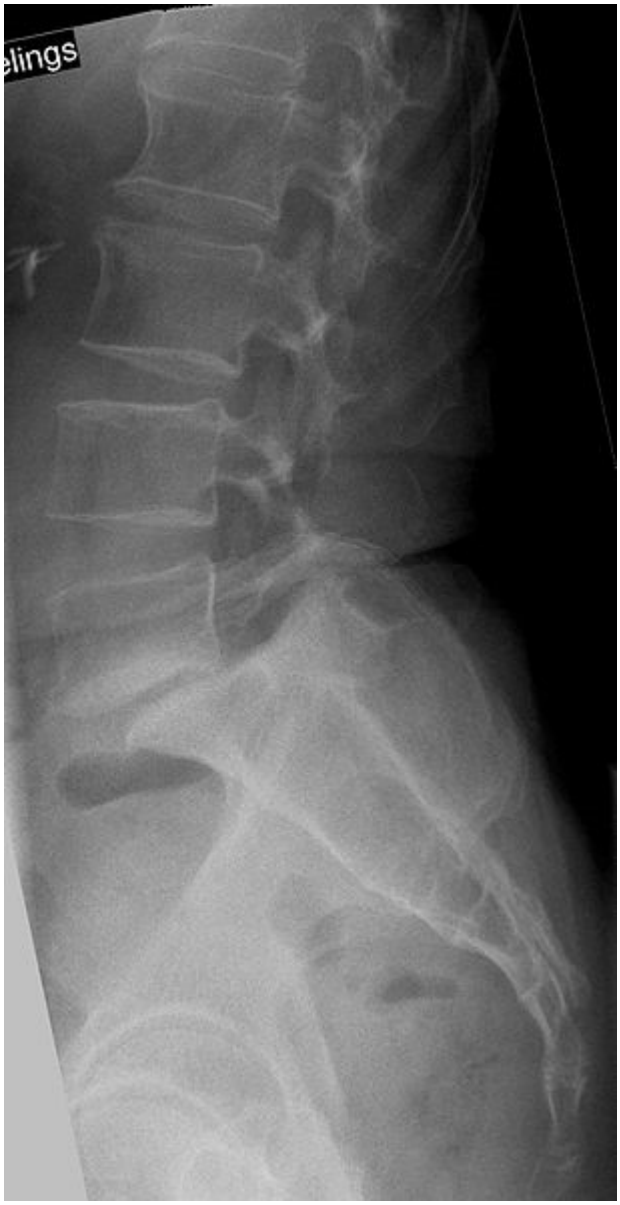
Forward displacement of a proximal vertebra in relation to its adjacent vertebra in association with an intact neural arch, and in the presence of degenerative changes is known as degenerative spondylolisthesis. Degenerative spondylolisthesis narrows the spinal canal and symptoms of spinal stenosis are common. Of these, neural claudication is most common. Any forward slipping of one vertebra on another can cause spinal stenosis by narrowing the canal. If this forward slipping narrows the canal sufficiently, and impinges on the contents of the spinal column, it is spinal stenosis by definition. If there are associated symptoms of narrowing, the diagnosis of spinal stenosis is confirmed. With increasing age, the occurrence of degenerative spondylolisthesis becomes more common. The most common spondylolisthesis occurs with slipping of L4 on L5. Frymoyer showed that spondylolisthesis with canal stenosis is more common in diabetic women who have undergone oophorectomy (removal of ovaries). The cause of symptoms in the legs can be difficult to determine. A peripheral neuropathy secondary to diabetes can have the same symptoms as spinal stenosis.

Ankylosing spondylitis

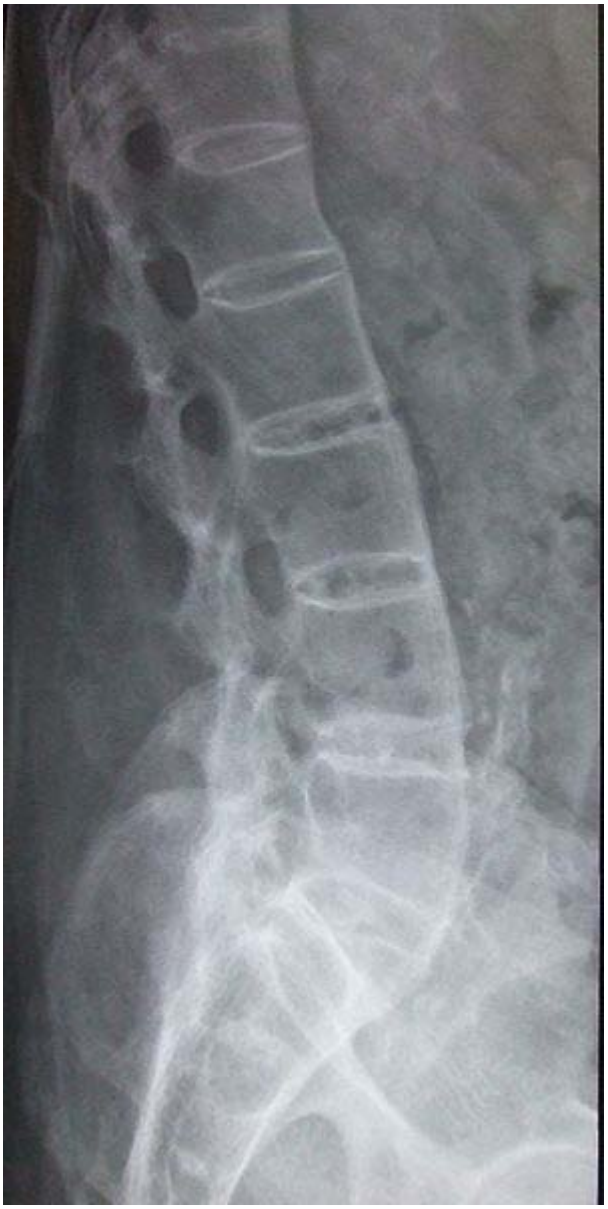
In a retrospective analysis of vertebral fractures in patients with ankylosing spondylitis, it was shown that 74% experienced some form of trauma. Of these, greater than 60% revealed vertebral fractures with some neurologic symptoms. Of these, a significant number went on to develop spinal stenosis. Paravertebral hematomas (blood clots) were accompanied by a higher incidence of other complications. Females were at greater risk of death from the complications.



Drawing of a lumbar disc herniation which can cause a localized stenosis. Thoracic discs though rare are similar.

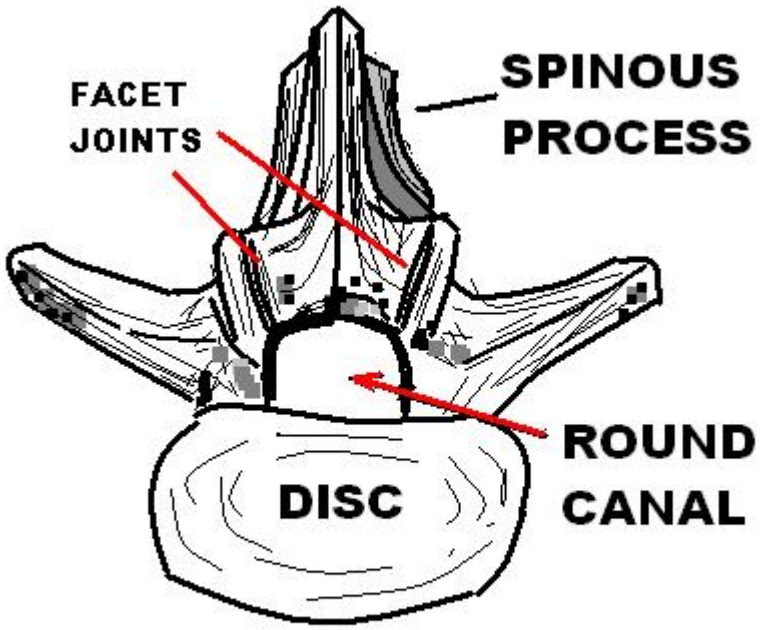


L5 S1 Spondylolisthesis Grade II with forward slipping of L5 on S1 <50%



Lumbar spine showing advanced ankylosing spondylitis which can lead to spinal stenosis

Diagnosis



Normal lumbar vertebra showing large, round spinal canal

The diagnosis is based on clinical findings; "neurologic findings on physical examination are unusual". Some patients can have a narrowed canal without symptoms, and do not require therapy. Stenosis can occur as either central stenosis (the narrowing of the entire canal) or foraminal stenosis (the narrowing of the foramen through which the nerve root exits the spinal canal). Severe narrowing of the lateral portion of the canal is called “lateral recess stenosis". The ligamentum flavum (yellow ligament), an important structural component intimately adjacent to the posterior portion of the dural sac (nerve sac) can become thickened and cause stenosis. The articular facets, also in the posterior portion of the bony spine can become thickened and enlarged causing stenosis. These changes are often called “trophic changes” or “facet trophism” in radiology reports. As the canal becomes smaller, resembling a triangular shape, it is called a "trefoil" canal.

The normal lumbar central canal has a midsagittal diameter (front to back) greater than 13 mm., with an area of 1.45 square cm. Relative stenosis is said to exist when the anterior-posterior canal diameter between 10 and 13 mm. Absolute stenosis of the lumbar canal exists anatomically when the anterior-posterior measurement is 10 mm. or less.

Plain x-rays of the lumbar or cervical spine may or may not show spinal stenosis. The definitive diagnosis is established by either CT (computerized tomography) or MRI scanning. Identifying the presence of a narrowed canal makes the diagnosis of spinal stenosis.

Bicycle test of van Gelderen

In 1977, Dyck and Doyle reported on the bicycle test of van Gelderen. The bicycle test is a simple procedure in which the patient is asked to pedal on a stationary bicycle. If the symptoms are caused by peripheral vascular disease, the patient will experience claudication (def: limping; experienced as a sensation of not getting enough blood to the legs); if the symptoms are caused by lumbar stenosis, symptoms will be relieved when the patient is leaning forward while bicycling. Despite the fact that diagnostic progress has been made with newer technical advances, the bicycle test remains an inexpensive and easy way to distinguish between claudication caused by vascular disease and spinal stenosis. Dyck and Doyle wrote in their 1977 article:

The authors describe a simple clinical adjunct to the routine neurological examination of patients with intermittent cauda equina compression syndrome. The "bicycle test" helps exclude intermittent claudication due to vascular insufficiency and frequently confirms the relationship of posture to radicular pain.

Magnetic resonance imaging

MRI is the preferred method of diagnosing and evaluating spinal stenosis of all areas of the spine, including cervical, thoracic and lumbar. MRI is useful to diagnose cervical spondylotic myelopathy (degenerative arthritis of the cervical spine with associated damage to the spinal cord). The finding of degeneration of the cervical spinal cord on MRI can be ominous; the condition is called myelomalacia or cord degeneration. It is seen as an increased signal on the MRI. In myelopathy (pathology of the spinal cord) from degenerative changes, the findings are usually permanent and decompressive laminectomy will not reverse the pathology. Surgery can stop the progression of the condition. In cases where the MRI changes are due to Vitamin B-12 deficiency, a brighter prospect for recovery can be expected.

The detection of spinal stenosis in the cervical, thoracic or lumbar spine confirms only the anatomic presence of a stenotic condition. This may or may not correlate with the diagnosis of spinal stenosis which is based on clinical findings of radiculopathy, neurogenic claudication, weakness, bowel and bladder dysfunction, spasticity, motor weakness, hyperreflexia and muscular atrophy. These findings, taken from the history and physical examination of the patient (along with the anatomic demonstration of stenosis with an MRI or CT scan), establish the diagnosis.

Management

Nonoperative therapies and laminectomy are the standard treatment for LSS.

A trial of conservative treatment including "activity modification, medications, physical therapy, home exercise therapy, and spinal injections" is recommended. Individuals are generally advised to avoid stressing the lower back, particularly with the spine extended. A physical therapy program to provide core strengthening and aerobic conditioning may

be recommended and is considered useful, although "high-level evidence is lacking for the direct benefit of physical therapy or exercise".

Medication

The evidence for the use of medical interventions for lumbar spinal stenosis is poor. Injectable but not nasal calcitonin may be useful for short term pain relief. Epidural blocks may also transiently decrease pain, but there is no evidence of long-term effect. Adding steroids to these injections does not improve the result; the use of epidural steroid injections (ESIs) is controversial and evidence of their efficacy is contradictory.

Non-steroidal anti-inflammatory drugs (NSAIDs), muscle relaxants and opioid analgesics are often used to treat low back pain, but evidence of their efficacy in treating LSS is lacking and they should have a limited role in treating LSS.

Surgery

Little "evidence is available to recommend specific nonsurgical treatments"; laminectomy is the most effective of the surgical treatments. In those who worsen despite conservative treatments surgery leads to improvement in 60–70% of cases. Another procedure using an interspinous distraction device known as X-STOP was less effective and more expensive when more than one spinal level is repaired. Both surgical procedures are more expensive than medical management.

Prognosis

Most people with mild to moderate symptoms do not get worse. While many improve in the short term after surgery this improvement decreases somewhat with time. A number of factors present before surgery are able to predict the outcome after surgery, with people with depression, cardiovascular disease and scoliosis doing in general worse while those with more severe stenosis before hand and better overall health doing better.

The natural evolution of disc disease and degeneration leads to stiffening of the intervertebral joint. This leads to osteophyte formation—a bony overgrowth about the joint. This process is called spondylosis, and is part of the normal aging of the spine. This has been seen in studies of normal and diseased spines. Degenerative changes begin to occur without symptoms as early as age 25–30 years. It is not uncommon for people to experience at least one severe case of low back pain by the age of 35 years. This can be expected to improve and become less prevalent as the individual develops osteophyte formation around the discs.

In the US workers' compensation system, once the threshold of two major spinal surgeries is reached, the vast majority of workers will never return to any form of gainful employment. Beyond two spinal surgeries, any more are likely to make the patient worse, not better. Very few studies in the worldwide surgical literature actually document return to work after spinal surgery, or lack thereof.

History

A description of LSS was published by Sachs and Frankel in 1900, but the first clinical description of LSS is usually attributed to the Dutch neurosurgeon Henk Verbiest, whose report appeared in 1954.

Spinal stenosis began to be recognized as an impairing condition in the 1960s and 1970s. Porter and colleagues discovered that individuals who experience back pain and other symptoms are likely to have smaller spinal canals than those who are asymptomatic. Rothman reported that a normal sized lumbar canal is rarely encountered in persons with either disc disease or those requiring a de-roofing (laminectomy) procedure.

During the 1970s and 1980s, multiple case reports showed successful surgical treatment rates based on subjective assessment by surgeons, "before studies with more standardized assessment techniques began to emerge in the 1990s". Studies "rarely reported on the clinical course of patients with stenosis who were treated with observation, and many surgeons held to the belief that the natural history was poor". In 1992, Johnsson, Rosén and Udén described the natural history of LSS, with different conclusions about prognosis and treatment: "70% of patients reported no significant change in symptoms, 15% showed significant improvement, whereas 15% showed some deterioration. The investigators concluded that observation is a reasonable treatment option for lumbar stenosis and that significant neurologic deterioration is rare."

As of 2010, there are "no widely accepted diagnostic or classification criteria for the diagnosis of LSS and, as a consequence, studies use widely differing eligibility criteria that limit the generalisability of reported findings" and "few studies have examined how its prevalence or incidence is changing".

Chapter 6

Falls in Older Adults

Every year, many older people suffer from falls. These **falls in older adults** are a significant cause of morbidity and mortality, and can have a serious effect on the person who falls. Falls can be caused by many things, and often the cause is multi-factorial, and require a multi-disciplinary approach to treat any injuries sustained during the fall, and to prevent any future falls.

Definition

The medical definition of a fall is: *An event which results in a person coming to rest inadvertently at a lower level, other than as a consequence of a violent stroke, loss of consciousness, or a sudden onset of paralysis*.

A person can also come to rest inadvertently at a lower level due to a faint or syncope, a stroke, transient ischaemic attack or some other cause of sudden paralysis.

Falls are one of the giants of geriatric medicine.

Incidence

Every year, the following proportion of people suffer from a fall:

>65 years	**>75 years**	**Institutional Care**	**Recurrent Fallers**	**Healthy Elderly**
28-35%	32-45%	>50%	60-70%	15%

Falls are the commonest presenting complaint to A&E in patients over the age of 65.

Causes of falls

Falls are often caused by a number of factors. The faller may live with many risk factors for falling and only have problems when another factor appears. As such, management is often tailored to treating the factor that caused the fall, rather than all of the risk factors a patient has for falling. Risk factors grouped into intrinsic and extrinsic factors.

Intrinsic Factors

- Balance and Gait

  As a result of stroke disease, Parkinsonism, arthritic changes, neuropathy, neuromuscular disease or vestibular disease.

- Medications
  - Polypharmacy is common in older people
  - Sedatives significantly increase the risk of falling
  - Cardiovascular medications can contribute towards falls
- Visual imparement
  - Glaucoma, macular degeneration and retinopathy increase the risk of falling
  - Bifocals can increase the risk of falling as the lower portion of corrective lenses are optimized for distances approximately 18 inches, thus precluding clear vision of one's feet/floor, approximately 4.5 to 5.5 feet below one's eyes.
- Cognitive problems
  - Dementia increases the likelihood of falls
- Cardiovascular causes
  - Orthostatic hypotension
  - Postprandial hypotension
  - Carotid sinus syndrome
  - Neurocardiogenic syncope - the commonest cause of syncope in A&E patients
  - Cardiac arrhythmias
  - Structural heart disease, such as valvular heart disease
- Urinary incontinence

Extrinsic Factors

- Poor lighting
- Stairs
- Rugs/floor surfaces
- Clothing/footwear
- Lack of equipment/aids

Consequences of falls

- **Trauma**
  - Soft tissue injuries. Bilateral orbital haematomas (two black eyes) suggests that the faller was probably not conscious as they fell, as they did not manage to protect their face as they hit the ground.
  - Fractures and dislocations. 5% of fallers end up having a fracture as a result of their fall, and 1% fracture their neck of femur.

- **"Long Lies"**
  - Pneumonia
  - Pressure sores
  - Dehydration
  - Hypothermia
- **Psychological**
  - A fear of falling

Presentation and assessment

When assessing a patient who has fallen, it is important to try to get an eye-witness account of the incident. As the faller may have had some loss of consciousness, they may not give an accurate description of the fall. However, in practice, these eye-witness accounts are often unavailable. It is also important to remember than 30% of cognitively intact older people are unable to remember a documented fall three months later. Important features to ask about include:

- The number of falls
- Eye witness account
- Associated features
- Risk factors for falling
- What drugs the faller is taking
- How much alcohol the faller drinks

Investigations

It is good practice to exclude anaemia, renal failure, and electrolyte imbalance, and to perform an ECG and a chest x-ray. Other tests should be tailored to the cause of the fall.

Interventions

A large body of evidence shows that a multi-disciplinary approach to assessment and treatment results in the best outcome.

Possible interventions include:

- Hip protectors
- Regular exercise
- Treatment for osteoporosis
- Review - monitoring of medications and ongoing medical problems
- Tackling environmental issues

Chapter 7

Geriatric Depression

Geriatric depression is the prolonged occurrence of depression in elderly-aged people. A meta-analysis done by the University of Liverpool found a 3.86% prevalence rate of depressed elderly in The People's Republic of China, compared to a 12% prevalence in Western Europe. Factors for depression in **Chinese elderly** are affected by Chinese culture, social expectations, and living conditions. There is dispute to whether the low-level reported rates are due to differences in culture and traditions.

Symptoms and Diagnosis

The most common used method of measuring depressive symptoms for many studies on Chinese elderly is the Geriatric Depression Scale (GDS) by Yesavage & Brink. The Chinese version of the GDS was translated by Chu Lee Hing of the Chinese University of Hong Kong. A study in Hong Kong found its "[brief] and simple response format [to be] particularly favourable for use among the elderly" and was found to be "satisfactory" for screening depression in elderly Chinese.

The use of the GDS analyzes simple behavior symptoms of crying, loss of appetite, sleep, weight, memory, concentration, energy, and enjoyment, whereas analysis of pure feelings may have different cultural connotations.

The General Health Questionnare (GHQ) was also deemed reliable in another study but not as sensitive as the GDS. This study also sampled Hong Kong elderly. Another assessment that has been used among Chinese old-aged is the Geriatric Mental State Schedule (GMS). It is an interview for assessing psychopathology in 65+ aged patients which classifies by symptom type and any changes over time within that type. Further detailed diagnosis can made with the Automated Geriatric Examination for Computer Assisted Taxonomy (AGECAT) by using the scores from the GMS.

Cultural Differences

The differences between Chinese and Western definitions of depression have long been studied. "In traditional Chinese medicine, mental illness is often attributed to maladies of the heart" writes Greg Miller, a mental health journalist for the *Science Magazine.* The *Harvard Review of Psychiatry* found that Traditional Chinese medicine has no conception of emotional disorders; rather, it has a concept of physical imbalance. It was

reported that patients with depression described their being as "emotional…disturbance combined with references to the body, especially the heart…these references were not just metaphors; some patients literally felt their depression as discomfort inside or over the heart" in a Harvard study on the ethnographic differences in depressive experiences. Phrases like *xinhuang* (heart panic), *xinfan* (heart vexed), and *xintong* (heart pain) are used by depressed patients to describe literal discomfort in the body.

Maoist doctrine teaches that unhappiness in a people is a result of poor politics, and this led to an outlawing of clinical psychology in the mainland during 1950-1980—an attempt to prevent the diagnosis of unhappiness. The following excerpt illustrates how far politics affected emotional health in a labor camp during the Maoist era:

I never met a man in the camps at this time who talked about his parents, wife, lover or children in warm, earnest, loving terms – not even the shortest sentence . . . A mention of one's home, that is one's real home, was bound to be related to receiving a package of things to eat in the mail . . . Other than that, home had no place in a man's emotions, because he had lost his emotions.

Patients in the Harvard study rarely described their feelings as sadness, as it is generally viewed as shameful, a sign of weakness in character. The culturally stoic Chinese, as a result, are more willing to accept physical ailments, such as heart pain or sleeplessness, than emotional problems.

Neurasthenia, "lack of nerve strength," became the preferred diagnosis for mental problems once it was introduced to China in the early 1900s. Translation of neurasthenia to Chinese, *shenjing shuairuo,* describes a weakness in the flow of vital energy (qi) throughout the body. This gave an appeal of physical disease, with physical symptoms of fatigue, nonspecific aches and pains on the body, dizziness, upset stomach, appetite loss, poor memory, and insomnia. It was not until the pragmatic era of *Deng Xiaoping* that politics allowed "the demarcation between public and private space to reemerge," thus relaxing the social acceptability to admit to feelings and leading to the study and treatment of emotional disorder. By the 1980s the *shenjing shuairuo* labeling was removed and the Western label of "depression" used.

In Regards to the Elderly

Chinese culture holds great importance on caring for the elderly. Physical, financial, and emotional care are traditionally provided by the children as a way to show honor, believed to come from Confucianism. At the same time, elders' expectations lie heavily on contributing to their community with their advice and service than receiving it themselves—also called *renqing.* For elderly who adhere to tradition, old-aged life's purpose and one's self-worth is measured by the positive impact one has on their family.

Regarding Chinese filial culture and the financial care of elderly, of a sample of Mainland Chinese-Canadian immigrants, 23.2% were assessed to have depressive

symptoms, and among that depressed group, 17.3% were considered to have an unstable financial status —study done for the *Chinese Medical Journal.*

Overall it can be said that the number of women sampled in many of the studies, compared to men, was significantly greater. This may be caused by the socialization in Chinese societies—that men are to suppress emotions and that any need for help with emotional matters is viewed as a sign of weakness. A study funded by the National Health Research Institute of Taiwan found a high prevalence of depression in Taiwanese elderly, contradictory to many studies held previously in Asia and "comparable to rates reported in some studies of UK samples." Furthermore, the study found lowly educated widows in urban communities were higher risk for depressive disorders.

Possible Factors

Physical

The same study by Chong et al. also observed that the main stress factor for the sampled Taiwanese elderly was health problems. A separate study found that Chinese elderly who participated in tai chi were found to reduce depressive symptoms in comparison with elderly with no treatment at all, as found in a study for the *International Journal for Geriatric Psychiatry* Physical abilities and health problems affect a patient's perceived quality of life which affects level of depression, according to a study done by the Chinese University of Hong Kong. Confirmed by data from a study published in *Stroke,* post-stroke depression is common. Stroke decreased the activities of daily living and had a strong effect on the severity of depression in rural Chinese elderly. Another study in rural China found that "undetected" hypertension had a significant relation to depression, suggesting that "hypertension screening among older populations may be warranted for preventing depression and cardiovascular disease."

It has also been learned that "current smokers and former smokers are more likely to have depressive symptoms than never smokers," as found in a study on Chinese elderly in Hong Kong.

Living Conditions

According to research, the living set-up of most Chinese elderly in 1987 was 65% living with two (and some-times three) generations of family and 18% with one generation, while 11% of couples lived together without their children and only 4% lived alone (although they had children). 2% were alone (i.e. single). It was observed that loneliness increased prevalence of depression in old-aged women more than old-aged men in Hong Kong. The study concluded that because of the known trend of older men (who could not find a wife in Hong Kong) marrying women across the border in the mainland, lifestyles adapted to the separation families.

Economic

In 1999, 48 % of Chinese elderly relied on their spouses and 40% on their children, indicates Li Hong and Martin Tracy's survey. "Worry about not having enough money to cover medical care is a new source of stress among urban residents" claims Rongjun Sun of Cleveland State University. The results of Sun's research show that "adequacy of medical care coverage has a substantial impact" on the elders' well-being and that "of all family support measures, emotional support from children is found to have significant buffering effects on the elders' depression."

Different from income, financial strain—the ability to pay for daily expenses and the worry felt when "the need for unexpected expenditures arise" —affects depression. This study on Hong Kong elderly further found that women with physical problems were more likely to worsen in depression from financial strain. Furthermore, it was concluded that a better social support did not necessarily lessen the impact of financial strain on depression—which contradicts Sun's findings (previously mentioned) of "buffering effects". A 1998 study of Wuhan elders found that "anticipated support" was the source of reduced impact of financial strain on depression. Anticipated support brought about feelings of security whereas "received support" usually aroused a sense of guilt in the elderly.

Question of Depression

Some sources argue that reported low-prevalence of depression is faulty because of the differences in culture while others argue that the difference in cultures is the cause of low-prevalence. Gordon Parker et al. suggests most Chinese deny depression, that "depression appears to be less evident in the Chinese and more likely to be expressed somatically, as a result of a rich set of interconnecting influences," whereas Mjelde-Mossey et al. suggests that holding onto "tradition was found to be negatively associated with depression and thus a protective factor" against depression. Three reasons for the lower prevalence of depression give by R. Chen, et al. based on a study on rural Chinese elders:

First, there were higher levels of social support and positive life values among older people in China. Second, working and living environments in rural areas were more relaxed (eg, less stressful work and more physical farming activity). Third, the causes of diseases within populations may differ from the factors that explain differences between populations.

Contributors to low-prevalence rates, from Parker's research :

- low level of reporting depression
- "idiomatic reporting" of neurasthenia
- "lack of criterion-based classification" which leads to problems in detection of depression

- coping mechanisms of stoicism, cultural support, and lower level of urbanization

Frequency distribution of the items in the Chinese tradition scale used in the Mjolde-Mossey study :

Chinese Tradition Scale Item	Agree (%)
Count on children when you are ill	79.4
Seek help from children on financial difficulties	74.9
Children should take responsibility for financial needs of elderly	71.6
Source of income from children	62.9
Help people around with household tasks	56.4
Receive financial assistance from children when in need	51.5
Comfort immediate family members when they feel down	50.1
Other people talk to you for important decisions	41.9
Comfort extended relatives when they feel down	22.2

Prognosis

It is predicted that by the middle of the 22nd century, 25% of the world's elderly population will consist of **Chinese elders**. With such a statistic, understanding how to prevent depression in Chinese elderly will serve to improve some of the problems that may come in caring for the well-being of the elderly and their families.

Sun's research found that elderly that lived near their children were associated with better well-being than those that lived in the same household as or lived far from their children. Because of the complex nature of human relationships and the variables that effect measuring methods, it is important to note that family support is not a consistent positive effect on elderly well-being, "nevertheless, [Sun's] study confirms that family ties play a critical role in buffering the impact of undesirable social event."

In regards to China's future family situation, the one-child policy presents an issue for the single child sons/daughters that face two pairs of parents to support.

The previously mentioned study by Mjelde-Mossey et al. concluded that because adherence to traditions is known to reduce depression an elder can achieve a level of mental stability by applying the purpose of their traditional beliefs to whatever non-traditional situations and relationships come into their life. With this kind of background, Chinese elderly can change the way they are impacted by changes in society—independent children, less contact between family members, and westernized traditions that support youth-self-centeredness.

Chapter 8

Geriatric Intensive-Care Unit

Geriatric intensive care unit is a special type of intensive care unit dedicated to management of critically ill elderly.

Geriatric intensive care unit's goal is to restore physiologic stability, prevent complications, maintain comfort and safety, and preserve pre-illness functional ability and quality of life (QOL) in older adults admitted to critical-care units.

Origin

Geriatric intensive care units appeared in response to the world's population aging. Managing Geriatrics diseases is not like managing adults or pediatrics diseases, especially if they are critically ill. Geriatric medicine was not included in the curricula of undergraduate or advanced medical training until recently, so not all critical care physicians were oriented by the pecularties of geriatric patients. Despite the fact that geriatric patients constitute many of the critically ill patients, the training of critical care team still lacks the training on the geriatrics giants.

Critically ill older adult: a person, age 65 or older, who is currently experiencing or at risk for some form of physiologic instability or alteration warranting urgent or emergent, advanced nursing/medical interventions and monitoring.

- More than half (55.8%) of all ICU days are incurred by patients older than 65.
- Older adults are living longer, are more racially and ethnically diverse, often have multiple chronic conditions, and more than one-quarter report difficulty performing one or more activities of daily living (ADLs). These factors may affect both the course and outcome of critical illness.
- Once hospitalized for a life-threatening illness, older adults often:

1. Experience high ICU, hospital, and long-term crude mortality rates.
2. Are at risk for deterioration in functional ability and post-discharge institutional care.

- Older age is also a factor that may lead to:

1. Physician bias in refusing ICU admission.

2. The decision to withhold mechanical ventilation, surgery, or dialysis.
3. An increased likelihood of an established resuscitation directive.

- Most critically ill older adults:

1. Demonstrate resiliency.
2. Report being satisfied with their QOL post-discharge.
3. Would reaccept ICU care and mechanical ventilation if needed.

- Chronologic age alone is not an acceptable or accurate predictor of poor outcomes after critical illness.
- Factors that may influence an older adult's ability to survive a catastrophic illness include:

1. Severity of illness
2. Nature and extent of co-morbidities
3. Diagnosis, reason for/duration of mechanical ventilation
4. Complications length of ICU/hospital stay.

Goal

Goal is to restore physiologic stability, prevent complications, maintain comfort and safety, and preserve pre-illness functional ability and quality of life (QOL) in older adults admitted to critical-care units.

Distribution in the world

Geriatric intensive care units are starting to be disseminated and are currently present in Japan, USA, China, Egypt, India & Europe (France, Italy, Poland, Germany).

Practice issues

Critical care practice by necessity is focused on the physiological parameters of the patients being served. Thus, the most important effort revolves around maintaining physiological function and restoring homeostasis for the person who is critically ill. However, when the urgent episode subsides, inappropriate practice guidelines and clinical approaches are often used in the care of older adults. Older individuals have less physiological reserve than younger ones and, therefore, are more likely to have dire consequences following critical care events such as cardiac or respiratory arrest. Further, there are associated geriatric syndromes, medication issues and problems that can be prevented if they are anticipated. Sleep disorders are prevalent in the elderly. During a critical care episode, sleeping and waking cycles are disturbed. Because of the noise in an ICU, less sleep and more noise may trigger delirium. Improving critical care practice for the elderly requires attention to sleep deficits, which means appropriate rest and recovery time.

Altered Eating and Feeding Patterns are more common in geriatric intensive care units. Tubes and other devices, which can impede the ability to obtain adequate nutrition, are common in an intensive care unit. While total parenteral nutrition lines can be inserted to provide calories, the pleasure of eating is lost, as is the sensory stimulation (i.e., smell, taste, texture) of the food, which might increase appetite. Careful attention must be paid to weight loss in the elderly during the critical care episode. Because albumin levels may already be potentially compromised, the older individual will be at risk for pressure ulcers if their nutrition falls to critically low levels. Other reasons for impaired nutrition include mouth sores; dry, cracked mouths; or a lack of dentures. These issues may be overlooked in busy units.

Foley catheters are regularly inserted in patients in the intensive care unit to monitor fluid balance, this should be changed. urinary catheters are known to cause urinary tract infections, which are potentially lethal to the elderly. Thus, when possible, catheters should be avoided in the ICU. In addition, the use of incontinence undergarments should be avoided, given the propensity for skin irritation and breakdown.

The ICU environment has been linked to delirium in the elderly. Disorientation to time or place because of overstimulation, pain and metabolic imbalances frequently results in cognitive changes. Optimally, critical care nurses must obtain a baseline mental status on the older patient upon admission and follow the changes through the use of a standardized assessment instrument such as a Mini-Mental State Examination. Early detection and intervention can reduce the use of either physical or chemical restraints.

Elderly admitted to intensive care units need special management as regard pharmacotherapy. They can suffer from special cardiovascular diseases, severe infections as MRSA of systemic fungal infections. And may need special posoperative analgesia. Also elderly need assessment by special instruments to predict the prognosis of ICU patients older than 75 years.

Ethical issues

Geriatrics critical care dictate many ethical issues which have been put into the focus of some researches & discussions. Also visiting hours in the geriatric ICU need special organisation different from other ICUs.

Not only do critical care units utilize up to a third of hospital expenditures and about 1% of GNP, the critically ill elderly consume a disproportionate amount of ICU resources. Outcome prediction models for very elderly critically ill patients have been proposed with age as one of numerous model variables; but such models have not been widely validated. Despite the burgeoning emphasis on evidence-based population approach to health care, there is insufficient research to guide the critical care clinician. There remains a modicum of subjectivity in crucial decisions that affect the elderly patient receiving intensive care.

Older age is also one of the factors that lead to a physician bias in refusing ICU admission. Many Critical care physicians generally consider their older patients' quality of life to be worse than do the patients, although other studies that have assessed the quality of live show no age-related differences among ICU survivors. Furthermore, physicians' estimations of patient quality of life significantly influence physicians' attitudes to futility of care issues, in contrast to patients' perceptions.

Threshold for life-sustaining treatment in the elderly will continue to be different among the ICUs. Clinical decisions will be subjected to many ethical, legal, and socioeconomic pressures. Personal and religious beliefs will inevitably influence societal expectations and clinician practices. Severity of illness has the biggest influence on outcome in a critical illness. Age alone is not a predictor of short-term or long-term outcome in the older patient who is critically ill. Critical illness in the elderly remains a fertile area for future research. Also some people tend to put a stigma on the geriatric intensive-care patient in community and in games.

Some studies suggest that patients who are perceived not to benefit from critical care are more often refused intensive care unit admission; refusal is associated with an increased risk of hospital death. During times of decreased critical bed availability, several factors, including age, illness severity, and medical diagnosis, are used to triage patients, although their relative importance is uncertain.

Some studies suggest the solution of subintensive care units. Which are now present in many places.

Training & education programs

Geriatric intensive care unit physicians are trained in geriatric medicine & critical care medicine. Some Universities & medical schools offer training sessions on Geritric critical care medicine. Some books focusing on older patients in the emergency department and critical care unit are available. And other online resources

Geriatric intensive care unit nurses receive special training in critical care of elderly in their basic training, advanced and clinical training. Some Nursing school faculties are establishing research in Geriatric critical care nursing. And a Geriatric Critical Care Nursing Research (GCCNR) Group was established, the purpose of this group is to serve as a forum to share, query, and exchange ideas and strategies related to the research involving and benefiting older ICU patients.

Chapter 9

Dementia

Dementia	
ICD-10	F00.-F07.
ICD-9	290-294
DiseasesDB	29283
MedlinePlus	000739
MeSH	D003704

Dementia (taken from Latin, originally meaning "madness", from *de-* "without" + *ment*, the root of *mens* "mind") is a serious loss of cognitive ability in a previously unimpaired person, beyond what might be expected from normal aging. It may be static, the result of a unique global brain injury, or progressive, resulting in long-term decline due to damage or disease in the body. Although dementia is far more common in the geriatric population, it may occur in any stage of adulthood.

This age cutoff is defining, as similar sets of symptoms due to organic brain syndrome or dysfunction, are given different names in populations younger than adult. Up to the end of the 19th century, dementia was a much broader clinical concept. Well into the second half of the 20th century, dementia of the elderly was called **senile dementia** or **senility** and viewed as a normal aspect of growing old rather than as being caused by any specific diseases, while Alzheimer's disease was seen as a rare disease of middle age, until the neurologist Robert Katzmann signaled a link between "senile dementia" and Alzheimer's.

Dementia is a non-specific illness syndrome (set of signs and symptoms) in which affected areas of cognition may be memory, attention, language, and problem solving. It is normally required to be present for at least 6 months to be diagnosed; cognitive dysfunction that has been seen only over shorter times, in particular less than weeks, must be termed delirium. In all types of general cognitive dysfunction, higher mental functions are affected first in the process.

Especially in the later stages of the condition, affected persons may be disoriented in time (not knowing what day of the week, day of the month, or even what year it is), in place (not knowing where they are), and in person (not knowing who they are or others around

them). Dementia, though often treatable to some degree, is usually due to causes that are progressive and incurable.

Symptoms of dementia can be classified as either reversible or irreversible, depending upon the etiology of the disease. Less than 10% of cases of dementia are due to causes that may presently be reversed with treatment. Causes include many different specific disease processes, in the same way that symptoms of organ dysfunction such as shortness of breath, jaundice, or pain are attributable to many etiologies.

Without careful assessment of history, the short-term syndrome of delirium (often lasting days to weeks) can easily be confused with dementia, because they have all symptoms in common, save duration. Some mental illnesses, including depression and psychosis, may also produce symptoms that must be differentiated from both delirium and dementia.

Chronic use of substances such as alcohol can also predispose the patient to cognitive changes suggestive of dementia, although moderate intake may have a protective effect.

Signs and symptoms

Comorbidities

Dementia is not merely a problem of memory. It reduces the ability to learn, reason, retain or recall past experience and there is also loss of patterns of thoughts, feelings and activities (Gelder et al 2005). Additional mental and behavioral problems often affect people who have dementia, and may influence quality of life, caregivers, and the need for institutionalization. As dementia worsens individuals may neglect themselves and may become disinhibited, the individual may become incontinent as their condition worsens. (Gelder et al 2005).

Depression affects 20–30% of people who have dementia, and about 20% have anxiety. Psychosis (often delusions of persecution) and agitation/aggression also often accompany dementia. Each of these needs to be assessed and treated independent of the underlying dementia.

Risk to self and others

The Canadian Medical Association Journal has reported that driving with dementia could lead to severe injury or even death to self and others. Doctors should advise appropriate testing on when to quit driving.

In the United States, Florida's Baker Act allows law enforcement and the judiciary to force mental evaluation for those suspected of suffering from dementia or other mental incapacities.

In the United Kingdom, as with all mental disorders, where a sufferer could potentially be a danger to themselves or others, they can be detained under the Mental Health Act 1983

for the purposes of assessment, care and treatment. This is a last resort, and usually avoided if the patient has family or friends who can ensure care.

The United Kingdom DVLA (Driving & Vehicle Licensing Agency) states that dementia sufferers who specifically suffer with poor short term memory, disorientation, lack of insight or judgment are almost certainly not fit to drive—and in these instances, the DVLA must be informed so said license can be revoked. They do however acknowledge low-severity cases and early sufferers, and those drivers may be permitted to drive pending medical report.

Causes

Fixed cognitive impairment

Various types of brain injury, occurring as a single event, may cause irreversible but fixed cognitive impairment. Traumatic brain injury may cause generalized damage to the white matter of the brain (diffuse axonal injury), or more localized damage (as also may neurosurgery). A temporary reduction in the brain's supply of blood or oxygen may lead to hypoxic-ischemic injury. Strokes (ischemic stroke, or intracerebral, subarachnoid, subdural or extradural hemorrhage) or infections (meningitis and/or encephalitis) affecting the brain, prolonged epileptic seizures and acute hydrocephalus may also have long-term effects on cognition. Excessive alcohol use may cause alcohol dementia, Wernicke's encephalopathy and/or Korsakoff's psychosis, and certain other recreational drugs may cause substance-induced persisting dementia; once overuse ceases, the cognitive impairment is persistent but not progressive.

Slowly progressive dementia

Dementia which begins gradually and worsens progressively over several years is usually caused by neurodegenerative disease; that is, by conditions affecting only or primarily the neurons of the brain and causing gradual but irreversible loss of function of these cells. Less commonly, a non-degenerative condition may have secondary effects on brain cells, which may or may not be reversible if the condition is treated.

The causes of dementia depend on the age at which symptoms begin. In the elderly population (usually defined in this context as over 65 years of age), a large majority of cases of dementia are caused by Alzheimer's disease, vascular dementia or both. Dementia with Lewy bodies is another fairly common cause, which again may occur alongside either or both of the other causes. Hypothyroidism sometimes causes slowly progressive cognitive impairment as the main symptom, and this may be fully reversible with treatment. Normal pressure hydrocephalus, though relatively rare, is important to recognize since treatment may prevent progression and improve other symptoms of the condition. However, significant cognitive improvement is unusual.

Dementia is much less common under 65 years of age. Alzheimer's disease is still the most frequent cause, but inherited forms of the disease account for a higher proportion of

cases in this age group. Frontotemporal lobar degeneration and Huntington's disease account for most of the remaining cases. Vascular dementia also occurs, but this in turn may be due to underlying conditions (including antiphospholipid syndrome, CADASIL, MELAS, homocystinuria, moyamoya and Binswanger's disease). People who receive frequent head trauma, such as boxers or some martial artists, are at risk of dementia pugilistica.

In young adults (up to 40 years of age) who were previously of normal intelligence, it is very rare to develop dementia without other features of neurological disease, or without features of disease elsewhere in the body. Most cases of progressive cognitive disturbance in this age group are caused by psychiatric illness, alcohol or other drugs, or metabolic disturbance. However, certain genetic disorders can cause true neurodegenerative dementia at this age. These include familial Alzheimer's disease, SCA17 (dominant inheritance); adrenoleukodystrophy (X-linked); Gaucher's disease type 3, metachromatic leukodystrophy, Niemann-Pick disease type C, pantothenate kinase-associated neurodegeneration, Tay-Sachs disease and Wilson's disease (all recessive). Wilson's disease is particularly important since cognition can improve with treatment.

At all ages, a substantial proportion of patients who complain of memory difficulty or other cognitive symptoms are suffering from depression rather than a neurodegenerative disease. Vitamin deficiencies and chronic infections may also occur at any age; they usually cause other symptoms before dementia occurs, but occasionally mimic degenerative dementia. These include deficiencies of vitamin B_{12}, folate or niacin, and infective causes including cryptococcal meningitis, HIV, Lyme disease, progressive multifocal leukoencephalopathy, subacute sclerosing panencephalitis, syphilis and Whipple's disease.

Rapidly progressive dementia

Creutzfeldt-Jakob disease typically causes a dementia which worsens over weeks to months, being caused by prions. The common causes of slowly progressive dementia also sometimes present with rapid progression: Alzheimer's disease, dementia with Lewy bodies, frontotemporal lobar degeneration (including corticobasal degeneration and progressive supranuclear palsy).

On the other hand, encephalopathy or delirium may develop relatively slowly and resemble dementia. Possible causes include brain infection (viral encephalitis, subacute sclerosing panencephalitis, Whipple's disease) or inflammation (limbic encephalitis, Hashimoto's encephalopathy, cerebral vasculitis); tumors such as lymphoma or glioma; drug toxicity (e.g. anticonvulsant drugs); metabolic causes such as liver failure or kidney failure; and chronic subdural hematoma.

Dementia as a feature of other conditions

There are many other medical and neurological conditions in which dementia only occurs late in the illness, or as a minor feature. For example, a proportion of patients with

Parkinson's disease develop dementia, though widely varying figures are quoted for this proportion. When dementia occurs in Parkinson's disease, the underlying cause may be dementia with Lewy bodies or Alzheimer's disease, or both. Cognitive impairment also occurs in the Parkinson-plus syndromes of progressive supranuclear palsy and corticobasal degeneration (and the same underlying pathology may cause the clinical syndromes of frontotemporal lobar degeneration). Chronic inflammatory conditions of the brain may affect cognition in the long term, including Behçet's disease, multiple sclerosis, sarcoidosis, Sjögren's syndrome and systemic lupus erythematosus. Although the acute porphyrias may cause episodes of confusion and psychiatric disturbance, dementia is a rare feature of these rare diseases.

Aside from those mentioned above, inherited conditions which may cause dementia alongside other features include:

- Alexander disease
- Canavan disease
- Cerebrotendinous xanthomatosis
- DRPLA
- Fragile X-associated tremor/ataxia syndrome
- Glutaric aciduria type 1
- Krabbe's disease
- Maple syrup urine disease
- Niemann Pick disease type C
- Kufs' disease
- Neuroacanthocytosis
- Organic acidemias
- Pelizaeus-Merzbacher disease
- Urea cycle disorders
- Sanfilippo syndrome type B
- Spinocerebellar ataxia type 2
- Huntington’s Disease
- Multiple sclerosis
- Multi-infarct Dementia
- AIDS Dementia complex

Diagnosis

Proper differential diagnosis between the types of dementia (cortical and subcortical) will require, at the least, referral to a specialist, e.g., a geriatric internist, geriatric psychiatrist, neurologist, neuropsychologist or geropsychologist. Duration of symptoms must evident for at least six months for a diagnosis of dementia or organic brain syndrome to be made (ICD-10).

Cognitive testing

Sensitivity and specificity of common tests for dementia

Test	Sensitivity	Specificity	Reference
MMSE	71%-92%	56%-96%	
3MS	83%-93.5%	85%-90%	
AMTS	73%-100%	71%-100%	

There exist some brief tests (5–15 minutes) that have reasonable reliability and can be used in the office or other setting to screen cognitive status. Examples of such tests include the abbreviated mental test score (AMTS), the mini mental state examination (MMSE), Modified Mini-Mental State Examination (3MS), the Cognitive Abilities Screening Instrument (CASI), and the clock drawing test. Scores must be interpreted in the context of the person's educational and other background, and the particular circumstances; for example, a person highly depressed or in great pain will not be expected to do well on many tests of mental ability.

While many tests have been studied, and some may emerge as better alternatives to the MMSE, presently the MMSE is the best studied and most commonly used.

Another approach to screening for dementia is to ask an informant (relative or other supporter) to fill out a questionnaire about the person's everyday cognitive functioning. Informant questionnaires provide complementary information to brief cognitive tests. Probably the best known questionnaire of this sort is the Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE). On the other hand the General Practitioner Assessment Of Cognition combines both, a patient assessment and an informant interview. It was specifically designed for the use in the primary care setting and is also available as a web-based test.

Further evaluation includes retesting at another date, and administration of other tests of mental function.

Laboratory tests

Routine blood tests are also usually performed to rule out treatable causes. These tests include vitamin B_{12}, folic acid, thyroid-stimulating hormone (TSH), C-reactive protein, full blood count, electrolytes, calcium, renal function, and liver enzymes. Abnormalities may suggest vitamin deficiency, infection or other problems that commonly cause confusion or disorientation in the elderly. The problem is complicated by the fact that these cause confusion more often in persons who have early dementia, so that "reversal" of such problems may ultimately only be temporary.

Testing for alcohol and other known dementia-inducing drugs may be indicated.

Imaging

A CT scan or magnetic resonance imaging (MRI scan) is commonly performed, although these modalities do not have optimal sensitivity for the diffuse metabolic changes associated with dementia in a patient that shows no gross neurological problems (such as paralysis or weakness) on neurological exam. CT or MRI may suggest normal pressure hydrocephalus, a potentially reversible cause of dementia, and can yield information relevant to other types of dementia, such as infarction (stroke) that would point at a vascular type of dementia.

The functional neuroimaging modalities of SPECT and PET are more useful in assessing long-standing cognitive dysfunction, since they have shown similar ability to diagnose dementia as a clinical exam. The ability of SPECT to differentiate the vascular cause from the Alzheimer's disease cause of dementias, appears to be superior to differentiation by clinical exam.

Recent research has established the value of PET imaging using carbon-11 Pittsburgh Compound B as a radiotracer (PIB-PET) in predictive diagnosis of various kinds of dementia, in particular Alzheimer's disease. Studies from Australia have found PIB-PET to be 86% accurate in predicting which patients with mild cognitive impairment would develop Alzheimer's disease within two years. In another study, carried out using 66 patients seen at the University of Michigan, PET studies using either PIB or another radiotracer, carbon-11 dihydrotetrabenazine (DTBZ), led to more accurate diagnosis for more than one-fourth of patients with mild cognitive impairment or mild dementia.

Prevention

It appears that the regular moderate consumption of alcohol (beer, wine, or distilled spirits) and a Mediterranean diet may reduce risk. A study has shown a link between high blood pressure and developing dementia. The study, published in the *Lancet Neurology* journal July 2008, found that blood pressure lowering medication reduced dementia by 13%.

Brain-derived neurotrophic factor (BDNF) expression is associated with some dementia types.

A Canadian study found that a lifetime of bilingualism delays the onset of dementia by an average of four years when compared to monolingual patients.

Management

Except for the treatable types listed above, there is no cure to this illness. Cholinesterase inhibitors are often used early in the disease course. Cognitive and behavioral interventions may also be appropriate. Educating and providing emotional support to the caregiver (or carer) is of importance as well.

Pain and dementia

As people age, they experience more health problems, and most health problems associated with aging carry a substantial burden of pain; so, between 25% and 50% of older adults experience persistent pain. Seniors with dementia experience the same prevalence of conditions likely to cause pain as seniors without dementia. Pain is often overlooked in older adults and, when screened for, often poorly assessed, especially among those with dementia. Beyond the issue of humane care, unrelieved pain has functional implications. Persistent pain can lead to decreased ambulation, depressed mood, sleep disturbances, impaired appetite and exacerbation of cognitive impairment, and pain-related interference with activity is a factor contributing to falls in the elderly.

Although persistent pain in the person with dementia is difficult to communicate, diagnose and treat, failure to address persistent pain has profound functional, psychosocial and quality of life implications for this vulnerable population. Health professionals often lack the skills and usually lack the time needed to recognize, accurately assess and adequately monitor pain in people with dementia. Family members and friends can make a valuable contribution to the care of a person with dementia by learning to recognize and assess their pain. Educational resources (such as the Understand Pain and Dementia tutorial) and observational assessment tools are available.

Medications

- Acetylcholinesterase inhibitors: Tacrine (Cognex), donepezil (Aricept), galantamine (Razadyne), and rivastigmine (Exelon) are approved by the United States Food and Drug Administration (FDA) for treatment of dementia induced by Alzheimer's disease. They may be useful for other similar diseases causing dementia such as Parkinsons or vascular dementia.
- N-methyl-D-aspartate Blockers. Memantine (Namenda) is a drug representative of this class. It can be used in combination with acetylcholinesterase inhibitors.

Off label

- Amyloid deposit inhibitors: Minocycline and Clioquinoline, antibiotics, may help reduce amyloid deposits in the brains of persons with Alzheimer's disease.
- Antidepressant drugs: Depression is frequently associated with dementia and generally worsens the degree of cognitive and behavioral impairment. Antidepressants effectively treat the cognitive and behavioral symptoms of depression in patients with Alzheimer's disease, but evidence for their use in other forms of dementia is weak.
- Anxiolytic drugs: Many patients with dementia experience anxiety symptoms. Although benzodiazepines like diazepam (Valium) have been used for treating anxiety in other situations, they are often avoided because they may increase agitation in persons with dementia and are likely to worsen cognitive problems or are too sedating. Buspirone (Buspar) is often initially tried for mild-to-moderate anxiety. There is little evidence for the effectiveness of benzodiazepines in

dementia, whereas there is evidence for the effectivess of antipsychotics (at low doses).

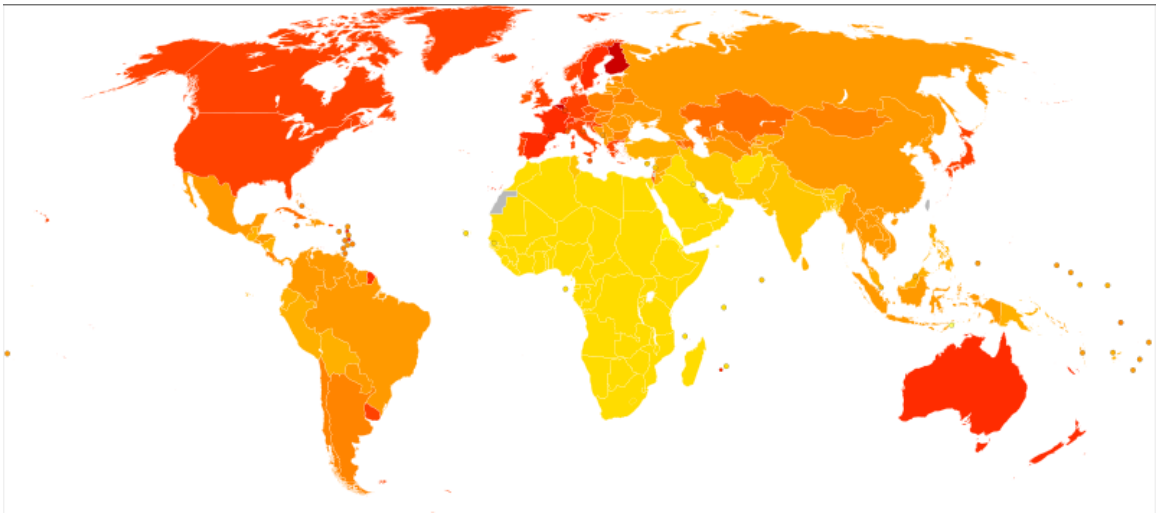
- Selegiline, a drug used primarily in the treatment of Parkinson's disease, appears to slow the development of dementia. Selegiline is thought to act as an antioxidant, preventing free radical damage. However, it also acts as a stimulant, making it difficult to determine whether the delay in onset of dementia symptoms is due to protection from free radicals or to the general elevation of brain activity from the stimulant effect.
- Antipsychotic drugs: Both typical antipsychotics (such as Haloperidol) and atypical antipsychotics such as (risperidone) increase the risk of death in dementia-associated psychosis. This means that any use of antipsychotic medication for dementia-associated psychosis is off-label and should only be considered after discussing the risks and benefits of treatment with these drugs, and after other treatment modalities have failed. In the UK around 144,000 dementia sufferers are unnecessarily prescribed antipsychotic drugs, around 2000 patients die as a result of taking the drugs each year.

Services

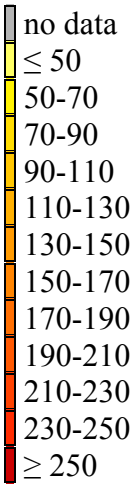
Adult daycare centers as well as special care units in nursing homes often provide specialized care for dementia patients. Adult daycare centers offer supervision, recreation, meals, and limited health care to participants, as well as providing respite for caregivers.

While some preliminary studies have found that music therapy may be useful in helping patients with dementia, their quality has been low and no reliable conclusions can be drawn from them.

Epidemiology



Disability-adjusted life year for Alzheimer and other dementias per 100,000 inhabitants in 2002.



In a study issued by European researchers, it is estimated that about 35 million people have dementia worldwide. They said that figure is likely to double every 20 years, to nearly 66 million in 2030 and 115 million in 2050.

Chapter 10

Late Life Depression

Late Life Depression refers to a major depressive episode occurring for the first time in an older person (usually over 50 or 60 years of age). Depression is a normal part of aging. Concurrent medical problems and lower functional expectations of elderly patients often obscure the degree of impairment. Typically, elderly patients with depression do not report depressed moods, but instead present with less specific symptoms such as insomnia, anorexia, and fatigue. Elderly persons sometimes dismiss less severe depression as an acceptable response to life stress or a normal part of aging.

Epidemiology of late life depression

Major depression of late life

Major Depression is a mental disorder characterized by an all-encompassing low mood accompanied by low self-esteem, and loss of interest or pleasure in normally enjoyable activities.Nearly 5 million of the 31 million Americans who are 65 years or older are clinically depressed, and 1 million have major depression. Approximately 3 percent of healthy elderly persons living in the community have major depression. Recurrence may be as high as 40 percent. Suicide rates are nearly twice as high in depressed patients as in the general population. Major depression is more common in medically ill patients who are older than 70 years and hospitalized or institutionalized.4 Severe or chronic diseases associated with high rates of depression include stroke (30 to 60 percent), coronary heart disease (8 to 44 percent),cancer (1 to 40 percent), Parkinson's disease (40 percent), Alzheimer's disease (20 to 40 percent), and dementia (17 to 31 percent).

Minor depression of late life

Minor depression is a clinically significant depressive disorder that does not fulfill the duration criterion or the number of symptoms necessary for the diagnosis of major depression.11 Minor depression, which is more common than major depression in elderly patients, may follow a major depressive episode. It also can be a reaction to routine stressors in older populations. Fifteen to 50 percent of patients with minor depression develop major depression within two years.

Symptoms and diagnosis of late life depression

To meet criteria for a major depressive episode, a patient must have 5 of these 9 symptoms nearly every day for at least 2 weeks.

1. Depressed or sad mood
2. Anhedonia (loss of interest in pleasurable activities)
3. Sleep disturbance (increased or decreased sleep)
4. Appetite disturbance (increased or decreased appetite) typically with weight change
5. Energy disturbance (increased or decreased energy/activity level), usually fatigue
6. Poor memory and/or concentration
7. Feelings of guilt or worthlessness
8. Psychomotor retardation or agitation (a change in mental and physical speed perceived by other people)
9. Thoughts of wishing you were dead; suicidal ideation or suicide attempts

Causes

The exact changes in brain chemistry and function that cause either late life or earlier-onset depression are unknown. It is known, however, that brain changes can be triggered by the stresses of certain life events such as illness, childbirth, death of a loved one, life transitions (such as retirement), interpersonal conflicts, or social isolation.Risk factors for depression in elderly persons include a history of depression, chronic medical illness, female sex, being single or divorced, brain disease, alcohol abuse, use of certain medications, and stressful life events.

Treatments

Ttreatment is effective in about 80% of identified cases, when treatment is provided. Effective management requires a biopsychosocial approach, combining pharmacotherapy and psychotherapy. Therapy generally results in improved quality of life, enhanced functional capacity, possible improvement in medical health status, increased longevity, and lower health care costs. Improvement should be evident as early as two weeks after the start of therapy, but full therapeutic effects may require several months of treatment. Psychotherapy and medication are the two primary treatment approaches.Therapy for older patients should be continued for longer periods than are typically used in younger patients.

Psychotherapy

Psychologic therapies are recommended for elderly patients with depression because of this group's vulnerability to adverse effects and high rates of medical problems and medication use. Psychotherapeutic approaches include cognitive-behavior therapy, supportive psychotherapy, problem-solving therapy, and interpersonal therapy.The potential benefit of psychotherapy is not diminished by increasing age. Older adults often

have better treatment compliance, lower dropout rates, and more positive responses to psychotherapy than younger patients.

Pharmacotherapy

Pharmacotherapy for acute episodes of depression usually is effective and free of complications. Underuse or misuse of antidepressants and prescribing inadequate dosages are the most common mistakes physicians make when treating elderly patients for depression. Only 10 to 40 percent of depressed elderly patients are given medication. Antidepressants, in general, may also work by playing a neuroprotective role in how they relieve anxiety and depression. It's thought that antidepressants may increase the effects of brain receptors that help nerve cells keep sensitivity to glutamate which is an organic compound of a nonessential amino acid. This increased support of nerve cells lowers glutamate sensitivity, providing protection against the glutamate overwhelming and exciting key brain areas related to depression. Antidepressant medications are often the first treatment choice for adults with moderate or severe depression, sometimes along with psychotherapy. Although antidepressants may not cure depression, they can help you achieve remission which is the disappearance or nearly complete reduction of depression symptoms.

Selective Serotonin Reuptake Inhibitors

Selective serotonin reuptake inhibitors (SSRIs) are a popular class of antidepressant medications. The first drug in this class was fluoxetine (Prozac), which hit the U.S. market in 1987. Precisely how SSRIs affect depression isn't clear. Certain brain chemicals called neurotransmitters are associated with depression, including the neurotransmitter serotonin (ser-oh-TOE-nin). Some research suggests that abnormalities in neurotransmitter activity affect mood and behavior. SSRIs seem to relieve symptoms of depression by blocking the reabsorption (reuptake) of serotonin by certain nerve cells in the brain. This leaves more serotonin available in the brain. Increased serotonin enhances neurotransmission, the sending of nerve impulses, and improves mood. SSRIs are called selective because they seem to affect only serotonin, not other neurotransmitters.

Tricyclic Antidepressants

Tricyclic antidepressants (TCAs) are a class of psychoactive drugs used primarily as antidepressants, which were first discovered in the early 1950s, and subsequently introduced later in the decade. They are named after their chemical structure, which contains three rings of atoms, and are closely related to the tetracyclic antidepressants (TeCAs), which contain four rings of atoms.

Monoamine Oxidase Inhibitors (MAOIs)

Researchers believe MAOIs relieve depression by preventing the enzyme monoamine oxidase from metabolizing the neurotransmitters norepinephrine (nor-ep-ih-NEF-rin),

serotonin (ser-oh-TOE-nin) and dopamine (DOE-puh-mene) in the brain. As a result, these levels remain high in the brain, boosting mood.

Other Antidepressants

Other antidepressants exist that have different ways of working than the SSRIs, tricyclics, and MAOIs. Commonly used ones are venlafaxine, nefazadone, bupropion, mirtazapine and trazodone.

Electroconvulsive Therapy (ECT)

Electroconvulsive therapy (ECT) is a first-line option in patients with depression and psychotic features who have not responded to antipsychotic and antidepressant medications,and patients with severe nonpsychotic depression who have not responded to adequate trials of two antidepressants.

ECT is a procedure in which electric currents are passed through the brain, deliberately triggering a brief seizure. This seizure releases many chemicals in the brain. These chemicals, called neurotransmitters, deliver messages from one brain cell to another. The release of these chemicals makes the brain cells work better. A person's mood will improve when his or her brain cells and chemical messengers work better. Although electroconvulsive therapy can still cause side effects and complications, it now uses precisely calculated electrical currents administered in a controlled setting to achieve the most benefit with the fewest possible risks.

Deep Brain Stimulation (DBS)

Deep brain stimulation (DBS) is a surgical treatment involving the implantation of a medical device called a brain pacemaker, which sends electrical impulses to specific parts of the brain. DBS in select brain regions has provided remarkable therapeutic benefits for otherwise treatment-resistant movement and affective disorders such as chronic pain, Parkinson’s disease, tremor and dystonia. Despite the long history of DBS, its underlying principles and mechanisms are still not clear. DBS directly changes brain activity in a controlled manner, its effects are reversible (unlike those of lesioning techniques) and is one of only a few neurosurgical methods that allows blinded studies.

Transcranial Magnetic Stimulation (TMS)

Transcranial magnetic stimulation (TMS) is a procedure that uses magnetic fields to stimulate nerve cells in the brain to improve symptoms of depression. Transcranial magnetic stimulation is one of the newer types of brain-stimulation methods designed to treat depression when standard treatment hasn't worked. There are different ways to perform transcranial magnetic stimulation. But in general, a large electromagnetic coil is placed against your scalp near your forehead. The electromagnet creates painless electric currents that stimulate nerve cells in the region of your brain involved in mood regulation and depression.

Vagus Nerve Stimulation (VNS)

Vagus nerve stimulation (VNS) is a neurological procedure that sends electrical impulses into your brain in an effort to improve chronic depression symptoms. Vagus nerve stimulation is one of several newer types of brain stimulation methods designed to treat depression when standard treatment hasn't worked. Vagus nerve stimulation is sometimes called vagal nerve stimulation. With vagus nerve stimulation, a device called a pulse generator is surgically implanted in your chest. A wire threaded under your skin connects the pulse generator to the left vagus nerve in your neck. The pulse generator sends out electrical signals along the vagus nerve to your brain. These signals affect mood centers of your brain, possibly improving depression symptoms. Vagus nerve stimulation is recommended only for certain cases of severe or chronic depression.

Research

Genetics Research

Researchers are increasingly certain that genes play an important role in vulnerability to depression. In recent years, the search for a single, defective gene responsible for each mental illness has given way to the understanding that multiple gene variants, acting together with yet unknown environmental risk factors or developmental events, account for the expression of depression.

Brain Imaging Research

Brain imaging (functional/structural MRI) may help direct the search for microscopic abnormalities in brain structure and function responsible for late life depression. Ultimately, imaging technologies may serve as tools for early diagnosis and subtyping of depression.

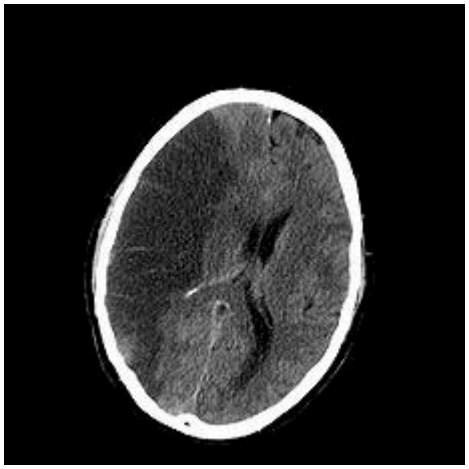
Hormonal Abnormalities Research

The hormonal system that regulates the body's response to stress, the hypothalamic-pituitary-adrenal (HPA) axis, is overactive in many patients with depression. Researchers are investigating whether this phenomenon contributes to the development of depression.

Chapter 11

Stroke

Stroke



CT scan slice of the brain showing a right-hemispheric ischemic stroke (left side of image).

ICD-10	I61.-I64.
ICD-9	434.91
OMIM	601367
DiseasesDB	2247
MedlinePlus	000726
eMedicine	neuro/9 emerg/558 emerg/557 pmr/187
MeSH	D020521

A **stroke**, previously known medically as a **cerebrovascular accident (CVA)**, is the rapidly developing loss of brain function(s) due to disturbance in the blood supply to the brain. This can be due to ischemia (lack of blood flow) caused by blockage (thrombosis, arterial embolism), or a hemorrhage (leakage of blood). As a result, the affected area of the brain is unable to function, leading to inability to move one or more limbs on one side

of the body, inability to understand or formulate speech, or an inability to see one side of the visual field.

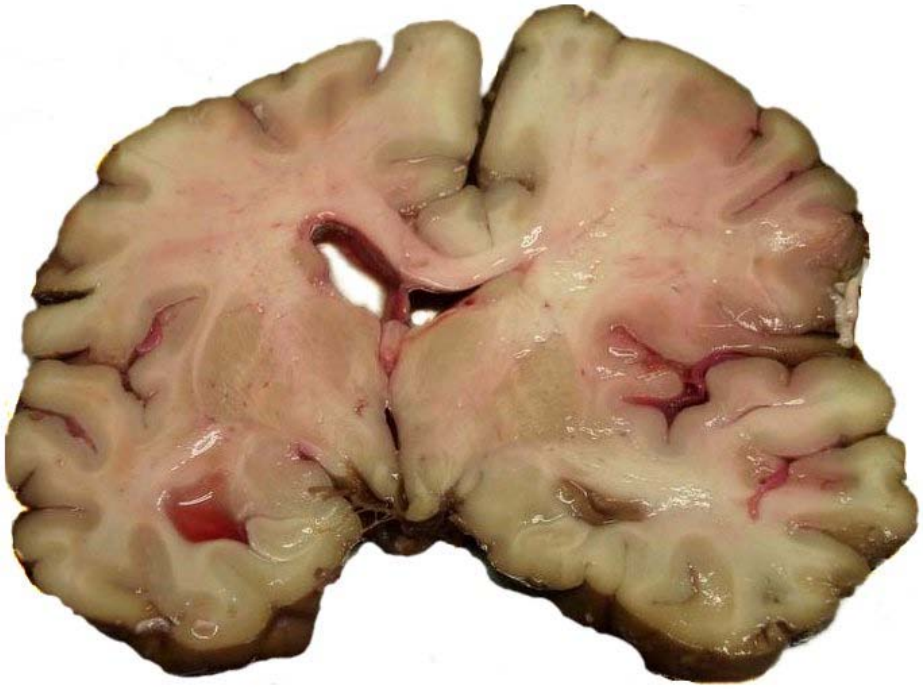
A stroke is a medical emergency and can cause permanent neurological damage, complications, and lead to death. It is the leading cause of adult disability in the United States and Europe and it is the second leading cause of death worldwide. Risk factors for stroke include advanced age, hypertension (high blood pressure), previous stroke or transient ischemic attack (TIA), diabetes, high cholesterol, cigarette smoking and atrial fibrillation. High blood pressure is the most important modifiable risk factor of stroke.

An ischemic stroke is occasionally treated in a hospital with thrombolysis (also known as a "clot buster"), and some hemorrhagic strokes benefit from neurosurgery. Treatment to recover any lost function is stroke rehabilitation, ideally in a stroke unit and involving health professions such as speech and language therapy, physical therapy and occupational therapy. Prevention of recurrence may involve the administration of antiplatelet drugs such as aspirin and dipyridamole, control and reduction of hypertension, and the use of statins. Selected patients may benefit from carotid endarterectomy and the use of anticoagulants.

Definition

The traditional definition of stroke, devised by the World Health Organization in the 1970s, is a "neurological deficit of cerebrovascular cause that persists beyond 24 hours or is interrupted by death within 24 hours". This definition was supposed to reflect the reversibility of tissue damage and was devised for the purpose, with the time frame of 24 hours being chosen arbitrarily. The 24-hour limit divides stroke from transient ischemic attack, which is a related syndrome of stroke symptoms that resolve completely within 24 hours. With the availability of treatments that, when given early, can reduce stroke severity, many now prefer alternative concepts, such as **brain attack** and **acute ischemic cerebrovascular syndrome** (modeled after heart attack and acute coronary syndrome respectively), that reflect the urgency of stroke symptoms and the need to act swiftly.

Classification



A slice of brain from the autopsy of a person who suffered an acute middle cerebral artery (MCA) stroke

Strokes can be classified into two major categories: ischemic and hemorrhagic. Ischemic strokes are those that are caused by interruption of the blood supply, while hemorrhagic strokes are the ones which result from rupture of a blood vessel or an abnormal vascular structure. About 87% of strokes are caused by ischemia, and the remainder by hemorrhage. Some hemorrhages develop inside areas of ischemia ("hemorrhagic transformation"). It is unknown how many hemorrhages actually start as ischemic stroke.

Ischemic

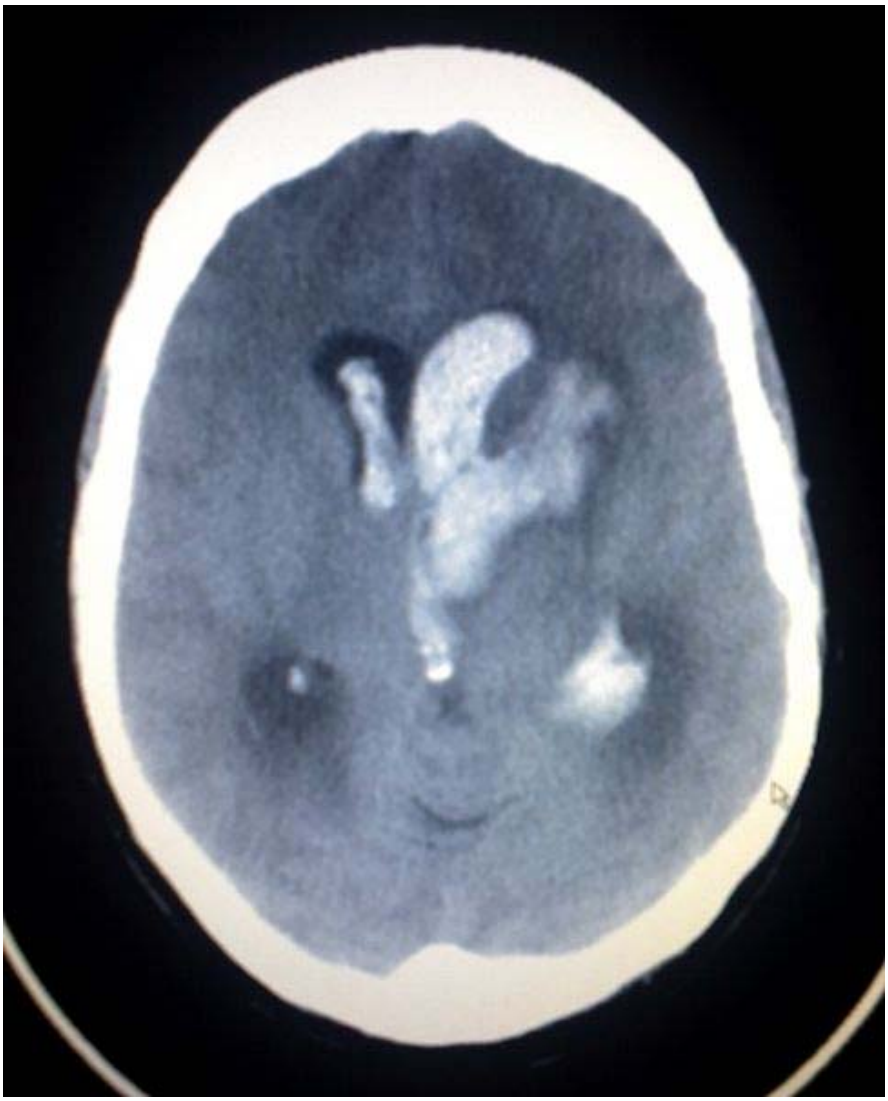
In an ischemic stroke, blood supply to part of the brain is decreased, leading to dysfunction of the brain tissue in that area. There are four reasons why this might happen:

1. Thrombosis (obstruction of a blood vessel by a blood clot forming locally)
2. Embolism (obstruction due to an embolus from elsewhere in the body),
3. Systemic hypoperfusion (general decrease in blood supply, e.g. in shock)
4. Venous thrombosis.

Stroke without an obvious explanation is termed "cryptogenic" (of unknown origin); this constitutes 30-40% of all ischemic strokes.

There are various classification systems for acute ischemic stroke. The Oxford Community Stroke Project classification (OCSP, also known as the Bamford or Oxford classification) relies primarily on the initial symptoms; based on the extent of the symptoms, the stroke episode is classified as total anterior circulation infarct (TACI), partial anterior circulation infarct (PACI), lacunar infarct (LACI) or posterior circulation infarct (POCI). These four entities predict the extent of the stroke, the area of the brain affected, the underlying cause, and the prognosis. The TOAST (Trial of Org 10172 in Acute Stroke Treatment) classification is based on clinical symptoms as well as results of further investigations; on this basis, a stroke is classified as being due to (1) thrombosis or embolism due to atherosclerosis of a large artery, (2) embolism of cardiac origin, (3) occlusion of a small blood vessel, (4) other determined cause, (5) undetermined cause (two possible causes, no cause identified, or incomplete investigation).

Hemorrhagic



CT scan showing an intracerebral hemorrhage with associated intraventricular hemorrhage

Intracranial hemorrhage is the accumulation of blood anywhere within the skull vault. A distinction is made between intra-axial hemorrhage (blood inside the brain) and extra-axial hemorrhage (blood inside the skull but outside the brain). Intra-axial hemorrhage is due to intraparenchymal hemorrhage or intraventricular hemorrhage (blood in the ventricular system). The main types of extra-axial hemorrhage are epidural hematoma (bleeding between the dura mater and the skull), subdural hematoma (in the subdural space) and subarachnoid hemorrhage (between the arachnoid mater and pia mater). Most of the hemorrhagic stroke syndromes have specific symptoms (e.g. headache, previous head injury).

Signs and symptoms

Stroke symptoms typically start suddenly, over seconds to minutes, and in most cases do not progress further. The symptoms depend on the area of the brain affected. The more extensive the area of brain affected, the more functions that are likely to be lost. Some forms of stroke can cause additional symptoms. For example, in intracranial hemorrhage, the affected area may compress other structures. Most forms of stroke are not associated with headache, apart from subarachnoid hemorrhage and cerebral venous thrombosis and occasionally intracerebral hemorrhage.

Early recognition

Various systems have been proposed to increase recognition of stroke by patients, relatives and emergency first responders. A systematic review, updating a previous systematic review from 1994, looked at a number of trials to evaluate how well different physical examination findings are able to predict the presence or absence of stroke. It was found that sudden-onset face weakness, arm drift (e.g. if a person, when asked to raise both arms, involuntarily lets one arm drift downward) and abnormal speech are the findings most likely to lead to the correct identification of a case of stroke (+ likelihood ratio of 5.5 when at least one of these is present). Similarly, when all three of these are absent, the likelihood of stroke is significantly decreased (– likelihood ratio of 0.39). While these findings are not perfect for diagnosing stroke, the fact that they can be evaluated relatively rapidly and easily make them very valuable in the acute setting.

Proposed systems include FAST (stroke) (face, arm, speech, and time), as advocated by the Department of Health (United Kingdom) and The Stroke Association, the American Stroke Association, National Stroke Association, the Los Angeles Prehospital Stroke Screen (LAPSS) and the Cincinnati Prehospital Stroke Scale (CPSS). Use of these scales is recommended by professional guidelines.

For people referred to the emergency room, early recognition of stroke is deemed important as this can expedite diagnostic tests and treatments. A scoring system called ROSIER (recognition of stroke in the emergency room) is recommended for this purpose; it is based on features from the medical history and physical examination.

Subtypes

If the area of the brain affected contains one of the three prominent central nervous system pathways—the spinothalamic tract, corticospinal tract, and dorsal column (medial lemniscus), symptoms may include:

- hemiplegia and muscle weakness of the face
- numbness
- reduction in sensory or vibratory sensation

In most cases, the symptoms affect only one side of the body (unilateral). Depending on the part of the brain affected, the defect in the brain is *usually* on the opposite side of the body. However, since these pathways also travel in the spinal cord and any lesion there can also produce these symptoms, the presence of any one of these symptoms does not necessarily indicate a stroke.

In addition to the above CNS pathways, the *brainstem* also consists of the 12 cranial nerves. A stroke affecting the brain stem therefore can produce symptoms relating to deficits in these cranial nerves:

- altered smell, taste, hearing, or vision (total or partial)
- drooping of eyelid (ptosis) and weakness of ocular muscles
- decreased reflexes: gag, swallow, pupil reactivity to light
- decreased sensation and muscle weakness of the face
- balance problems and nystagmus
- altered breathing and heart rate
- weakness in sternocleidomastoid muscle with inability to turn head to one side
- weakness in tongue (inability to protrude and/or move from side to side)

If the *cerebral cortex* is involved, the CNS pathways can again be affected, but also can produce the following symptoms:

- aphasia (difficulty with verbal expression, auditory comprehension, reading and/or writing Broca's or Wernicke's area typically involved)
- dysarthria (motor speech disorder resulting from neurological injury)
- apraxia (altered voluntary movements)
- visual field defect
- memory deficits (involvement of temporal lobe)
- hemineglect (involvement of parietal lobe)
- disorganized thinking, confusion, hypersexual gestures (with involvement of frontal lobe)
- anosognosia (persistent denial of the existence of a, usually stroke-related, deficit)

If the *cerebellum* is involved, the patient may have the following:

- trouble walking

- altered movement coordination
- vertigo and or disequilibrium

Associated symptoms

Loss of consciousness, headache, and vomiting usually occurs more often in hemorrhagic stroke than in thrombosis because of the increased intracranial pressure from the leaking blood compressing the brain.

If symptoms are maximal at onset, the cause is more likely to be a subarachnoid hemorrhage or an embolic stroke.

Causes

Thrombotic stroke

In thrombotic stroke a thrombus (blood clot) usually forms around atherosclerotic plaques. Since blockage of the artery is gradual, onset of symptomatic thrombotic strokes is slower. A thrombus itself (even if non-occluding) can lead to an embolic stroke if the thrombus breaks off, at which point it is called an "embolus." Two types of thrombosis can cause stroke:

- *Large vessel disease* involves the common and internal carotids, vertebral, and the Circle of Willis. Diseases that may form thrombi in the large vessels include (in descending incidence): atherosclerosis, vasoconstriction (tightening of the artery), aortic, carotid or vertebral artery dissection, various inflammatory diseases of the blood vessel wall (Takayasu arteritis, giant cell arteritis, vasculitis), noninflammatory vasculopathy, Moyamoya disease and fibromuscular dysplasia.
- *Small vessel disease* involves the smaller arteries inside the brain: branches of the circle of Willis, middle cerebral artery, stem, and arteries arising from the distal vertebral and basilar artery. Diseases that may form thrombi in the small vessels include (in descending incidence): lipohyalinosis (build-up of fatty hyaline matter in the blood vessel as a result of high blood pressure and aging) and fibrinoid degeneration (stroke involving these vessels are known as lacunar infarcts) and microatheroma (small atherosclerotic plaques).

Sickle cell anemia, which can cause blood cells to clump up and block blood vessels, can also lead to stroke. A stroke is the second leading killer of people under 20 who suffer from sickle-cell anemia.

Embolic stroke

An embolic stroke refers to the blockage of an artery by an arterial embolus, a travelling particle or debris in the arterial bloodstream originating from elsewhere. An embolus is most frequently a thrombus, but it can also be a number of other substances including fat (e.g. from bone marrow in a broken bone), air, cancer cells or clumps of bacteria (usually from infectious endocarditis).

Because an embolus arises from elsewhere, local therapy solves the problem only temporarily. Thus, the source of the embolus must be identified. Because the embolic blockage is sudden in onset, symptoms usually are maximal at start. Also, symptoms may be transient as the embolus is partially resorbed and moves to a different location or dissipates altogether.

Emboli most commonly arise from the heart (especially in atrial fibrillation) but may originate from elsewhere in the arterial tree. In paradoxical embolism, a deep vein thrombosis embolises through an atrial or ventricular septal defect in the heart into the brain.

Cardiac causes can be distinguished between high and low-risk:

- High risk: atrial fibrillation and paroxysmal atrial fibrillation, rheumatic disease of the mitral or aortic valve disease, artificial heart valves, known cardiac thrombus of the atrium or ventricle, sick sinus syndrome, sustained atrial flutter, recent myocardial infarction, chronic myocardial infarction together with ejection fraction <28 percent, symptomatic congestive heart failure with ejection fraction <30 percent, dilated cardiomyopathy, Libman-Sacks endocarditis, Marantic endocarditis, infective endocarditis, papillary fibroelastoma, left atrial myxoma and coronary artery bypass graft (CABG) surgery
- Low risk/potential: calcification of the annulus (ring) of the mitral valve, patent foramen ovale (PFO), atrial septal aneurysm, atrial septal aneurysm *with* patent foramen ovale, left ventricular aneurysm without thrombus, isolated left atrial "smoke" on echocardiography (no mitral stenosis or atrial fibrillation), complex atheroma in the ascending aorta or proximal arch

Systemic hypoperfusion

Systemic hypoperfusion is the reduction of blood flow to all parts of the body. It is most commonly due to cardiac pump failure from cardiac arrest or arrhythmias, or from reduced cardiac output as a result of myocardial infarction, pulmonary embolism, pericardial effusion, or bleeding. Hypoxemia (low blood oxygen content) may precipitate the hypoperfusion. Because the reduction in blood flow is global, all parts of the brain may be affected, especially "watershed" areas - border zone regions supplied by the major cerebral arteries. A watershed stroke refers to the condition when blood supply to these areas is compromised. Blood flow to these areas does not necessarily stop, but instead it may lessen to the point where brain damage can occur. This phenomenon is also referred to as "last meadow" to point to the fact that in irrigation the last meadow receives the least amount of water.

Venous thrombosis

Cerebral venous sinus thrombosis leads to stroke due to locally increased venous pressure, which exceeds the pressure generated by the arteries. Infarcts are more likely to

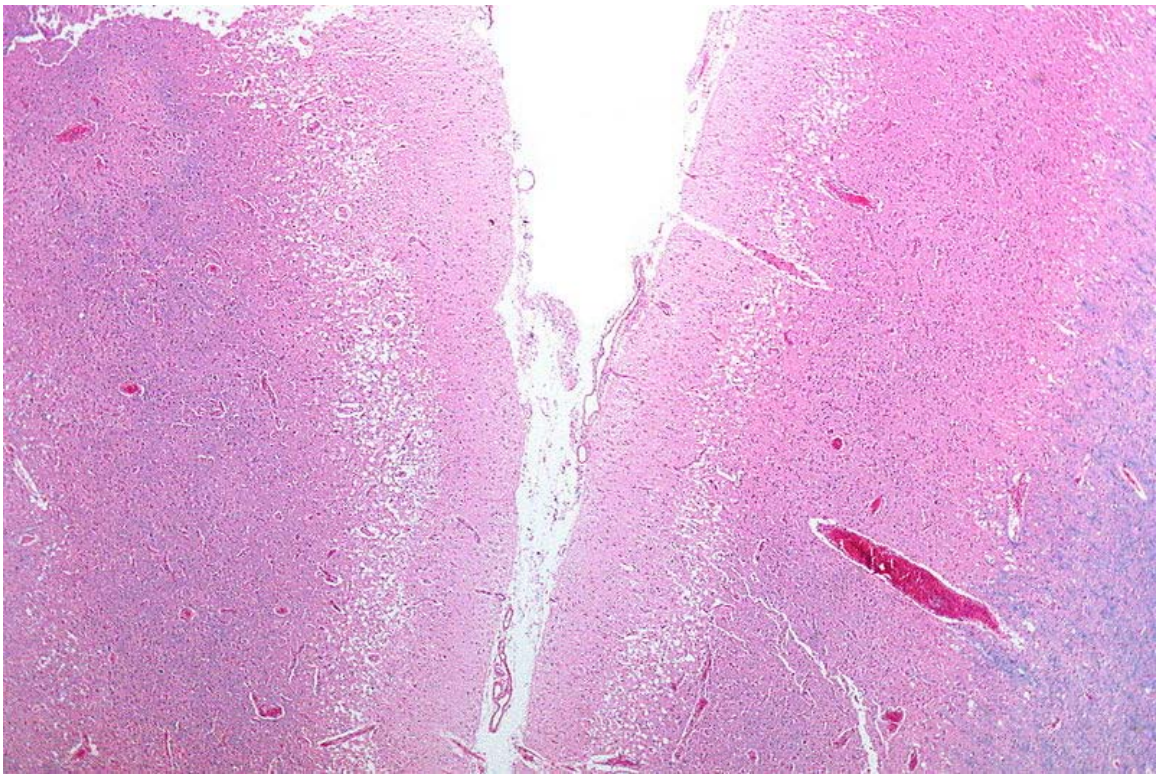
undergo hemorrhagic transformation (leaking of blood into the damaged area) than other types of ischemic stroke.

Intracerebral hemorrhage

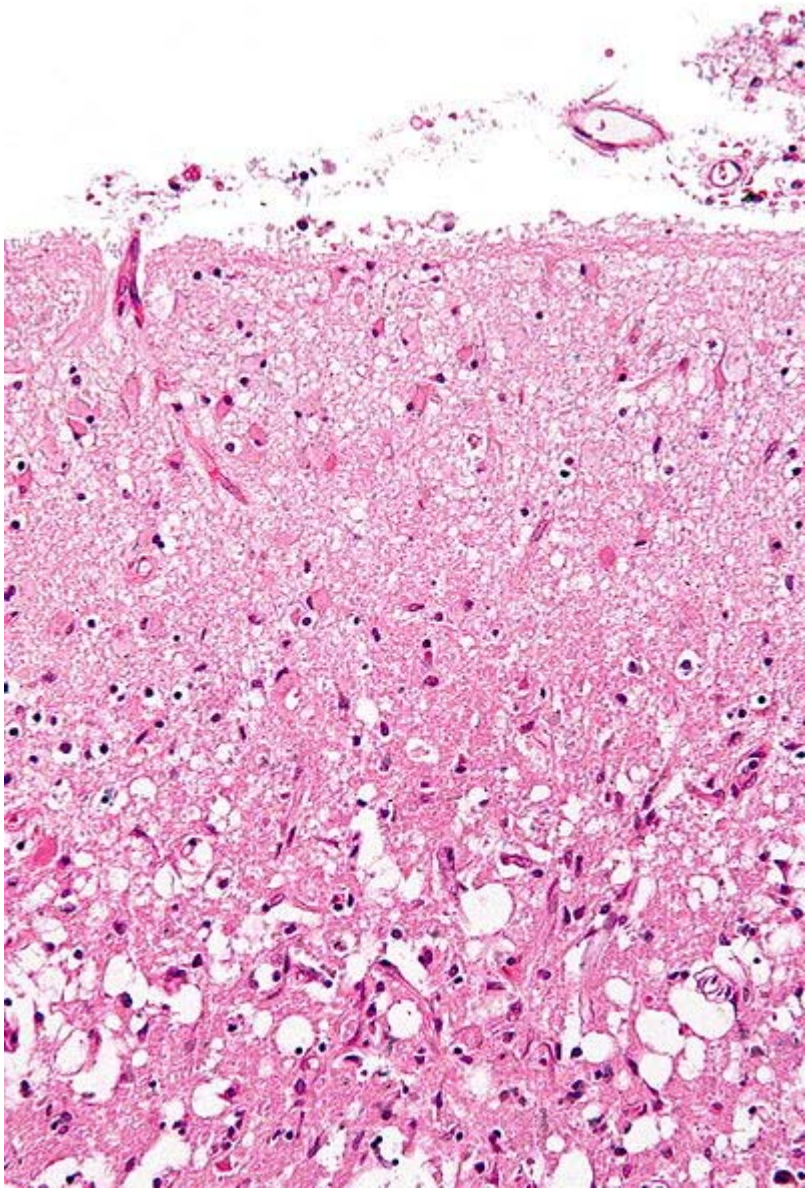
It generally occurs in small arteries or arterioles and is commonly due to hypertension, intracranial vascular malformations (including cavernous angiomas or arteriovenous malformations), cerebral amyloid angiopathy, or infarcts into which secondary haemorrhage has occurred. Other potential causes are trauma, bleeding disorders, amyloid angiopathy, illicit drug use (e.g. amphetamines or cocaine). The hematoma enlarges until pressure from surrounding tissue limits its growth, or until it decompresses by emptying into the ventricular system, CSF or the pial surface. A third of intracerebral bleed is into the brain's ventricles. ICH has a mortality rate of 44 percent after 30 days, higher than ischemic stroke or even the very deadly subarachnoid hemorrhage (which, however, also may be classified as a type of stroke).

Pathophysiology

Ischemic



Micrograph showing cortical pseudolaminar necrosis, a finding seen in strokes on medical imaging and at autopsy. H&E-LFB stain.



Micrograph of the superficial cerebral cortex showing neuron loss and reactive astrocytes in a person that suffered a stroke. H&E-LFB stain.

Ischemic stroke occurs due to a loss of blood supply to part of the brain, initiating the ischemic cascade. Brain tissue ceases to function if deprived of oxygen for more than 60 to 90 seconds and after approximately three hours, will suffer irreversible injury possibly leading to death of the tissue, i.e., infarction. (This is why TPA's (e.g. Streptokinase, Altapase) are given only until three hours since the onset of the stroke.) Atherosclerosis may disrupt the blood supply by narrowing the lumen of blood vessels leading to a reduction of blood flow, by causing the formation of blood clots within the vessel, or by releasing showers of small emboli through the disintegration of atherosclerotic plaques. Embolic infarction occurs when emboli formed elsewhere in the circulatory system, typically in the heart as a consequence of atrial fibrillation, or in the carotid arteries,

break off, enter the cerebral circulation, then lodge in and occlude brain blood vessels. Since blood vessels in the brain are now occluded, the brain becomes low in energy, and thus it resorts into using anaerobic respiration within the region of brain tissue affected by ischemia. Unfortunately, this kind of respiration produces less adenosine triphosphate (ATP) but releases a by-product called lactic acid. Lactic acid is an irritant which could potentially destroy cells since it is an acid and disrupts the normal acid-base balance in the brain. The ischemia area is referred to as the "ischemic penumbra".

Then, as oxygen or glucose becomes depleted in ischemic brain tissue, the production of high energy phosphate compounds such as adenosine triphosphate (ATP) fails, leading to failure of energy-dependent processes (such as ion pumping) necessary for tissue cell survival. This sets off a series of interrelated events that result in cellular injury and death. A major cause of neuronal injury is release of the excitatory neurotransmitter glutamate. The concentration of glutamate outside the cells of the nervous system is normally kept low by so-called uptake carriers, which are powered by the concentration gradients of ions (mainly Na^+) across the cell membrane. However, stroke cuts off the supply of oxygen and glucose which powers the ion pumps maintaining these gradients. As a result the transmembrane ion gradients run down, and glutamate transporters reverse their direction, releasing glutamate into the extracellular space. Glutamate acts on receptors in nerve cells (especially NMDA receptors), producing an influx of calcium which activates enzymes that digest the cells' proteins, lipids and nuclear material. Calcium influx can also lead to the failure of mitochondria, which can lead further toward energy depletion and may trigger cell death due to apoptosis.

Ischemia also induces production of oxygen free radicals and other reactive oxygen species. These react with and damage a number of cellular and extracellular elements. Damage to the blood vessel lining or endothelium is particularly important. In fact, many antioxidant neuroprotectants such as uric acid and NXY-059 work at the level of the endothelium and not in the brain *per se*. Free radicals also directly initiate elements of the apoptosis cascade by means of redox signaling.

These processes are the same for any type of ischemic tissue and are referred to collectively as the *ischemic cascade*. However, brain tissue is especially vulnerable to ischemia since it has little respiratory reserve and is completely dependent on aerobic metabolism, unlike most other organs.

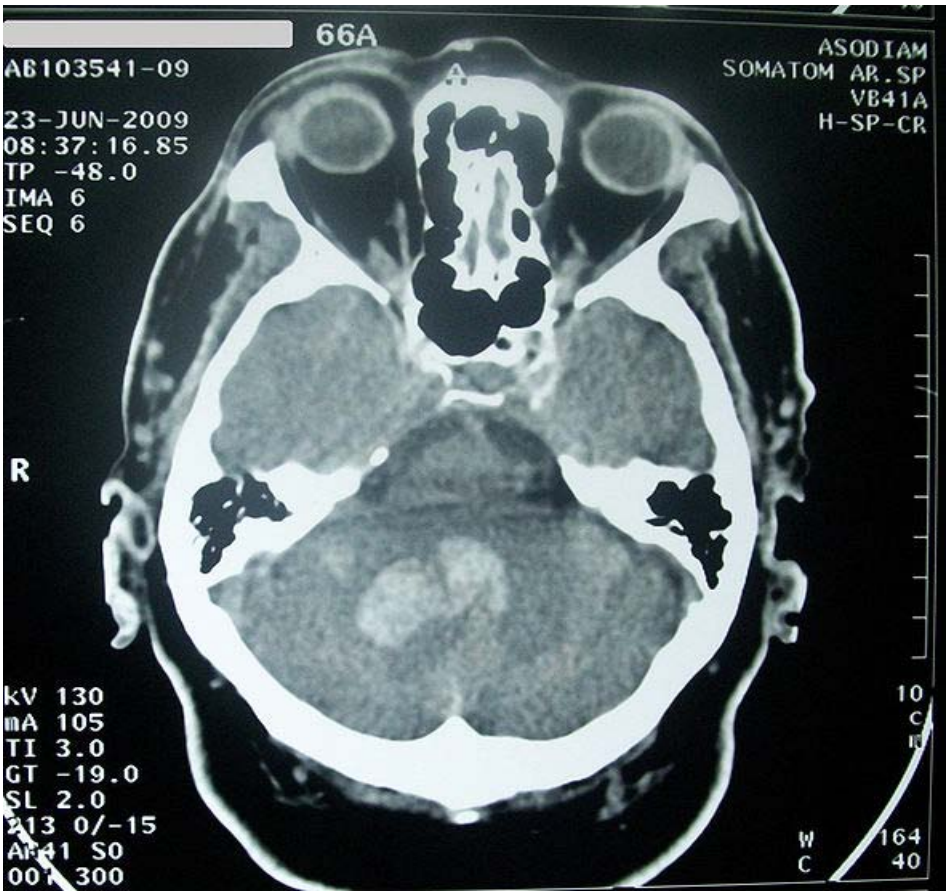
Brain tissue survival can be improved to some extent if one or more of these processes is inhibited. Drugs that scavenge reactive oxygen species, inhibit apoptosis, or inhibit excitatory neurotransmitters, for example, have been shown experimentally to reduce tissue injury due to ischemia. Agents that work in this way are referred to as being *neuroprotective*. Until recently, human clinical trials with neuroprotective agents have failed, with the probable exception of deep barbiturate coma. However, more recently NXY-059, the disulfonyl derivative of the radical-scavenging spintrap phenylbutylnitrone, is reported to be neuroprotective in stroke. This agent appears to work at the level of the blood vessel lining or endothelium. Unfortunately, after

producing favorable results in one large-scale clinical trial, a second trial failed to show favorable results.

In addition to injurious effects on brain cells, ischemia and infarction can result in loss of structural integrity of brain tissue and blood vessels, partly through the release of matrix metalloproteases, which are zinc- and calcium-dependent enzymes that break down collagen, hyaluronic acid, and other elements of connective tissue. Other proteases also contribute to this process. The loss of vascular structural integrity results in a breakdown of the protective blood brain barrier that contributes to cerebral edema, which can cause secondary progression of the brain injury.

As is the case with any type of brain injury, the immune system is activated by cerebral infarction and may under some circumstances exacerbate the injury caused by the infarction. Inhibition of the inflammatory response has been shown experimentally to reduce tissue injury due to cerebral infarction, but this has not proved out in clinical studies.

Hemorrhagic



Head CT showing deep intracerebral hemorrhage due to bleeding within the cerebellum, approximately 30 hours old.

Hemorrhagic strokes result in tissue injury by causing compression of tissue from an expanding hematoma or hematomas. This can distort and injure tissue. In addition, the pressure may lead to a loss of blood supply to affected tissue with resulting infarction, and the blood released by brain hemorrhage appears to have direct toxic effects on brain tissue and vasculature.

Diagnosis

Stroke is diagnosed through several techniques: a neurological examination (such as the Nihss), CT scans (most often without contrast enhancements) or MRI scans, Doppler ultrasound, and arteriography. The diagnosis of stroke itself is clinical, with assistance from the imaging techniques. Imaging techniques also assist in determining the subtypes and cause of stroke. There is yet no commonly used blood test for the stroke diagnosis itself, though blood tests may be of help in finding out the likely cause of stroke.

Physical examination

A physical examination, including taking a medical history of the symptoms and a neurological status, helps giving an evaluation of the location and severity of a stroke. It can give a standard score on e.g. the NIH stroke scale.

Imaging

For diagnosing ischemic stroke in the emergency setting:

- CT scans (*without* contrast enhancements)

  sensitivity= 16%
  specificity= 96%

- MRI scan

  sensitivity= 83%
  specificity= 98%

For diagnosing hemorrhagic stroke in the emergency setting:

- CT scans (*without* contrast enhancements)

  sensitivity= 89%
  specificity= 100%

- MRI scan

  sensitivity= 81%
  specificity= 100%

For detecting chronic hemorrhages, MRI scan is more sensitive.

For the assessment of stable stroke, nuclear medicine scans SPECT and PET/CT may be helpful. SPECT documents cerebral blood flow and PET with FDG isotope the metabolic activity of the neurons.

Underlying etiology

When a stroke has been diagnosed, various other studies may be performed to determine the underlying etiology. With the current treatment and diagnosis options available, it is of particular importance to determine whether there is a peripheral source of emboli. Test selection may vary, since the cause of stroke varies with age, comorbidity and the clinical presentation. Commonly used techniques include:

- an ultrasound/doppler study of the carotid arteries (to detect carotid stenosis) or dissection of the precerebral arteries
- an electrocardiogram (ECG) and echocardiogram (to identify arrhythmias and resultant clots in the heart which may spread to the brain vessels through the bloodstream)
- a Holter monitor study to identify intermittent arrhythmias
- an angiogram of the cerebral vasculature (if a bleed is thought to have originated from an aneurysm or arteriovenous malformation)
- blood tests to determine hypercholesterolemia, bleeding diathesis and some rarer causes such as homocysteinuria

Prevention

Given the disease burden of strokes, prevention is an important public health concern. Primary prevention is less effective than secondary prevention (as judged by the number needed to treat to prevent one stroke per year). Recent guidelines detail the evidence for primary prevention in stroke. Because stroke may indicate underlying atherosclerosis, it is important to determine the patient's risk for other cardiovascular diseases such as coronary heart disease. Conversely, aspirin prevents against first stroke in patients who have suffered a myocardial infarction or patients with a high cardiovascular risk.

Risk factors

The most important modifiable risk factors for stroke are high blood pressure and atrial fibrillation (although magnitude of this effect is small: the evidence from the Medical Research Council trials is that 833 patients have to be treated for 1 year to prevent one stroke). Other modifiable risk factors include high blood cholesterol levels, diabetes, cigarette smoking (active and passive), heavy alcohol consumption and drug use, lack of physical activity, obesity and unhealthy diet. Alcohol use could predispose to ischemic stroke, and intracerebral and subarachnoid hemorrhage via multiple mechanisms (for example via hypertension, atrial fibrillation, rebound thrombocytosis and platelet aggregation and clotting disturbances). The drugs most commonly associated with stroke

are cocaine, amphetamines causing hemorrhagic stroke, but also over-the-counter cough and cold drugs containing sympathomimetics.

No high quality studies have shown the effectiveness of interventions aimed at weight reduction, promotion of regular exercise, reducing alcohol consumption or smoking cessation. Nonetheless, given the large body of circumstantial evidence, best medical management for stroke includes advice on diet, exercise, smoking and alcohol use. Medication or drug therapy is the most common method of stroke prevention; carotid endarterectomy can be a useful surgical method of preventing stroke.

Blood pressure

Hypertension accounts for 35-50% of stroke risk. Epidemiological studies suggest that even a small blood pressure reduction (5 to 6 mmHg systolic, 2 to 3 mmHg diastolic) would result in 40% fewer strokes. Lowering blood pressure has been conclusively shown to prevent both ischemic and hemorrhagic strokes. It is equally important in secondary prevention. Even patients older than 80 years and those with isolated systolic hypertension benefit from antihypertensive therapy. Studies show that intensive antihypertensive therapy results in a greater risk reduction. The available evidence does not show large differences in stroke prevention between antihypertensive drugs — therefore, other factors such as protection against other forms of cardiovascular disease should be considered and cost.

Atrial fibrillation

Patients with atrial fibrillation have a risk of 5% each year to develop stroke, and this risk is even higher in those with valvular atrial fibrillation. Depending on the stroke risk, anticoagulation with medications such as coumarins or aspirin is warranted for stroke prevention.

Blood lipids

High cholesterol levels have been inconsistently associated with (ischemic) stroke. Statins have been shown to reduce the risk of stroke by about 15%. Since earlier meta-analyses of other lipid-lowering drugs did not show a decreased risk, statins might exert their effect through mechanisms other than their lipid-lowering effects.

Diabetes mellitus

Patients with diabetes mellitus are 2 to 3 times more likely to develop stroke, and they commonly have hypertension and hyperlipidemia. Intensive disease control has been shown to reduce microvascular complications such as nephropathy and retinopathy but not macrovascular complications such as stroke.

Anticoagulation drugs

Oral anticoagulants such as warfarin have been the mainstay of stroke prevention for over 50 years. However, several studies have shown that aspirin and antiplatelet drugs are highly effective in secondary prevention after a stroke or transient ischemic attack. Low doses of aspirin (for example 75–150 mg) are as effective as high doses but have fewer side effects; the lowest effective dose remains unknown. Thienopyridines (clopidogrel, ticlopidine) "might be slightly more effective" than aspirin and have a decreased risk of gastrointestinal bleeding, but they are more expensive. Their exact role remains controversial. Ticlopidine has more skin rash, diarrhea, neutropenia and thrombotic thrombocytopenic purpura. Dipyridamole can be added to aspirin therapy to provide a small additional benefit, even though headache is a common side effect. Low-dose aspirin is also effective for stroke prevention after sustaining a myocardial infarction. Except for in atrial fibrillation, oral anticoagulants are not advised for stroke prevention —any benefit is offset by bleeding risk.

In primary prevention however, antiplatelet drugs did not reduce the risk of ischemic stroke while increasing the risk of major bleeding. Further studies are needed to investigate a possible protective effect of aspirin against ischemic stroke in women.

Surgery

Surgical procedures such as carotid endarterectomy or carotid angioplasty can be used to remove significant atherosclerotic narrowing (stenosis) of the carotid artery, which supplies blood to the brain. There is a large body of evidence supporting this procedure in selected cases. Endarterectomy for a significant stenosis has been shown to be useful in the secondary prevention after a previous symptomatic stroke. Carotid artery stenting has not been shown to be equally useful. Patients are selected for surgery based on age, gender, degree of stenosis, time since symptoms and patients' preferences. Surgery is most efficient when not delayed too long —the risk of recurrent stroke in a patient who has a 50% or greater stenosis is up to 20% after 5 years, but endarterectomy reduces this risk to around 5%. The number of procedures needed to cure one patient was 5 for early surgery (within two weeks after the initial stroke), but 125 if delayed longer than 12 weeks.

Screening for carotid artery narrowing has not been shown to be a useful screening test in the general population. Studies of surgical intervention for carotid artery stenosis without symptoms have shown only a small decrease in the risk of stroke. To be beneficial, the complication rate of the surgery should be kept below 4%. Even then, for 100 surgeries, 5 patients will benefit by avoiding stroke, 3 will develop stroke despite surgery, 3 will develop stroke or die due to the surgery itself, and 89 will remain stroke-free but would also have done so without intervention.

Nutritional and metabolic interventions

Nutrition, specifically the Mediterranean-style diet, has the potential of more than halving stroke risk.

With regards to lowering homocysteine, a meta-analysis of previous trials has concluded that lowering homocysteine with folic acid and other supplements may reduce stroke risk. However, the two largest randomized controlled trials included in the meta-analysis had conflicting results. One reported positive results; whereas the other was negative.

The European Society of Cardiology and the European Association for Cardiovascular Prevention and Rehabilitation have developed an interactive tool for prediction and managing the risk of heart attack and stroke in Europe. HeartScore is aimed at supporting clinicians in optimising individual cardiovascular risk reduction. The Heartscore Programme is available in 12 languages and offers web based or PC version.

Treatment

Stroke unit

Ideally, people who have had a stroke are admitted to a "stroke unit", a ward or dedicated area in hospital staffed by nurses and therapists with experience in stroke treatment. It has been shown that people admitted to a stroke unit have a higher chance of surviving than those admitted elsewhere in hospital, even if they are being cared for by doctors without experience in stroke.

When an acute stroke is suspected by history and physical examination, the goal of early assessment is to determine the cause. Treatment varies according to the underlying cause of the stroke, thromboembolic (ischemic) or hemorrhagic. A non-contrast head CT scan can rapidly identify a hemorrhagic stroke by imaging bleeding in or around the brain. If no bleeding is seen, a presumptive diagnosis of ischemic stroke is made.

Treatment of ischemic stroke

An ischemic stroke is caused by a thrombus (blood clot) occluding blood flow to an artery supplying the brain. Definitive therapy is aimed at removing the blockage by breaking the clot down (thrombolysis), or by removing it mechanically (thrombectomy). The more rapidly blood flow is restored to the brain, the fewer brain cells die.

Other medical therapies are aimed at minimizing clot enlargement or preventing new clots from forming. To this end, treatment with medications such as aspirin, clopidogrel and dipyridamole may be given to prevent platelets from aggregating.

In addition to definitive therapies, management of acute stroke includes control of blood sugars, ensuring the patient has adequate oxygenation and adequate intravenous fluids. Patients may be positioned with their heads flat on the stretcher, rather than sitting up, to

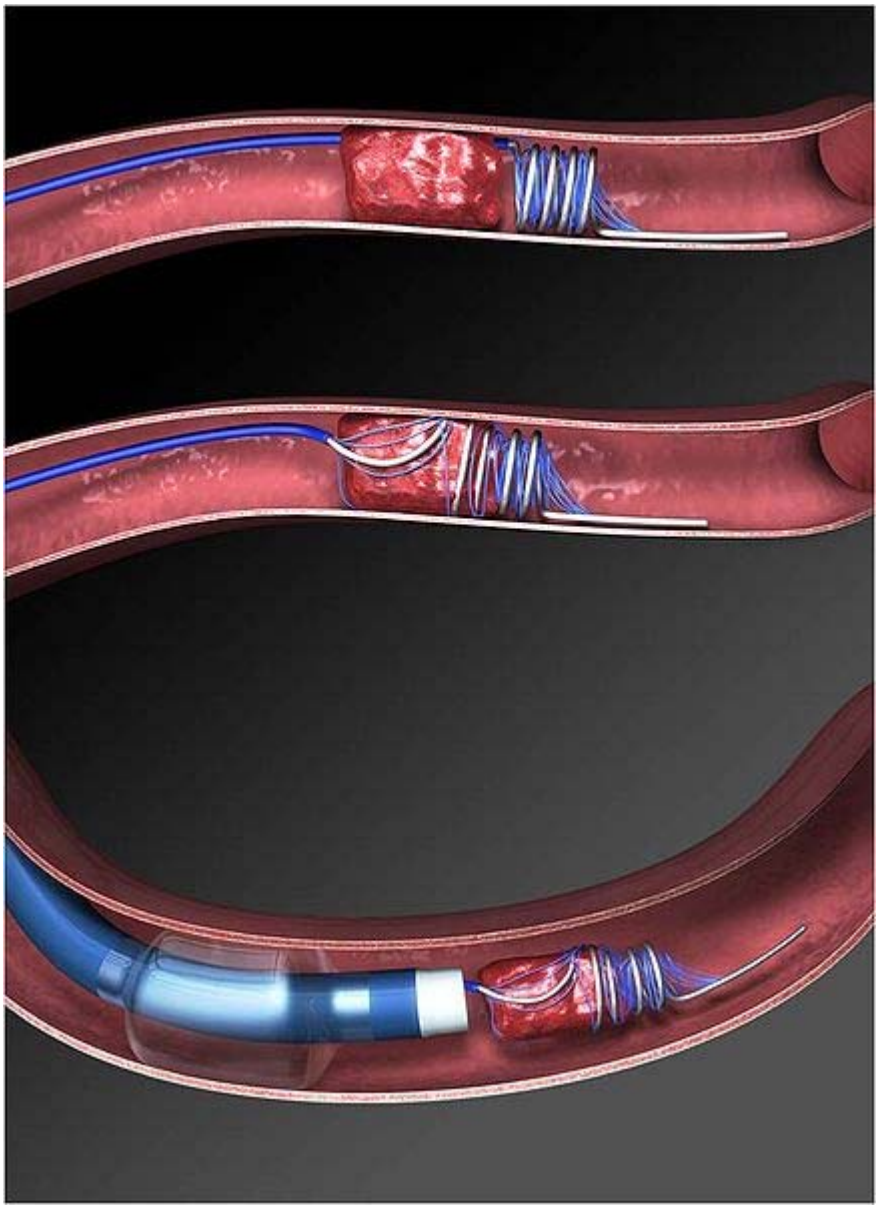
increase blood flow to the brain. It is common for the blood pressure to be elevated immediately following a stroke. Although high blood pressure may cause some strokes, hypertension during acute stroke is desirable to allow adequate blood flow to the brain.

Thrombolysis

In increasing numbers of primary stroke centers, pharmacologic thrombolysis ("clot busting") with the drug tissue plasminogen activator (tPA), is used to dissolve the clot and unblock the artery. However, the use of tPA in acute stroke is controversial. On one hand, it is endorsed by the American Heart Association and the American Academy of Neurology as the recommended treatment for acute stroke within three hours of onset of symptoms as long as there are not other contraindications (such as abnormal lab values, high blood pressure, or recent surgery). This position for tPA is based upon the findings of two studies by one group of investigators which showed that tPA improves the chances for a good neurological outcome. When administered within the first three hours, 39% of all patients who were treated with tPA had a good outcome at three months, only 26% of placebo controlled patients had a good functional outcome. A recent study using alteplase for thrombolysis in ischemic stroke suggests clinical benefit with administration 3 to 4.5 hours after stroke onset. However, in the NINDS trial 6.4% of patients with large strokes developed substantial brain hemorrhage as a complication from being given tPA. A recent study found the mortality to be higher among patients receiving tPA versus those who did not. Additionally, it is the position of the American Academy of Emergency Medicine that objective evidence regarding the efficacy, safety, and applicability of tPA for acute ischemic stroke is insufficient to warrant its classification as standard of care.

Intra-arterial fibrinolysis, where a catherter is passed up an artery into the brain and the medication is injected at the site of thrombosis, has been found to improve outcomes in people with acute ischemic stroke.

Mechanical thrombectomy



Merci Retriever L5

Another intervention for acute ischemic stroke is removal of the offending thrombus directly. This is accomplished by inserting a catheter into the femoral artery, directing it into the cerebral circulation, and deploying a corkscrew-like device to ensnare the clot, which is then withdrawn from the body. Mechanical embolectomy devices have been demonstrated effective at restoring blood flow in patients who were unable to receive thrombolytic drugs or for whom the drugs were ineffective, though no differences have been found between newer and older versions of the devices. The devices have only been tested on patients treated with mechanical clot embolectomy within eight hours of the onset of symptoms.

Angioplasty and stenting

Angioplasty and stenting have begun to be looked at as possible viable options in treatment of acute ischemic stroke. In a systematic review of six uncontrolled, single-center trials, involving a total of 300 patients, of intra-cranial stenting in symptomatic intracranial arterial stenosis, the rate of technical success (reduction to stenosis of <50%) ranged from 90-98%, and the rate of major peri-procedural complications ranged from 4-10%. The rates of restenosis and/or stroke following the treatment were also favorable. This data suggests that a large, randomized controlled trial is needed to more completely evaluate the possible therapeutic advantage of this treatment.

Secondary prevention of ischemic stroke

Anticoagulation can prevent recurrent stroke. Among patients with nonvalvular atrial fibrillation, anticoagulation can reduce stroke by 60% while antiplatelet agents can reduce stroke by 20%. However, a recent meta-analysis suggests harm from anti-coagulation started early after an embolic stroke. Stroke prevention treatment for atrial fibrillation is determined according to the CHADS/CHADS2 system. The most widely used anticoagulant to prevent thromboembolic stroke in patients with nonvalvular atrial fibrillation is the oral agent Warfarin while dabigatran is a new alternative which does not require prothrombin time monitoring.

If studies show carotid stenosis, and the patient has residual function in the affected side, carotid endarterectomy (surgical removal of the stenosis) may decrease the risk of recurrence if performed rapidly after stroke.

Treatment of hemorrhagic stroke

Patients with intracerebral hemorrhage require neurosurgical evaluation to detect and treat the cause of the bleeding, although many may not need surgery. Anticoagulants and antithrombotics, key in treating ischemic stroke, can make bleeding worse and cannot be used in intracerebral hemorrhage. Patients are monitored for changes in the level of consciousness, and their blood pressure, blood sugar, and oxygenation are kept at optimum levels.

Care and rehabilitation

Stroke rehabilitation is the process by which patients with disabling strokes undergo treatment to help them return to normal life as much as possible by regaining and relearning the skills of everyday living. It also aims to help the survivor understand and adapt to difficulties, prevent secondary complications and educate family members to play a supporting role.

A rehabilitation team is usually multidisciplinary as it involves staff with different skills working together to help the patient. These include nursing staff, physiotherapy, occupational therapy, speech and language therapy, and usually a physician trained in

rehabilitation medicine. Some teams may also include psychologists, social workers, and pharmacists since at least one third of the patients manifest post stroke depression. Validated instruments such as the Barthel scale may be used to assess the likelihood of a stroke patient being able to manage at home with or without support subsequent to discharge from hospital.

Good nursing care is fundamental in maintaining skin care, feeding, hydration, positioning, and monitoring vital signs such as temperature, pulse, and blood pressure. Stroke rehabilitation begins almost immediately.

For most stroke patients, physical therapy (PT) and occupational therapy (OT), speech-language pathology (SLP) are the cornerstones of the rehabilitation process. Often, assistive technology such as a wheelchair, walkers, canes, and orthosis may be beneficial. PT and OT have overlapping areas of working but their main attention fields are; PT involves re-learning functions as transferring, walking and other gross motor functions. OT focusses on exercises and training to help relearn everyday activities known as the Activities of daily living (ADLs) such as eating, drinking, dressing, bathing, cooking, reading and writing, and toileting. Speech and language therapy is appropriate for patients with the speech production disorders: dysarthria and apraxia of speech, aphasia, cognitive-communication impairments and/or dysphagia (problems with swallowing).

Patients may have particular problems, such as complete or partial inability to swallow, which can cause swallowed material to pass into the lungs and cause aspiration pneumonia. The condition may improve with time, but in the interim, a nasogastric tube may be inserted, enabling liquid food to be given directly into the stomach. If swallowing is still deemed unsafe, then a percutaneous endoscopic gastrostomy (PEG) tube is passed and this can remain indefinitely.

Stroke rehabilitation should be started as quickly as possible and can last anywhere from a few days to over a year. Most return of function is seen in the first few months, and then improvement falls off with the "window" considered officially by U.S. state rehabilitation units and others to be closed after six months, with little chance of further improvement. However, patients have been known to continue to improve for years, regaining and strengthening abilities like writing, walking, running, and talking. Daily rehabilitation exercises should continue to be part of the stroke patient's routine. Complete recovery is unusual but not impossible and most patients will improve to some extent : proper diet and exercise are known to help the brain to recover.

Prognosis

Disability affects 75% of stroke survivors enough to decrease their employability. Stroke can affect patients physically, mentally, emotionally, or a combination of the three. The results of stroke vary widely depending on size and location of the lesion. Dysfunctions correspond to areas in the brain that have been damaged.

Some of the physical disabilities that can result from stroke include muscle weakness, numbness, pressure sores, pneumonia, incontinence, apraxia (inability to perform learned movements), difficulties carrying out daily activities, appetite loss, speech loss, vision loss, and pain. If the stroke is severe enough, or in a certain location such as parts of the brainstem, coma or death can result.

Emotional problems resulting from stroke can result from direct damage to emotional centers in the brain or from frustration and difficulty adapting to new limitations. Post-stroke emotional difficulties include anxiety, panic attacks, flat affect (failure to express emotions), mania, apathy, and psychosis.

30 to 50% of stroke survivors suffer post stroke depression, which is characterized by lethargy, irritability, sleep disturbances, lowered self esteem, and withdrawal. Depression can reduce motivation and worsen outcome, but can be treated with antidepressants.

Emotional lability, another consequence of stroke, causes the patient to switch quickly between emotional highs and lows and to express emotions inappropriately, for instance with an excess of laughing or crying with little or no provocation. While these expressions of emotion usually correspond to the patient's actual emotions, a more severe form of emotional lability causes patients to laugh and cry pathologically, without regard to context or emotion. Some patients show the opposite of what they feel, for example crying when they are happy. Emotional lability occurs in about 20% of stroke patients.

Cognitive deficits resulting from stroke include perceptual disorders, speech problems, dementia, and problems with attention and memory. A stroke sufferer may be unaware of his or her own disabilities, a condition called anosognosia. In a condition called hemispatial neglect, a patient is unable to attend to anything on the side of space opposite to the damaged hemisphere.

Up to 10% of all stroke patients develop seizures, most commonly in the week subsequent to the event; the severity of the stroke increases the likelihood of a seizure.

Epidemiology

Stroke could soon be the most common cause of death worldwide. Stroke is currently the second leading cause of death in the Western world, ranking after heart disease and before cancer, and causes 10% of deaths worldwide. Geographic disparities in stroke incidence have been observed, including the existence of a "stroke belt" in the southeastern United States, but causes of these disparities have not been explained.

The incidence of stroke increases exponentially from 30 years of age, and etiology varies by age. Advanced age is one of the most significant stroke risk factors. 95% of strokes occur in people age 45 and older, and two-thirds of strokes occur in those over the age of 65. A person's risk of dying if he or she does have a stroke also increases with age. However, stroke can occur at any age, including in childhood.

Family members may have a genetic tendency for stroke or share a lifestyle that contributes to stroke. Higher levels of Von Willebrand factor are more common amongst people who have had ischemic stroke for the first time. The results of this study found that the only significant genetic factor was the person's blood type. Having had a stroke in the past greatly increases one's risk of future strokes.

Men are 25% more likely to suffer strokes than women, yet 60% of deaths from stroke occur in women. Since women live longer, they are older on average when they have their strokes and thus more often killed (NIMH 2002). Some risk factors for stroke apply only to women. Primary among these are pregnancy, childbirth, menopause and the treatment thereof (HRT).

History

Hippocrates first described the sudden paralysis that is often associated with stroke

Episodes of stroke and familial stroke have been reported from the 2nd millennium BC onward in ancient Mesopotamia and Persia. Hippocrates (460 to 370 BC) was first to describe the phenomenon of sudden paralysis that is often associated with ischemia. Apoplexy, from the Greek word meaning "struck down with violence," first appeared in Hippocratic writings to describe this phenomenon.

The word *stroke* was used as a synonym for apoplectic seizure as early as 1599, and is a fairly literal translation of the Greek term.

In 1658, in his *Apoplexia*, Johann Jacob Wepfer (1620–1695) identified the cause of hemorrhagic stroke when he suggested that people who had died of apoplexy had bleeding in their brains. Wepfer also identified the main arteries supplying the brain, the vertebral and carotid arteries, and identified the cause of ischemic stroke [also known as cerebral infarction] when he suggested that apoplexy might be caused by a blockage to those vessels.

Chapter 12

Parkinson's Disease

Parkinson's disease	

Illustration of Parkinson's disease by William Richard Gowers from *A Manual of Diseases of the Nervous System* in 1886

ICD-10	G20., F02.3
ICD-9	332
OMIM	168600 556500
DiseasesDB	9651
MedlinePlus	000755
eMedicine	neuro/304 neuro/635 in young pmr/99 rehab
GeneReviews	Parkinson Disease Overview

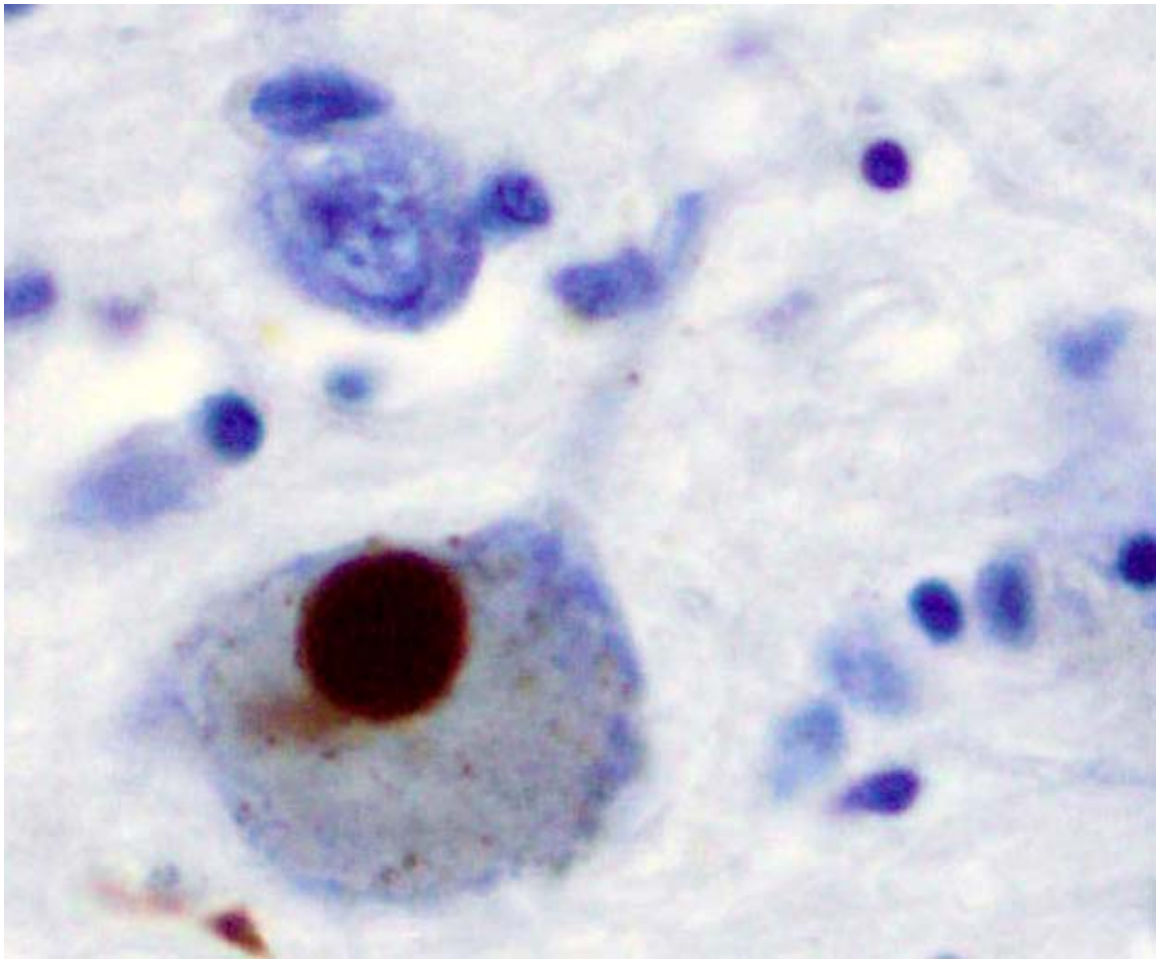
Parkinson's disease (also known as **Parkinson disease**, **Parkinson's**, **idiopathic parkinsonism**, **primary parkinsonism**, **PD** or **paralysis agitans**) is a progressive degenerative disorder of the central nervous system. Early in the course of the disease, the most obvious symptoms are movement-related, including shaking, rigidity, slowness of movement and difficulty with walking and gait. Later, cognitive and behavioural problems may arise, with dementia commonly occurring in the advanced stages of the disease. Other symptoms include sensory, sleep and emotional problems. PD typically becomes apparent around the age of 60 years and is unusual before the age of 40 years.

The main symptoms are collectively called parkinsonism, or sometimes a "parkinsonian syndrome". They can arise from a variety of causes. Parkinson's disease is often defined as a Parkinsonian syndrome that is idiopathic (has no known cause), although some atypical cases have a genetic origin. Many risk and protective factors have been investigated: the clearest evidence is for an increased risk of PD in people exposed to certain pesticides and a reduced risk in tobacco smokers. The pathology of the disease is characterized by the accumulation of a protein called alpha-synuclein into inclusions called Lewy bodies in neurons, and from insufficient formation and activity of dopamine produced in certain neurons of parts of the midbrain. Diagnosis of typical cases is mainly based on symptoms, with tests such as neuroimaging being used for confirmation.

Modern treatments are effective at managing the early motor symptoms of the disease, mainly through the use of levodopa and dopamine agonists. As the disease progresses and dopamine neurons continue to be lost, a point eventually arrives at which these drugs become ineffective at treating the symptoms, while at the same time produce a complication called dyskinesia, marked by writhing movements. Medications to treat other symptoms of PD exist. Diet and some forms of rehabilitation have shown some effectiveness at alleviating symptoms. Surgery and deep brain stimulation have been used to reduce motor symptoms as a last resort in severe cases where drugs are ineffective. Research directions include a search of new animal models of the disease and investigations of the potential usefulness of gene therapy, stem cell transplants and neuroprotective agents.

The disease is named after the English doctor James Parkinson, who published the first detailed description in *An Essay on the Shaking Palsy* (1817). PD is a costly disease to society: inpatient care and nursing homes account for the highest costs. The total burden may reach 23 billion dollars per year in the United States. Several major organizations promote research and improvement of quality of life of those with the disease and their families. Public awareness campaigns include Parkinson's disease day on the birthday of James Parkinson, April 11, and the use of a red tulip as the symbol of the disease. People with parkinsonism who have enhanced public awareness include Michael J. Fox and Muhammad Ali.

Classification



Positive alpha-synuclein staining of a Lewy body in a brain affected by Parkinson's disease. Presence of Lewy bodies in the brains of those with PD has led to the classification of the disease as a synucleinopathy.

The term parkinsonism is used for a motor syndrome whose main symptoms are tremor at rest, stiffness, slowing of movement and postural instability. Parkinsonian syndromes can be divided into four subtypes according to their origin: primary or idiopathic, secondary or acquired, hereditary parkinsonism, and parkinson plus syndromes or multiple system degeneration. Parkinson's disease is the most common form of parkinsonism and is usually defined as "idiopathic" parkinsonism, meaning parkinsonism with no identifiable cause.

PD is usually classified as a movement disorder, although it also gives rise to several non-motor types of symptoms such as cognitive difficulties or sleep problems. Parkinson plus diseases are primary parkinsonisms which present additional features. They include multiple system atrophy, progressive supranuclear palsy, corticobasal degeneration and dementia with Lewy bodies.

In terms of pathophysiology, PD is considered a synucleinopathy due to an abnormal accumulation of alpha-synuclein protein in the brain in the form of Lewy bodies, as opposed to other diseases such as Alzheimer's disease where the brain accumulates tau protein in the form of neurofibrillary tangles. Nevertheless, there is clinical and pathological overlap between tauopathies and synucleinopathies. The most typical symptom of Alzheimer's disease, dementia, occurs in advanced stages of PD, while it is common to find neurofibrillary tangles in brains affected by PD.

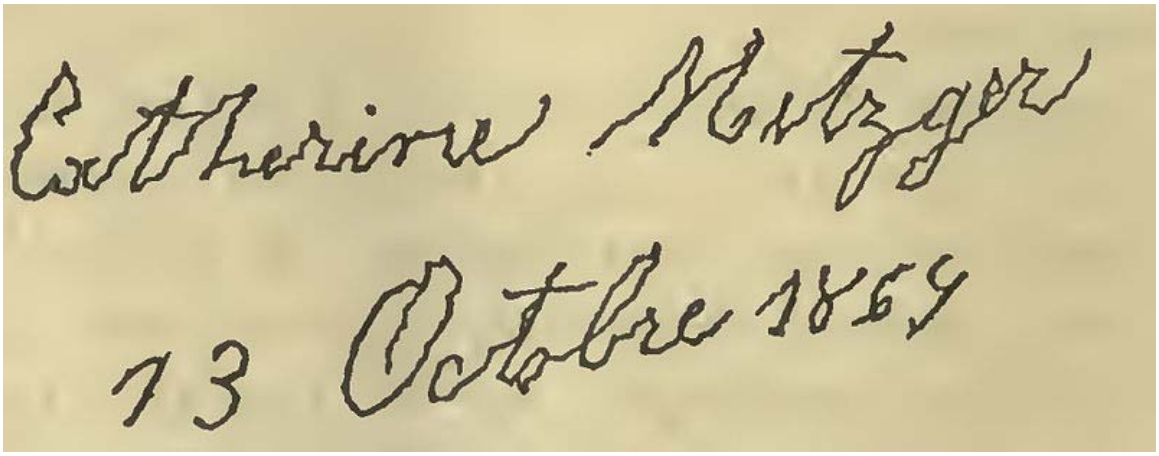
Dementia with Lewy bodies is another synucleinopathy that has many similarities with PD. Thus dementia with Lewy bodies and Parkinson's disease may be considered parts of the same continuum, and this is even more clear for the subset of PD cases with dementia. However the relationship between the two diseases is complex and still has to be clarified.

Signs and symptoms

Person with Parkinson's disease displaying a flexed walking posture pictured in 1892. Photo appeared in *Nouvelle Iconographie de la Salpètrière*, vol. 5.

Parkinson's disease affects movement, producing motor symptoms. Non-motor symptoms, which include autonomic dysfunction, neuropsychiatric problems (mood, cognition, behavior or thought alterations), and sensory and sleep difficulties, are common.

Motor



Handwriting of a person affected by PD in *Lectures on the diseases of the nervous system* by Charcot (1879)

Four motor symptoms are considered cardinal in PD: tremor, rigidity, slowness of movement, and postural instability.

Tremor is the most apparent and well-known symptom. It is the most common; though around 30% of individuals with PD do not have tremor at disease onset, most develop it as the disease progresses. It is usually a rest tremor: maximal when the limb is at rest and disappearing with voluntary movement and sleep. It affects to a greater extent the most distal part of the limb and at onset typically appears in only a single arm or leg, becoming bilateral later. Frequency of PD tremor is between 4 and 6 hertzs (cycles per second). A feature of tremor is "pill-rolling", a term used to describe the tendency of the index finger of the hand to get into contact with the thumb and perform together a circular movement. Such term was given due to the similarity of the movement in PD patients with the former pharmaceutical technique of manually making pills.

Bradykinesia (slowness of movement) is the most characteristic clinical feature of PD and is associated with difficulties along the whole course of the movement process, from planning to initiation and finally execution of a movement. The performance of sequential and simultaneous movements is hindered. Bradykinesia is the most disabling symptom in the early stages of the disease. Initial manifestations of bradykinesia are problems when performing daily life tasks requiring fine motor control such as writing, sewing or getting dressed. Clinical evaluation is based in similar tasks consisting such as alternating movements between both hands or feet. Bradykinesia is not equal for all movements or times. It is modified by the activity or emotional state of the subject to the

point of some patients barely able to walk yet being capable of riding a bicycle. Generally patients have less difficulty when some short of external cue is provided.

Rigidity is due to joint stiffness and increased muscle tone, which combined with a resting tremor produce a ratchety, "cogwheel rigidity" when the limb is passively moved. Rigidity may be associated with joint pain; such pain being a frequent initial manifestation of the disease. In the late stages postural instability is typical, which leads to impaired balance and frequent falls. Instability is often absent in the initial stages, especially in younger people.

Other motor symptoms include gait and posture disturbances such as festination (rapid shuffling steps and a forward-flexed posture when walking), speech and swallowing disturbances; mask-like face expression or small handwriting but there is a big range of motor problems that can appear.

Neuropsychiatric

Parkinson's disease causes neuropsychiatric disturbances, which include cognition, thought, mood and behavior alterations, and can be as disabling as motor symptoms.

A high proportion of people with PD will have mild cognitive impairment as the disease advances although in some cases cognitive disturbances can occur in the initial stages of the disease. The most common cognitive deficits in affected individuals without dementia are executive dysfunction. The executive system is responsible for planning, cognitive flexibility, abstract thinking, rule acquisition, initiating appropriate actions and inhibiting inappropriate actions, and selecting relevant sensory information. Individuals with PD may have problems with these cognitive processes. Fluctuations in attention and slowed cognitive speed are among other cognitive difficulties. Memory is affected, specifically in recalling learned information. Nevertheless, improvement appears when recall is aided by cues. Visuospatial difficulties are part of the disease, which are for example seen when the individual is asked to perform tests of facial recognition and perception of the orientation of drawn lines.

Deficits tend to aggravate with time, in many cases developing into dementia. A person with PD has a sixfold increased risk of suffering dementia, and the overall rate in people with the disease is around 30%. Prevalence of dementia increases in relation to disease duration, going up to 80%. Dementia has been associated with a reduced quality of life in people with PD and their caregivers, increased mortality and a higher probability of attending a nursing home.

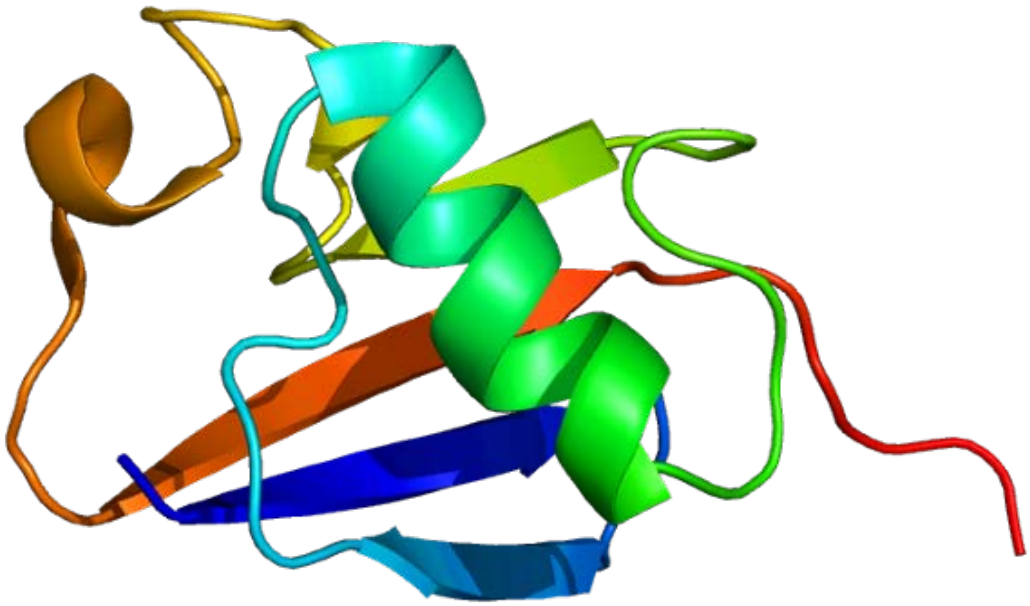
Cognitive problems and dementia are usually accompanied by behavior and mood alterations, although these kind of changes are more common in those without cognitive impairment than in the general population. Most frequent mood difficulties include depression, apathy and anxiety. Impulse control behaviors such as medication overuse and craving, binge eating, hypersexuality, or pathological gambling can appear in PD and

have been related to the medications for the disease. Psychotic symptoms—hallucinations or delusions—are common in late PD.

Other

In addition to cognitive and motor symptoms, PD can impair other body functions. Sleep problems are a core feature of the disease and can be worsened by medications. They can manifest as daytime drowsiness, disturbances in REM sleep, or insomnia. Alterations in the autonomic nervous system can lead to orthostatic hypotension, oily skin and seborrheic dermatitis, excessive sweating, urinary incontinence and altered sexual function. Constipation and gastric dysmotility can be severe enough to cause discomfort and even endanger health. PD is related to several eye and vision abnormalities such as decreased blink rate and alteration in the tear film leading to irritation of the eye surface, abnormalities in ocular pursuit and saccadic movements, and difficulties in directing gaze upward. Changes in perception may include an impaired sense of smell, sensation of pain, and paresthesia. All these symptoms occur in many cases years before diagnosis of the disease.

Causes



PDB rendering of Parkin

Most people with Parkinson's disease have idiopathic Parkinson's disease (having no specific known cause). A small proportion of cases, however, can be attributed to known genetic factors.

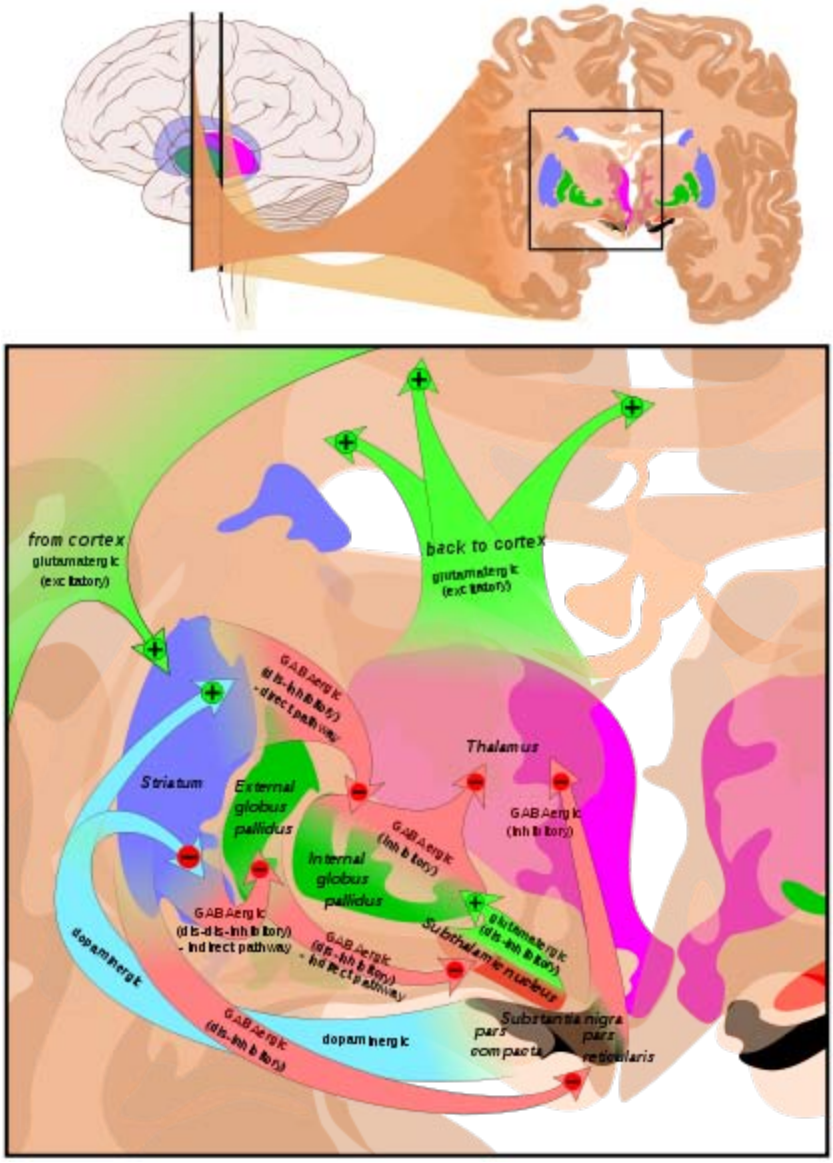
PD traditionally has been considered a non-genetic disorder, however, around 15% of individuals with PD have a first-degree relative who has the disease. At least 5% of people are now known to have forms of the disease that occur due to a mutation of one of several specific genes.

Mutations in specific genes have been conclusively shown to cause PD. These include alpha-synuclein (SNCA), ubiquitin carboxy-terminal hydrolase L1 (UCH-L1), parkin (PRKN), leucine-rich repeat kinase 2 (LRRK2 or dardarin), PTEN-induced putative kinase 1 (PINK1), DJ-1 and ATP13A2. In most cases, people with these mutations will develop PD. With the exception of LRRK2, however, they account for only a small minority of cases of PD. The most extensively studied PD-related genes are SNCA and LRRK2. Mutations in genes including SNCA, LRRK2 and glucocerebrosidase (GBA), have been found to be risk factors for sporadic PD. Mutations in GBA are known to cause Gaucher's disease. Genome-wide association studies, which search for mutated alleles with low penetrance in sporadic cases, have yielded few positive results, but such studies have been few in number and their size small.

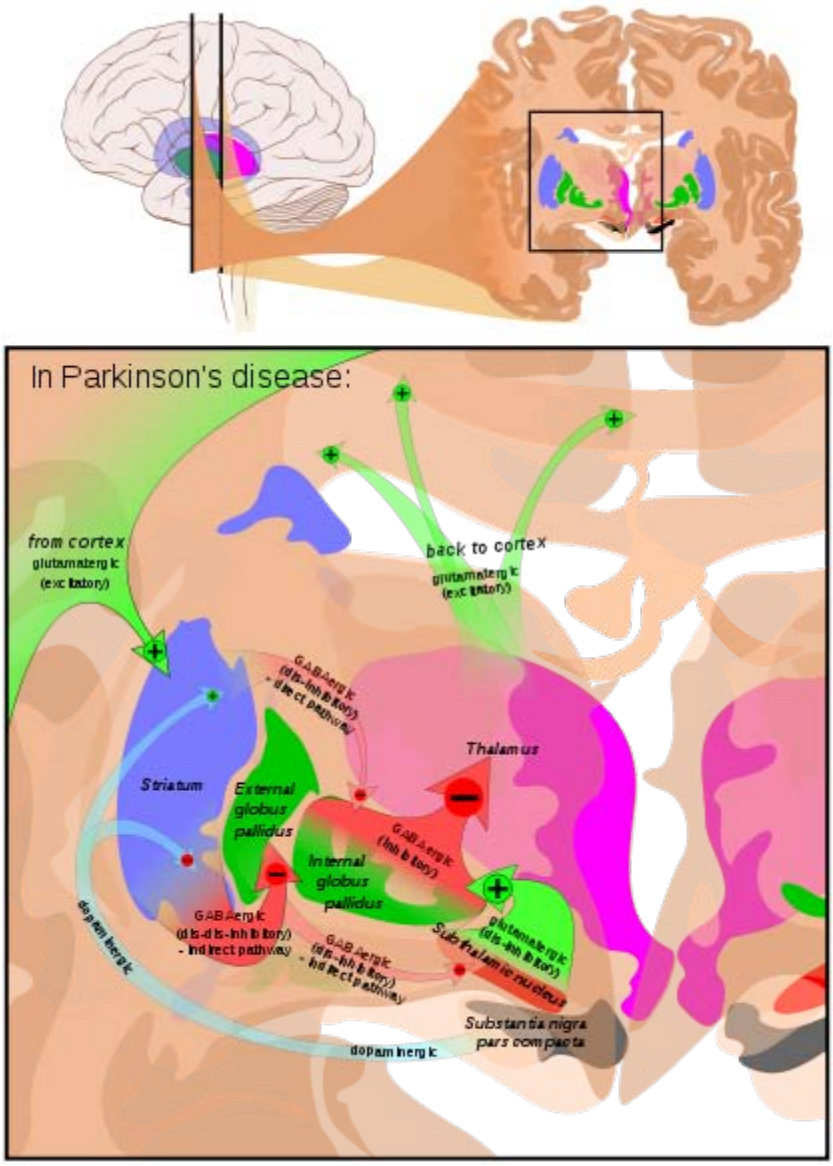
The role of the SNCA gene is important in PD because the alpha-synuclein protein is the main component of Lewy bodies. Missense mutations (mutation in which a single nucleotide is changed) of the gene, and duplications and triplications of the locus containing it, have been found in different groups with familial PD. Missense mutations are rare. On the other hand, multiplications of the SNCA locus account for around 2% of familial cases. Multiplications have been found in asymptomatic carriers, which indicate that penetrance is incomplete or age-dependent.

The LRRK2 gene (PARK8) encodes for a protein called dardarin. The name dardarin was taken from a Basque word for tremor, because this gene was first identified in families from England and the north of Spain. Mutations in LRRK2 are the most common known cause of familial and sporadic PD, accounting for up to 10% of individuals with a family history of the disease and 3% of sporadic cases. More than 40 different mutations of the gene have been found to be related to PD.

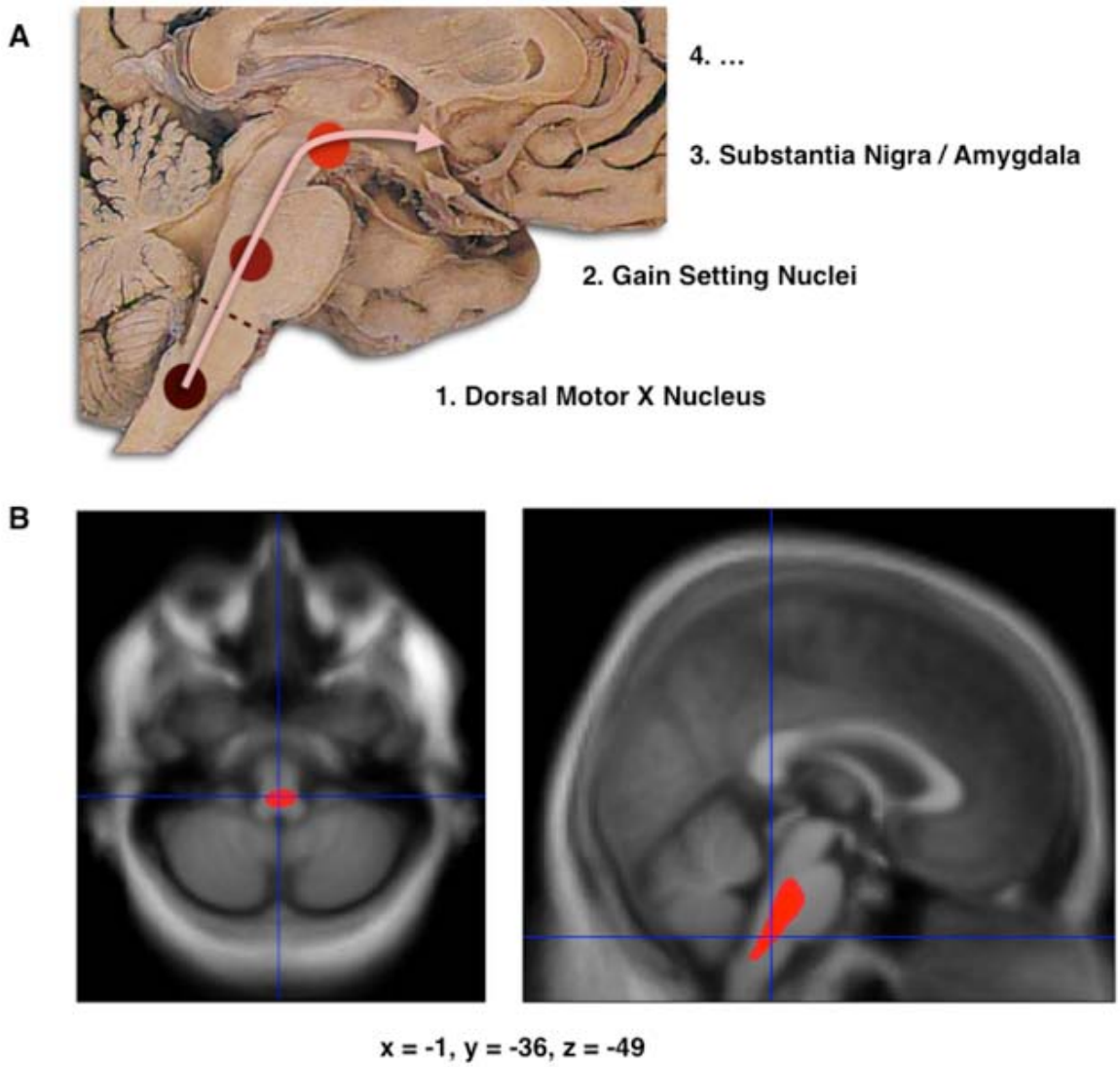
Pathophysiology



Connections of the basal ganglia in the normal state



Connections of the basal ganglia in Parkinson's disease, resulting from decreased activity of the pars compacta region of the substantia nigra. Larger and smaller arrows refer to pathways with increased and decreased activity, respectively, in Parkinson's disease.
Model of the circuits of the basal ganglia in the normal state (left) and PD (right). Substantia nigra is seen at bottom right. Pictures show 2 coronal slices that have been superimposed to include the involved basal ganglia structures. + and – signs at the point of the arrows indicate respectively whether the pathway is excitatory or inhibitory in effect. Green arrows refer to excitatory glutamatergic pathways, red arrows refer to inhibitory GABAergic pathways and turquoise arrows refer to dopaminergic pathways that are excitatory on the direct pathway and inhibitory on the indirect pathway. Dis-inhibitory pathways are in effect excitatory on the feedback to the cortex, while dis-dis-inhibitory pathways are inhibitory



A. Schematic initial progression of Lewy body deposits in the first stages of Parkinson's disease, as proposed by Braak and colleagues B. Localization of the area of significant brain volume reduction in initial PD compared with a group of participants without the disease in a neuroimaging study which concluded that brain stem damage may be the first identifiable stage of PD neuropathology

The basal ganglia, a group of "brain structures" innervated by the dopaminergic system, are the most seriously affected brain areas in PD. The primary symptoms of Parkinson's disease result from greatly reduced activity of dopamine-secreting cells due to cell death in the pars compacta region of the substantia nigra. The most characteristic pathological finding in PD is a progressive accumulation of Lewy bodies in the substantia nigra and several other brain regions.

There are five major pathways in the brain connecting other brain areas with the basal ganglia. These are known as the motor, oculo-motor, associative, limbic and orbitofrontal circuits, with names indicating the main projection area of each circuit. All of them are

affected in PD and their disruption explains many of the symptoms of the disease since these circuits are involved in a wide variety of functions including movement, attention and learning. Scientifically, the motor circuit has been examined the most intensively.

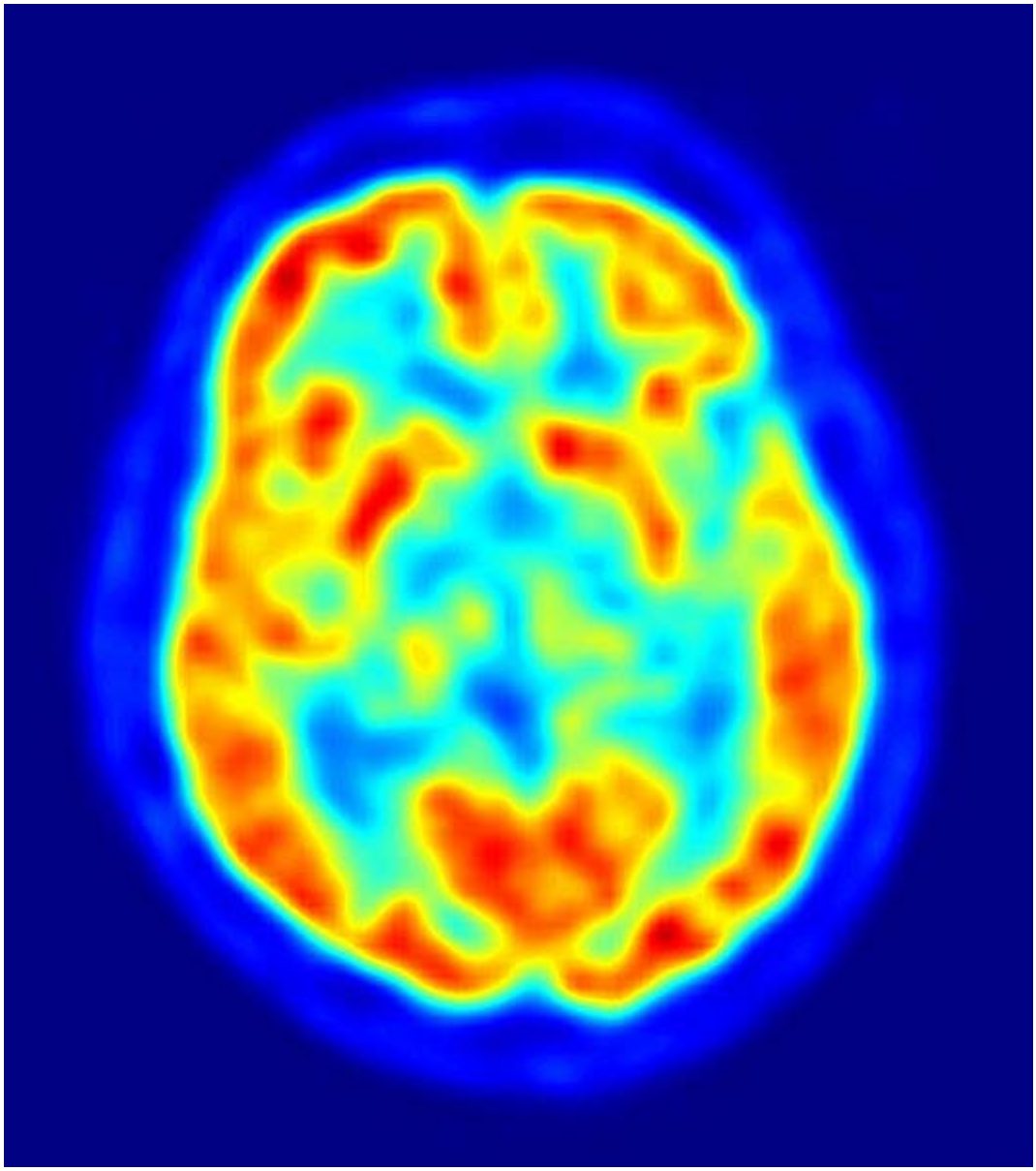
A particular conceptual model of the motor circuit and its alteration with PD has been of great influence since 1980, although some limitations have been pointed out which have led to modifications. In this model, the basal ganglia normally exert a constant inhibitory influence on a wide range of motor systems, preventing them from becoming active at inappropriate times. When a decision is made to perform a particular action, inhibition is reduced for the required motor system, thereby releasing it for activation. Dopamine acts to facilitate this release of inhibition, so high levels of dopamine function tend to promote motor activity, while low levels of dopamine function, such as occur in PD, demand greater exertions of effort for any given movement. Thus the net effect of dopamine depletion is to produce hypokinesia, an overall reduction in motor output. Drugs that are used to treat PD, conversely, may produce excessive dopamine activity, allowing motor systems to be activated at inappropriate times and thereby producing dyskinesias.

The main pathological characteristic of PD is cell death in the substantia nigra and, more specifically, the ventral (front) part of the pars compacta, affecting up to 70% of the cells by the time death occurs. Macroscopically alterations can be noticed inside the brainstem, where neuronal loss can be inferred from a reduction of melanin pigmentation in the substantia nigra and locus coeruleus. The study of the microscopic anatomy of the affected tissues (histology) shows that neuronal loss is accompanied by astrocytes (star-shaped glial cells) death and activation of the microglia (another type of glial cells).

There are several mechanisms by which the brain cells are lost. One mechanism consists of an abnormal accumulation of the protein alpha-synuclein bound to ubiquitin in the damaged cells. This protein accumulation forms insoluble inclusions called Lewy bodies. According to the Braak staging, a classification of the disease based on pathological findings, Lewy bodies (LB) first appear in the olfactory bulb, medulla oblongata and pontine tegmentum, with individuals at this stage being asymptomatic. As the disease progresses, LB later develop in the substantia nigra, areas of the midbrain and basal forebrain, and in a last step the neocortex. These brain sites are the main places of neuronal degeneration in PD, so it is believed that LB are related to cell death. In patients with dementia, a generalized presence of LB is common in cortical areas. Neurofibrillary tangles and senile plaques, characteristic of Alzheimer's disease, are not common unless the person is demented.

Other cell-death mechanisms include proteosomal and lysosomal system dysfunction and reduced mitochondrial activity. Iron accumulation in the substantia nigra is typically observed in conjunction with the protein inclusions. It may be related to oxidative stress, protein aggregation and neuronal death, but the mechanisms are not fully understood.

Diagnosis



Fludeoxyglucose (18F) PET scan of a healthy brain. A decreased dopamine activity in the basal ganglia can aid in diagnosing Parkinson's disease.

A diagnosis of Parkinson's disease is usually made based on the medical history and neurological examination. The physician conducts an interview, looking for cardinal motor symptoms, while attending to other possible symptoms that would exclude a diagnosis of PD. Reduction of motor impairment in response to administration of levodopa markedly increases the likelihood of PD. There is no definitive test for diagnosis, but finding Lewy bodies during autopsy has traditionally been considered the gold standard. Common presentations of the disease are usually easily diagnosed. On the other hand, diagnosis can be difficult when the symptoms are not fully typical of PD,

since parkinsonism can occur due to a range of causes and the difference with PD may be subtle, particularly in the early stages when symptoms may be mild.

Medical organizations have created diagnostic criteria to ease and standardize the diagnostic process, especially in the early stages of the disease. The most widely known criteria come from the UK Parkinson's Disease Society Brain Bank and the US National Institute of Neurological Disorders and Stroke. The PD Society Brain Bank criteria require slowness of movement (bradykinesia) plus either rigidity, resting tremor, or postural instability. Other possible causes for these symptoms need to be ruled out. Finally, three or more of the following features are required during onset or evolution: unilateral onset, tremor at rest, progression in time, asymmetry of motor symptoms, response to levodopa for at least five years, clinical course of at least ten years and appearance of dyskinesias induced by the intake of excessive levodopa. Accuracy of diagnostic criteria evaluated at autopsy is 75–90%, with specialists such as neurologists having the highest rates.

Differential diagnosis requires distinguishing PD from other kinds of tremors and other causes of parkinsonism. Other tremors include postural and action tremors or intention tremor. Other causes that can secondarily produce a parkinsonian syndrome are Alzheimer's disease, multiple cerebral infarction and drug-induced parkinsonism. Parkinson plus syndromes such as progressive supranuclear palsy and multiple system atrophy must be ruled out. Anti-Parkinson's medications are typically less effective at controlling symptoms in Parkinson plus syndromes. Faster progression rates, early cognitive dysfunction or postural instability, minimal tremor or symmetry at onset may indicate a Parkinson plus disease rather than PD itself. Genetic forms are usually classified as PD, although the terms *familial Parkinson's disease* and *familial parkinsonism* are used for disease entities with an autosomal dominant or recessive pattern of inheritance.

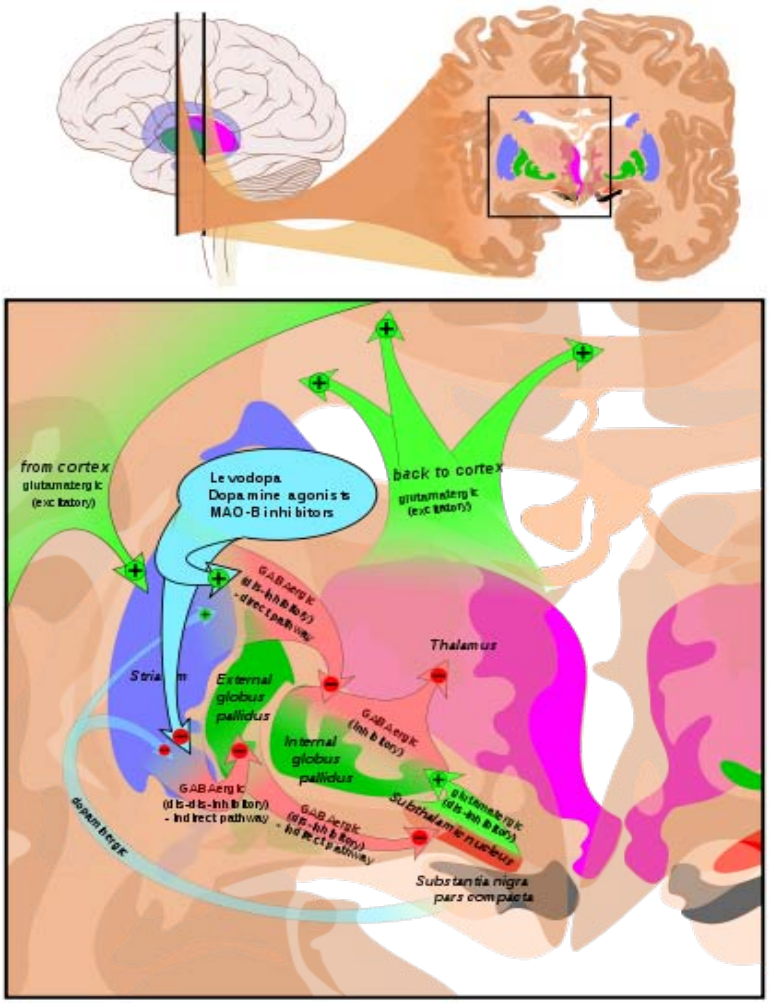
Computed tomography (CT) and magnetic resonance imaging (MRI) brain scans of people with PD usually appear normal. These techniques are nevertheless useful to rule out other diseases that can be secondary causes of parkinsonism, such as basal ganglia tumors, vascular pathology and hydrocephalus. A specific technique of MRI, diffusion MRI, has been reported to be useful at discriminating between typical and atypical parkinsonism, although its exact diagnostic value is still under investigation. Dopaminergic function in the basal ganglia can be measured with the help of different PET and SPECT radiotracers. Examples are ioflupane (^{123}I) (trade name *DaTSCAN*) and iometopane (*Dopascan*) for SPECT or fludeoxyglucose (^{18}F) for PET. A pattern of reduced dopaminergic activity in the basal ganglia, can aid in diagnosing PD.

Management

There is no cure for Parkinson's disease, but medications, surgery and multidisciplinary management can provide relief from the symptoms. The main families of drugs useful for treating motor symptoms are levodopa (usually combined with a dopa decarboxylase inhibitor or COMT inhibitor), dopamine agonists and MAO-B inhibitors. The stage of the

disease determines which group is most useful. Two stages are usually distinguished: an initial stage in which the individual with PD has already developed some disability for which he needs pharmacological treatment, then a second stage in which an individual develops motor complications related to levodopa usage. Treatment in the initial stage aims for an optimal tradeoff between good symptom control and side-effects resulting from enhancement of dopaminergic function. The start of L-DOPA treatment may be delayed by using other medications such as MAO-B inhibitors and dopamine agonists, in the hope of delaying the onset of dyskinesias. In the second stage the aim is to reduce symptoms while controlling fluctuations of the response to medication. Sudden withdrawals from medication or overuse have to be managed. When medications are not enough to control symptoms, surgery and deep brain stimulation can be of use. Palliative care is especially important in the late stages.

Levodopa



Circuits of the basal ganglia in treatment of Parkinson's disease. Model of the effect of medication on motor symptoms: levodopa, dopamine agonists and MAO-B inhibitors stimulate excitatory signals from the thalamus to the cortex by effects on the striatum,

compensating for decreased dopaminergic signals from substantia nigra (seen at bottom right).

Levodopa (or L-DOPA) has been the most widely used treatment for over 30 years. L-DOPA is converted into dopamine in the dopaminergic neurons by dopa decarboxylase. Since motor symptoms are produced by a lack of dopamine in the substantia nigra, the administration of L-DOPA temporarily diminishes the motor symptoms.

Only 5–10% of L-DOPA crosses the blood-brain barrier. The remainder is often metabolized to dopamine elsewhere, causing a variety of side effects including nausea, dyskinesias and joint stiffness. Carbidopa and benserazide are peripheral dopa decarboxylase inhibitors. They help to prevent the metabolism of L-DOPA before it reaches the dopaminergic neurons, therefore reducing side effects and increasing bioavailability. They are generally given as combination preparations with levodopa. Existing preparations are carbidopa/levodopa (co-careldopa, trade names *Sinemet*, *Parcopa*, *Atamet*) and benserazide/levodopa (co-beneldopa, trade name *Madopar*). Levodopa has been related to dopamine dysregulation syndrome, which is a compulsive overuse of the medication, and punding. There are controlled release versions of levodopa in the form intravenous and intestinal infusions that spread out the effect of the medication. These slow-release levodopa preparations have not shown an increased control of motor symptoms or motor complications when compared to immediate release preparations.

Tolcapone inhibits the COMT enzyme, which degrades dopamine, thereby prolonging the effects of levodopa. It has been used to complement levodopa; however, its usefulness is limited by possible side effects such as liver damage. A similarly effective drug, entacapone, has not been shown to cause significant alterations of liver function. Commercial preparations of entacapone contain entacapone alone (*COMTan*) or in combination with carbidopa and levodopa (*Stalevo*).

Levodopa preparations lead in the long term to the development of motor complications characterized by involuntary movements called dyskinesias and fluctuations in the response to medication. When this occurs a person with PD can change from phases with good response to medication and few symptoms ("on" state), to phases with no response to medication and significant motor symptoms ("off" state). For this reason levodopa doses are kept as low as possible while maintaining functionality. Delaying the initiation of therapy with levodopa by using alternatives (dopamine agonists and MAO-B inhibitors) is common practice. A former strategy to reduce motor complications was to withdraw L-DOPA medication for some time. This is discouraged now since it can bring dangerous side effects such as neuroleptic malignant syndrome. Most people with PD will eventually need levodopa and later develop motor side effects.

Dopamine agonists

Several dopamine agonists that bind to dopaminergic post-synaptic receptors in the brain have similar effects to levodopa. These were initially used for individuals experiencing

on-off fluctuations and dyskinesias as a complementary therapy to levodopa; they are now mainly used on their own as an initial therapy for motor symptoms with the aim of delaying motor complications. When used in late PD they are useful at reducing the off periods. Dopamine agonists include bromocriptine, pergolide, pramipexole, ropinirole, piribedil, cabergoline, apomorphine and lisuride.

Dopamine agonists produce significant, although usually mild, side effects including drowsiness, hallucinations, insomnia, nausea and constipation. Sometimes side effects appear even at a minimal clinically effective dose, leading the physician to search for a different drug. Compared with levodopa, dopamine agonists may delay motor complications but are less effective at controlling symptoms. Nevertheless, they are usually effective enough to manage symptoms in the initial years. They tend to be more expensive than levodopa. Dyskinesias due to dopamine agonists are rare in younger people who have PD, but along with other side effects, become more common with age at onset. Thus dopamine agonists are the preferred initial treatment for earlier onset as opposed to levodopa in later onset. Agonists have been related to a impulse control disorders (such as compulsive sexual activity and eating, and pathological gambling and shopping) even more strongly than levodopa.

Apomorphine, a non-orally administered dopamine agonist, may be used to reduce off periods and dyskinesia in late PD. It is administered by intermittent injections or continuous subcutaneous infusions. Since secondary effects such as confusion and hallucinations are common, individuals receiving apomorphine treatment should be closely monitored. Two dopamine agonists that are administered through skin patches (lisuride and rotigotine) have been recently found to be useful for patients in initial stages and preliminary positive results has been published on the control of off states in patients in the advanced state.

MAO-B inhibitors

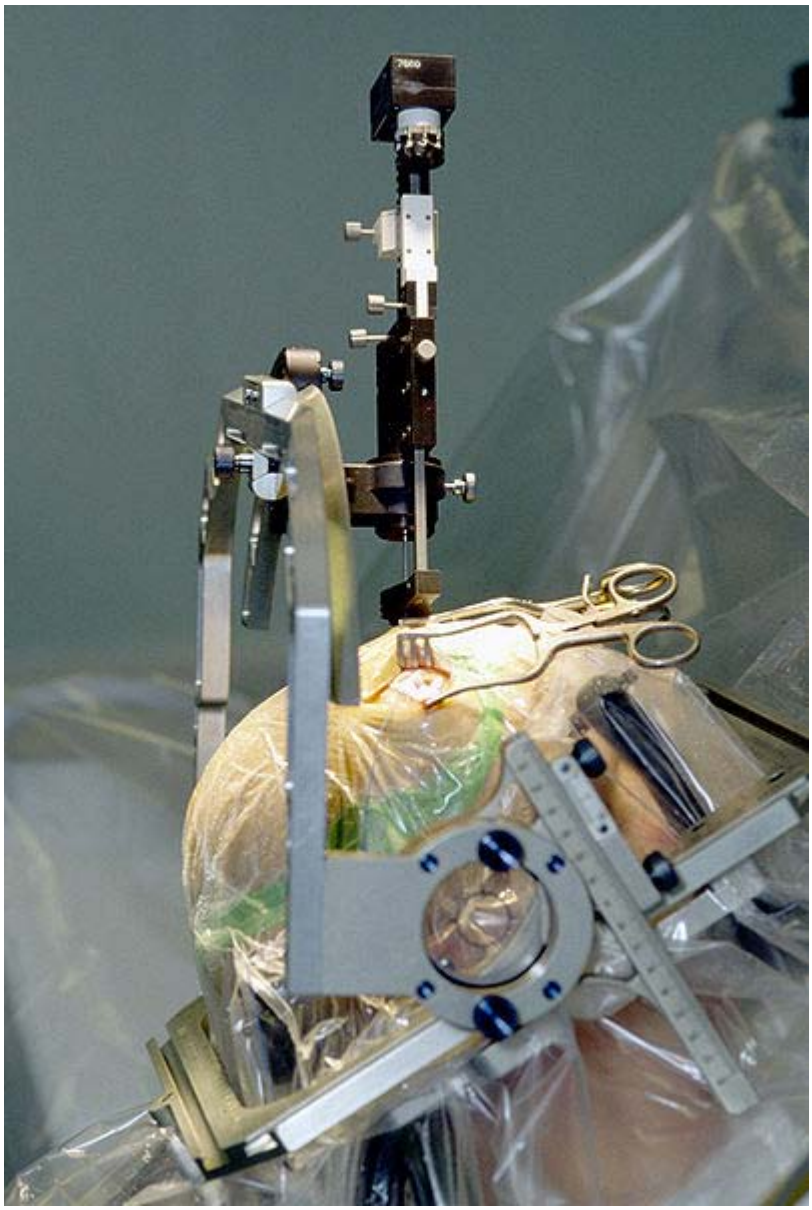
MAO-B inhibitors (selegiline and rasagiline) increase the level of dopamine in the basal ganglia by blocking its metabolism. They inhibit monoamine oxidase-B (MAO-B) which breaks down dopamine secreted by the dopaminergic neurons. The reduction in MAO-B activity results in increased L-DOPA in the striatum. Like dopamine agonists, MAO-B inhibitors used as monotherapy improve motor symptoms and delay the need for levodopa in early disease, but produce more adverse effects and are less effective than levodopa. There are few studies of their effectiveness in the advanced stage, although results suggest that they are useful to reduce fluctuations between on and off periods. An initial study indicated that selegiline in combination with levodopa increased the risk of death, but this was later disproven.

Other drugs

Other drugs such as amantadine and anticholinergics may be useful as treatment of motor symptoms. However, the evidence supporting them lacks quality, so they are not first choice treatments. In addition to motor symptoms, PD is accompanied by a range of

diverse symptoms. A number of drugs have been used to treat some of these problems. Examples are the use of clozapine for psychosis, cholinesterase inhibitors for dementia, and modafinil for daytime sleepiness.

Surgery and deep brain stimulation



Placement of an electrode, to be deep-seated in the brain

Treating motor symptoms with surgery was once a common practice, but since the discovery of levodopa, the number of operations has reduced. Studies in the past few decades have led to great improvements in surgical techniques, so that surgery is again being used in people with advanced PD for whom drug therapy is no longer sufficient. Deep brain stimulation (DBS) is the most commonly used surgical treatment. Other surgical therapies involve the formation of lesions in specific subcortical areas. DBS

involves the implantation of a medical device called a brain pacemaker, which sends electrical impulses to specific parts of the brain. Target areas for DBS or lesions include the thalamus, the globus pallidus (the lesion technique being called pallidotomy) or the subthalamic nucleus. DBS is recommended for people who have PD who suffer from motor fluctuations and tremor inadequately controlled by medication, or to those who are intolerant to medication, as long as they do not have severe neuropsychiatric problems.

Rehabilitation

There is some evidence that speech or mobility problems can improve with rehabilitation although studies are scarce and of low quality. Regular physical exercise and/or therapy can be beneficial to maintain and improve mobility, flexibility, strength, gait speed and quality of life. Exercise may improve constipation. One of the most widely practiced treatments for speech disorders associated with Parkinson's disease is the Lee Silverman voice treatment (LSVT). Speech therapy and specifically LSVT may improve speech. Occupational therapy (OT) aims to promote health and quality of life by helping people with the disease to participate in as many of their daily living activities as possible. There have been few studies on the effectiveness of OT and their quality is poor, although there is some indication that it may improve motor skills and quality of life for the duration of the therapy.

Diet

Muscles and nerves that control the digestive process may be affected by PD, resulting in constipation and gastroparesis (food remaining in the stomach for a longer period of time than normal). A balanced diet helps improve digestion. Diet should include high-fiber foods and plenty of water. As the disease advances, swallowing difficulties (dysphagia) may appear. In such cases it may be helpful to use thickening agents for liquid intake and an upright posture when eating, both measures reducing the risk of choking. Gastrostomy to deliver food directly into the stomach is possible in the worst cases.

Levodopa and proteins use the same transportation system in the intestine and the blood-brain barrier, thereby competing for access. When they are taken together, this results in a reduced effectiveness of the drug. Therefore, when levodopa is introduced, excessive protein consumption is discouraged. In advanced stages, additional intake of low-protein products such as bread or pasta is recommended for similar reasons. To minimize interaction with proteins, levodopa should be taken 30 minutes before meals. At the same time, regimens for PD restrict proteins during breakfast and lunch, allowing protein intake in the evening.

Palliative care

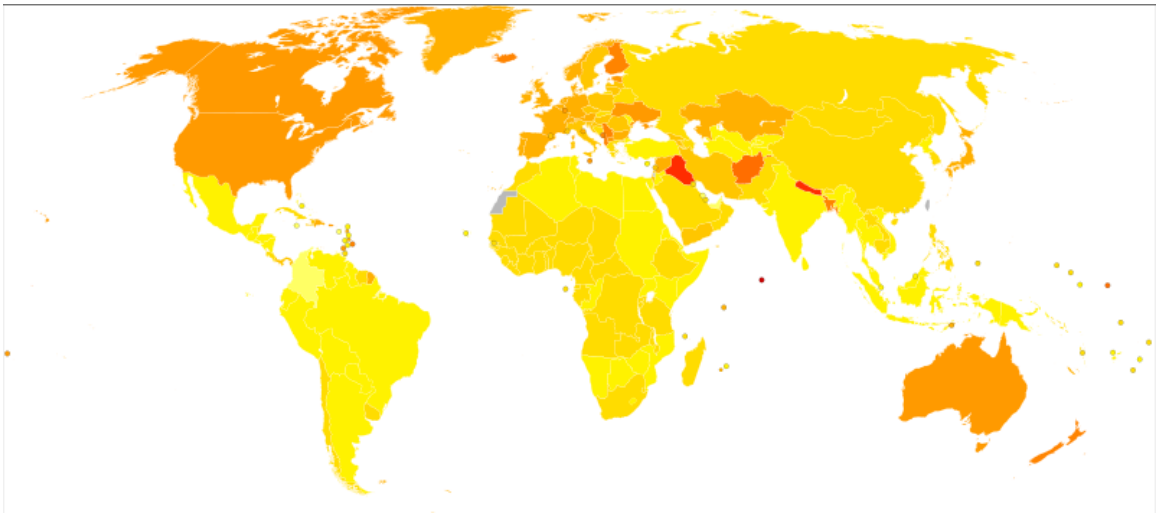
Palliative care is often required in the final stages of the disease when all other treatment strategies have become ineffective. The aim of palliative care is to maximize the quality of life for the person with the disease and those surrounding him or her. Some central issues of palliative care are: care in the community while adequate care can be given

there, reducing or withdrawing drug intake to reduce drug side effects, preventing pressure ulcers by management of pressure areas of inactive patients, and facilitating end-of-life decisions for the patient as well as involved friends and relatives.

Other treatments

Repetitive transcranial magnetic stimulation temporarily improves levodopa-induced dyskinesias. Its usefulness in PD is an open research topic. Several nutrients have been proposed as possible treatments; however there is no strong evidence that vitamins or food additives improve symptoms. There is not enough evidence to substantiate that acupuncture and practice of Qigong, or Tai chi, have any effect on symptoms. Fava beans and velvet beans are natural sources of levodopa and are eaten by many people with PD. While they have shown some effectiveness in clinical trials, their intake is not free of risks. Life-threatening adverse reactions have been described, such as the neuroleptic malignant syndrome.

Prognosis



Global burden of Parkinson's disease, measured in disability-adjusted life years per 100,000 inhabitants in 2004

- no data
- < 5
- 5–12.5
- 12.5–20
- 20–27.5
- 27.5–35
- 35–42.5
- 42.5–50
- 50–57.5
- 57.5–65
- 65–72.5
- 72.5–80
- > 80

PD invariably progresses with time. Motor symptoms, if not treated, advance aggressively in the early stages of the disease and more slowly later. Untreated, individuals are expected to lose independent ambulation after an average of eight years and be bedridden after ten years. However, it is uncommon to find untreated people nowadays and medication has improved the prognosis of motor symptoms, while at the same time it is a new source of disability due to the undesired effects of levodopa after years of use. In people taking levodopa, the mean progression of symptoms to a stage of high dependency takes around 15 years. However, it is hard to predict what course the disease will take for a given individual. Age is the best predictor of disease progression. The rate of motor decline is greater in those with less impairment at the time of diagnosis, while cognitive impairment is more frequent in those who are over 70 years of age at symptom onset.

Since current therapies improve motor symptoms, disability at present is mainly related to non-motor features of the disease. Nevertheless, the relationship between disease progression and disability is not linear. At first disability is related to motor symptoms and specially motor complications, which appear in up to 50% of individuals after 5 years of L-DOPA usage. As the disease advances disability is more related to motor symptoms that have a bad response to medication such as swallowing and speech difficulties and gait and balance problems. Finally after ten years most people with the disease have autonomic disturbances, sleep problems, mood alterations and cognitive decline. All of them, but specially the latter, greatly increase disability.

The life expectancy of people with PD is lower than for people who do not have the disease. Mortality ratios are around twice those of unaffected people. Cognitive decline and dementia, old age at onset, a more advanced disease state and presence of swallowing problems are all mortality risk factors. On the other hand a disease mainly characterized by tremor as opposed to rigidity predicts an improved survival. One specific cause of death twice as common in individuals with PD as in the healthy population is aspiration pneumonia.

Epidemiology

PD is the second most common neurodegenerative disorder after Alzheimer's disease. Two main measures are used in epidemiological studies: incidence and prevalence. Incidence is the number of new cases per unit of person–time at risk (usually number of new cases per thousand person–years); prevalence is the total number of cases of the disease in the population at a given time. The prevalence is estimated at 0.3% of the whole population in industrialized countries, rising to 1% in those over 60 years of age and to 4% of the population over 80. The mean age of onset is around 60 years, although 5–10% of cases, classified as young onset, begin between the ages of 20 and 50. PD may be less prevalent in those of African and Asian ancestry, although this finding is disputed. Some studies have proposed that it is more common in men than women, but others failed to detect any differences between the two sexes. The incidence of PD is between 8 and 18 per 100,000 person–years.

Many risk factors and protective factors have been proposed, sometimes in relation to theories concerning possible mechanisms of the disease, however none have been conclusively related to PD by empirical evidence. When epidemiological studies have been carried out in order to test the relationship between a given factor and PD, they have frequently been biased and their results have in some cases been contradictory. The most frequently replicated relationships are an increased risk of PD in those exposed to pesticides and a reduced risk in smokers.

Risk factors

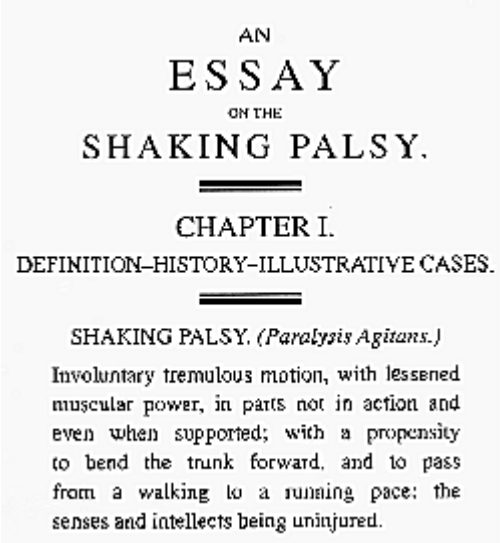
U.S. Army helicopter spraying Agent Orange over Vietnamese agricultural land during the Vietnam war. Agent Orange has been associated to PD.

Injections of the synthetic neurotoxin MPTP produce a range of symptoms similar to those of PD as well as selective damage to the dopaminergic neurons in the substantia nigra. This observation has led to theorizing that exposure to some environmental toxins may increase the risk of having PD. Toxins that have been consistently related to the disease are certain pesticides, such as rotenone or paraquat, and herbicides such as Agent Orange with exposure increasing the risk by as much as a factor of two. Indirect measures of exposure, such as living in rural environments, have been found to increase the risk of PD. Heavy metals exposure has been proposed to be a risk factor, through possible accumulation in the substantia nigra, however studies on the issue have been inconclusive.

Protective factors

Smoking has been related to a reduced risk of having PD. Smokers risk of having PD may be reduced down to a third when compared to non smokers. The basis for this effect is not known, but possibilities include an effect of nicotine as a dopamine stimulant. Caffeine consumption also protects against PD. Antioxidants, such as vitamin C and D, have been proposed to protect against the disease but results of studies have been contradictory and no positive effect has been proven. Regarding fat and fatty acids, the results have been contradictory, with protective effects, risk-enhancing effects, and no effects reported by various studies. Finally there have been preliminary indications of a possible protective role of estrogens and anti-inflammatory drugs.

History



AN

ESSAY

ON THE

SHAKING PALSY.

CHAPTER I.

DEFINITION–HISTORY–ILLUSTRATIVE CASES.

SHAKING PALSY. *(Paralysis Agitans.)*

Involuntary tremulous motion, with lessened muscular power, in parts not in action and even when supported; with a propensity to bend the trunk forward, and to pass from a walking to a running pace: the senses and intellects being uninjured.

First page of James Parkinson's classical essay on the Shaking palsy

The disease was not formally recognized and its symptoms were not documented until 1817, when British apothecary James Parkinson published *An Essay on the Shaking Palsy*. PD was then known as *paralysis agitans* (shaking palsy in English). The term "Parkinson's disease" was coined several decades later by French neurologist Jean-Martin Charcot.

Early descriptions

Several early sources describe symptoms resembling those of PD. An Egyptian papyrus from the 12th century B.C. mentions a king drooling with age and the Bible contains a number of references to tremor. An Ayurvedic medical treatise from the 10th century B.C. describes a disease that evolves with tremor, lack of movement, drooling and other symptoms of PD. Moreover, this disease was treated with remedies derived from the mucuna family, which is rich in L-DOPA. Galen wrote about a disease that almost

certainly was PD, describing tremors that occur only at rest, postural changes and paralysis.

After Galen there are no references unambiguously related to PD until the 17th century. In this and the following century several authors wrote about elements of the disease, preceding the description by Parkinson. Franciscus Sylvius, like Galen, distinguished tremor at rest from other tremors, while Johannes Baptiste Sagar and Hieronymus David Gaubius described festination, a term for the gait abnormalities characteristic of PD. John Hunter provided a thorough description of the disease, which may have given Parkinson the idea of collecting and describing patients with "paralysis agitans". Finally, Auguste François Chomel in his pathology treatise, which was contemporary to Parkinson's essay, included several descriptions of abnormal movements and rigidity matching those seen in PD.

19th century

A 1893 photograph of Jean-Martin Charcot, who made important contributions to the understanding of the disease and proposed its current name honoring James Parkinson

In 1817 James Parkinson published his essay reporting 6 cases of paralysis agitans. *An Essay on the Shaking Palsy* described the characteristic resting tremor, abnormal posture and gait, paralysis and diminished muscle strength, and the way that the disease progresses over time. He also acknowledged the contributions of many of the previously

mentioned authors to the understanding of PD. Although the article was later considered the seminal work on the disease, it received little attention over the forty years that followed. Nevertheless, early neurologists who made further additions to the knowledge of the disease include Trousseau, Gowers, Kinnier Wilson and Erb, and most notably Charcot, whose studies between 1868 and 1881 were a landmark in the understanding of the disease. Among other advances he made the distinction between rigidity, weakness and bradykinesia. He also championed the renaming of the disease in honor of James Parkinson.

20th century

The first speculations concerning the anatomical substrate of PD were made 80 years after Parkinson's essay, when Édouard Brissaud proposed that it had its origin in the subthalamus or cerebral peduncle and might be caused by an ischemic lesion. In 1912 Frederic Lewy described a pathologic finding in affected brains, later named "Lewy bodies". In 1919 Konstantin Tretiakoff reported that the substantia nigra was the main cerebral structure affected, but this finding was not widely accepted until it was confirmed by further studies published by Rolf Hassler in 1938. The underlying biochemical changes in the brain were identified in the 1950s, due largely to the work of Arvid Carlsson on the neurotransmitter dopamine and its role on PD. Carlsson was eventually awarded a Nobel Prize for this work. Synuclein proteins being the main component of Lewy bodies was discovered in 1997.

History of treatments

The positive albeit modest effects on tremor of anticholinergic alkaloids obtained from the plant of the belladona were described during 19th century by Charcot, Erb and others. Modern surgery for tremor, consisting of the lesioning of some of the basal ganglia structures was first tried in 1939 and was improved over the following 20 years. Before this date surgery consisted in lesioning the corticospinal pathway with paralysis instead of tremor as result. Anticholinergics and surgery were the only treaments until the arrival of levodopa, which reduced their use dramatically. Levodopa was first synthesized in 1911 by Casimir Funk, but it received little attention until the mid 20th century. It entered clinical practice in 1967, and the first large study reporting improvements in people with Parkinson's disease resulting from treatment with levodopa was published in 1968. Levodopa brought about a revolution in the management of PD. By the late 1980s deep brain stimulation emerged as a possible treatment and it was approved for clinical use by the FDA in 1997.

Research directions

There is little prospect of dramatic new PD treatments expected in a short time frame. Currently active research directions include the search for new animal models of the disease and studies of the potential usefulness of gene therapy, stem cell transplants and neuroprotective agents.

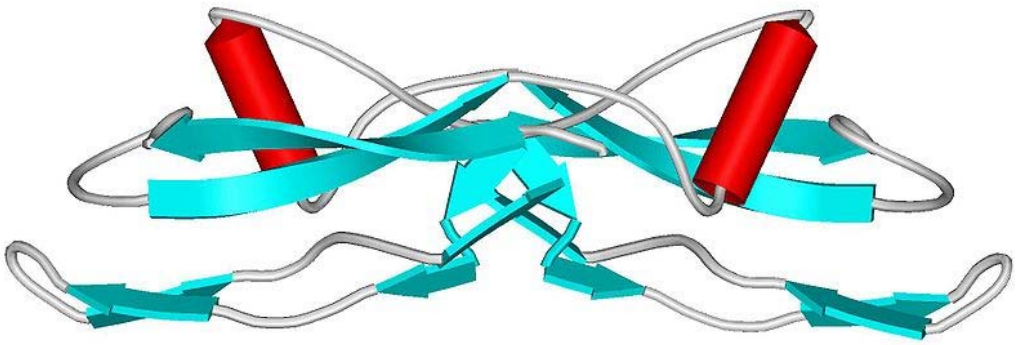
Animal models

PD is not known to occur naturally in any species other than humans. However, the appearance of parkinsonian symptoms in a group of drug addicts in the early 1980s who consumed a contaminated batch of the synthetic opiate MPPP led to the discovery of the chemical MPTP as an agent that causes a parkinsonian syndrome in non-human primates as well as in humans. Other predominant toxin-based models employ the insecticide rotenone, the herbicide paraquat and the fungicide maneb. Models based on toxins are most commonly used in primates. Transgenic rodent models that replicate various aspects of PD have been developed.

Gene therapy

Gene therapy involves the use of a non-infectious virus to shuttle a gene into a part of the brain. The gene used leads to the production of an enzyme which helps to manage PD symptoms or protects the brain from further damage. As of 2010 there are four clinical trials using gene therapy in PD. There have not been important adverse effects in these trials although the clinical usefulness of gene therapy is still unknown.

Neuroprotective treatments



While several chemical compounds such as GDNF (chemical structure pictured) have been proposed as neuroprotectors in PD, none have proven their efficacy.

Investigations on neuroprotection are at the forefront of PD research. Several molecules have been proposed as potential treatments. However, none of them have been conclusively demonstrated to reduce degeneration. Agents currently under investigation include anti-apoptotics (TCH346, CEP-1347), antiglutamatergics, monoamine oxidase

inhibitors (selegiline, rasagiline), promitochondrials (coenzyme Q10, creatine), calcium channel blockers (isradipine) and growth factors (GDNF). Preclinical research also targets alpha-synuclein.

Neural transplantation

Since early in the 1980s, fetal, porcine, carotid or retinal tissues have been used in cell transplants, in which dissociated cells are injected into the substantia nigra in the hope that they will incorporate themselves into the brain in a way that replaces the dopamine cells that have been lost. Although there was initial evidence of mesencephalic dopamine-producing cell transplants being beneficial, the best constructed studies up to date indicate that cell transplants produce no demonstrable long-term benefit. An additional significant problem was the excess release of dopamine by the transplanted tissue, leading to dystonias. Stem cell transplants are a recent main research target, because stem cells are easy to manipulate and stem cells transplanted into the brains of rodents and monkeys have been found to survive and to reduce behavioral abnormalities. Nevertheless, use of fetal stem cells is controversial. It has been proposed that effective treatments may be developed in a less controversial way by use of induced pluripotent stem cells taken from adults.

Chapter 13

Urinary Incontinence

Urinary incontinence	
ICD-10	N39.3-N39.4, R32.
ICD-9	788.3
DiseasesDB	6764
MedlinePlus	003142
eMedicine	med/2781
MeSH	D014549

Urinary incontinence (**UI**) is any involuntary leakage of urine. It is a common and distressing problem, which may have a profound impact on quality of life. Urinary incontinence almost always results from an underlying treatable medical condition but is under-reported to medical practitioners. There is also a related condition for defecation known as fecal incontinence.

Physiology of continence

Continence and micturition involve a balance between urethral closure and detrusor muscle activity. Urethral pressure normally exceeds bladder pressure, resulting in urine remaining in the bladder. The proximal urethra and bladder are both within the pelvis. Intraabdominal pressure increases (from coughing and sneezing) are transmitted to both urethra and bladder equally, leaving the pressure differential unchanged, resulting in continence. Normal voiding is the result of changes in both of these pressure factors: urethral pressure falls and bladder pressure rises.

Causes

- Polyuria (excessive urine production) of which, in turn, the most frequent causes are: uncontrolled diabetes mellitus, primary polydipsia (excessive fluid drinking), central diabetes insipidus and nephrogenic diabetes insipidus. Polyuria generally causes urinary urgency and frequency, but doesn't necessarily lead to incontinence.

- Caffeine or cola beverages also stimulate the bladder.
- Enlarged prostate is the most common cause of incontinence in men after the age of 40; sometimes prostate cancer may also be associated with urinary incontinence. Moreover drugs or radiation used to treat prostate cancer can also cause incontinence.
- Brain disorders like multiple sclerosis, Parkinson's disease, strokes and spinal cord injury can all interfere with nerve function of the bladder.

Types

- *Stress incontinence*, also known as **effort incontinence**, is due essentially to insufficient strength of the pelvic floor muscles.

- *Urge incontinence* is involuntary loss of urine occurring for no apparent reason while suddenly feeling the need or urge to urinate.

- *Overflow incontinence:* Sometimes people find that they cannot stop their bladders from constantly dribbling, or continuing to dribble for some time after they have passed urine. It is as if their bladders were like a constantly overflowing pan, hence the general name overflow incontinence.

- *Mixed incontinence* is not uncommon in the elderly female population and can sometimes be complicated by urinary retention, which makes it a treatment challenge requiring staged multimodal treatment.

- *Structural incontinence:* Rarely, structural problems can cause incontinence, usually diagnosed in childhood, for example an ectopic ureter. Fistulas caused by obstetric and gynecologic trauma or injury can also lead to incontinence. These types of vaginal fistulas include most commonly, vesicovaginal fistula, but more rarely ureterovaginal fistula. These may be difficult to diagnose. The use of standard techniques along with a vaginogram or radiologically viewing the vaginal vault with instillation of contrast media.

- *Functional incontinence* occurs when a person recognizes the need to urinate, but cannot physically make it to the bathroom in time due to limited mobility. The urine loss may be large. Causes of functional incontinence include confusion, dementia, poor eyesight, poor mobility, poor dexterity, unwillingness to toilet because of depression, anxiety or anger, drunkenness, or being in a situation in which it is impossible to reach a toilet. People with functional incontinence may have problems thinking, moving, or communicating that prevent them from reaching a toilet. A person with Alzheimer's Disease, for example, may not think well enough to plan a timely trip to a restroom. A person in a wheelchair may be blocked from getting to a toilet in time. Conditions such as these are often associated with age and account for some of the incontinence of elderly women and men in nursing homes. Disease or biology is not necessarily the cause of functional incontinence. For example, someone on a road trip may be between

rest stops and on the highway; also, there may be problems with the restrooms in the vicinity of a person.

- *Bedwetting* is episodic UI while asleep. It is normal in young children.

- *Transient incontinence* is a temporary version of incontinence. It can be triggered by medications, adrenal insufficiency, mental impairment, restricted mobility, and stool impaction (severe constipation), which can push against the urinary tract and obstruct outflow.

Diagnosis

Patients with incontinence should be referred to a medical practitioner specializing in this field. Urologists specialize in the urinary tract, and some urologists further specialize in the female urinary tract. A urogynecologist is a gynecologist who has special training in urological problems in women. Gynecologists and obstetricians specialize in the female reproductive tract and childbirth and some also treat urinary incontinence in women. Family practitioners and internists see patients for all kinds of complaints and can refer patients on to the relevant specialists.

A careful history taking is essential especially in the pattern of voiding and urine leakage as it suggests the type of incontinence faced. Other important points include straining and discomfort, use of drugs, recent surgery, and illness.

The physical examination will focus on looking for signs of medical conditions causing incontinence, such as tumors that block the urinary tract, stool impaction, and poor reflexes or sensations, which may be evidence of a nerve-related cause.

A test often performed is the measurement of bladder capacity and residual urine for evidence of poorly functioning bladder muscles.

Other tests include:

- Stress test – the patient relaxes, then coughs vigorously as the doctor watches for loss of urine.
- Urinalysis – urine is tested for evidence of infection, urinary stones, or other contributing causes.
- Blood tests – blood is taken, sent to a laboratory, and examined for substances related to causes of incontinence.
- Ultrasound – sound waves are used to visualize the kidneys, ureters, bladder, and urethra.
- Cystoscopy – a thin tube with a tiny camera is inserted in the urethra and used to see the inside of the urethra and bladder.
- Urodynamics – various techniques measure pressure in the bladder and the flow of urine.

Patients are often asked to keep a diary for a day or more, up to a week, to record the pattern of voiding, noting times and the amounts of urine produced.

Urinary incontinence in women

Bladder symptoms affect women of all ages. However, bladder problems are most prevalent among older women. Up to 35% of the total population over the age of 60 years is estimated to be incontinent, with women twice as likely as men to experience incontinence. One in three women over the age of 60 years are estimated to have bladder control problems.

Bladder control problems have been found to be associated with higher incidence of many other health problems such as obesity and diabetes. Difficulty with bladder control results in higher rates of depression and limited activity levels.

Incontinence is expensive both to individuals in the form of bladder control products and to the health care system and nursing home industry. Injury related to incontinence is a leading cause of admission to assisted living and nursing care facilities. More than 50% of nursing facility admissions are related to incontinence.

Coital incontinence (CI) is urinary leakage that occurs during either penetration or orgasm and can occur with a sexual partner or with masturbation. It has been reported to occur in 10% to 24% of sexually active women with pelvic floor disorders.

Urinary incontinence in men

Men tend to experience incontinence less often than women, and the structure of the male urinary tract accounts for this difference. But both women and men can become incontinent from neurologic injury, congenital defects, strokes, multiple sclerosis, and physical problems associated with aging.

While urinary incontinence affects older men more often than younger men, the onset of incontinence can happen at any age. Incontinence is treatable and often curable at all ages.

Incontinence in men usually occurs because of problems with muscles that help to hold or release urine. The body stores urine—water and wastes removed by the kidneys—in the urinary bladder, a balloon-like organ. The bladder connects to the urethra, the tube through which urine leaves the body.

During urination, muscles in the wall of the bladder contract, forcing urine out of the bladder and into the urethra. At the same time, sphincter muscles surrounding the urethra relax, letting urine pass out of the body. Incontinence will occur if the bladder muscles suddenly contract or muscles surrounding the urethra suddenly relax.

Treatment

The treatment options range from conservative treatment, behavior management, medications and surgery. In all cases, the least invasive treatment is started first. The success of treatment depends on the correct diagnoses in the first place.

Most treatment options are most appropriate for a specific underlying cause of the incontinence (though these can overlap if there is a mixed component to the incontinence.) However, some approaches (such as use of absorbent products) address the problem symptomatically, and can be applicable to more than one type. It is also sometimes possible to use a treatment for the pathophysiology of one type of incontinence to provide relief for an unrelated type of incontinence.

Absorbent pads and urinary catheters may help those individuals who continue to have incontinence. The absorbent pads are not bulky like in the old days but are close fitting underwear with liners. Men also can use a small urine collector that is worn around the penis.

Absorbent products include shields, undergarments, protective underwear, briefs, diapers, adult diapers and underpads.

Hospitals often use some type of incontinence pad, a small but highly absorbent sheet placed beneath the patient, to deal with incontinence or other unexpected discharges of bodily fluid. These pads are especially useful when it is not practical for the patient to wear a diaper.

Urinary incontinence in children

Urination, or voiding, is a complex activity. The bladder is a balloonlike muscle that lies in the lowest part of the abdomen. The bladder stores urine, then releases it through the urethra, the canal that carries urine to the outside of the body. Controlling this activity involves nerves, muscles, the spinal cord and the brain.

The bladder is made of two types of muscles: the detrusor, a muscular sac that stores urine and squeezes to empty, and the sphincter, a circular group of muscles at the bottom or neck of the bladder that automatically stay contracted to hold the urine in and automatically relax when the detrusor contracts to let the urine into the urethra. A third group of muscles below the bladder (pelvic floor muscles) can contract to keep urine back.

A baby's bladder fills to a set point, then automatically contracts and empties. As the child gets older, the nervous system develops. The child's brain begins to get messages from the filling bladder and begins to send messages to the bladder to keep it from automatically emptying until the child decides it is the time and place to void.

Failures in this control mechanism result in incontinence. Reasons for this failure range from the simple to the complex.

Incontinence happens less often after age 5: About 10 percent of 5-year-olds, 5 percent of 10-year-olds, and 1 percent of 18-year-olds experience episodes of incontinence. It is twice as common in girls as in boys.

Nocturnal enuresis

Causes of nighttime incontinence

After age 5, wetting at night—often called bedwetting or sleepwetting—is more common than daytime wetting in boys. Experts do not know what causes nighttime incontinence. Young people who experience nighttime wetting tend to be physically and emotionally normal. Most cases probably result from a mix of factors including slower physical development, an overproduction of urine at night, a lack of ability to recognize bladder filling when asleep, and, in some cases, anxiety. For many, there is a strong family history of bedwetting, suggesting an inherited factor.

Slower physical development

Between the ages of 5 and 10, incontinence may be the result of a small bladder capacity, long sleeping periods, and underdevelopment of the body's alarms that signal a full or emptying bladder. This form of incontinence will fade away as the bladder grows and the natural alarms become operational.

Excessive output of urine during sleep

Normally, the body produces a hormone that can slow the making of urine. This hormone is called antidiuretic hormone, or ADH. The body normally produces more ADH during sleep so that the need to urinate is lower. If the body does not produce enough ADH at night, the making of urine may not be slowed down, leading to bladder overfilling. If a child does not sense the bladder filling and awaken to urinate, then wetting will occur.

Anxiety

Experts suggest that anxiety-causing events occurring in the lives of children ages 2 to 4 might lead to incontinence before the child achieves total bladder control. Anxiety experienced after age 4 might lead to wetting after the child has been dry for a period of 6 months or more. Such events include angry parents, unfamiliar social situations, and overwhelming family events such as the birth of a brother or sister.

Incontinence itself is an anxiety-causing event. Strong bladder contractions leading to leakage in the daytime can cause embarrassment and anxiety that lead to wetting at night.

Genetics

Certain inherited genes appear to contribute to incontinence. In 1995, Danish researchers announced they had found a site on human chromosome 13 that is responsible, at least in part, for nighttime wetting. If both parents were bedwetters, a child has an 80 percent chance of being a bedwetter also. Experts believe that other, undetermined genes also may be involved in incontinence.

Obstructive sleep apnea

Nighttime incontinence may be one sign of another condition called obstructive sleep apnea, in which the child's breathing is interrupted during sleep, often because of inflamed or enlarged tonsils or adenoids. Other symptoms of this condition include snoring, mouth breathing, frequent ear and sinus infections, sore throat, choking, and daytime drowsiness. In some cases, successful treatment of this breathing disorder may also resolve the associated nighttime incontinence.

Structural problems

Finally, a small number of cases of incontinence are caused by physical problems in the urinary system in children. A condition known as urinary reflux or vesicoureteral reflux, in which urine backs up into one or both ureters, can cause urinary tract infections and incontinence. Rarely, a blocked bladder or urethra may cause the bladder to overfill and leak. Nerve damage associated with the birth defect spina bifida can cause incontinence. An ectopic ureter, a misplacement of the ureter outside the bladder, can also commonly cause incontinence. In these cases, the incontinence can appear as a constant dribbling of urine.

Diurnal enuresis

Causes of daytime incontinence

Daytime incontinence that is not associated with urinary infection or anatomic abnormalities is less common than nighttime incontinence and tends to disappear much earlier than the nighttime versions. One possible cause of daytime incontinence is an overactive bladder. Many children with daytime incontinence have abnormal voiding habits, the most common being infrequent voiding. This form of incontinence occurs more often in girls than in boys.

An overactive bladder

Muscles surrounding the urethra (the tube that takes urine away from the bladder) have the job of keeping the passage closed, preventing urine from passing out of the body. If the bladder contracts strongly and without warning, the muscles surrounding the urethra may not be able to keep urine from passing. This often happens as a consequence of urinary tract infection and is more common in girls.

Infrequent voiding

Infrequent voiding refers to a child's voluntarily holding urine for prolonged intervals. For example, a child may not want to use the toilets at school or may not want to interrupt enjoyable activities, so he or she ignores the body's signal of a full bladder. In these cases, the bladder can overfill and leak urine. Additionally, these children often develop urinary tract infections (UTIs), leading to an irritable or overactive bladder.

Other causes

Some of the same factors that contribute to nighttime incontinence may act together with infrequent voiding to produce daytime incontinence. These factors include a small bladder capacity, constipation and food containing caffeine, chocolate or artificial coloring.

Sometimes overly strenuous toilet training may make the child unable to relax the sphincter and the pelvic floor to completely empty the bladder. Retaining urine (incomplete emptying) sets the stage for urinary tract infections.

Treatment

Growth and development

Most urinary incontinence fades away naturally. Here are examples of what can happen over time:

- Bladder capacity increases.
- Natural body alarms become activated.
- An overactive bladder settles down.
- Production of ADH becomes normal.
- The child learns to respond to the body's signal that it is time to void.
- Stressful events or periods pass.

Many children overcome incontinence naturally (without treatment) as they grow older. The number of cases of incontinence goes down by 15 percent for each year after the age of 5.

Medications

Nighttime incontinence may be treated by increasing ADH levels. The hormone can be boosted by a synthetic version known as desmopressin, or DDAVP, which recently became available in pill form. Patients can also spray a mist containing desmopressin into their nostrils. Desmopressin is approved for use by children.

Another medication, called imipramine, is also used to treat sleepwetting. It acts on both the brain and the urinary bladder. Unfortunately, total dryness with either of the medications available is achieved in only about 20 percent of patients.

If a young person experiences incontinence resulting from an overactive bladder, a doctor might prescribe a medicine that helps to calm the bladder muscle. This medicine controls muscle spasms and belongs to a class of medications called anticholinergics.

Bladder training and related strategies

Bladder training consists of exercises for strengthening and coordinating muscles of the bladder and urethra, and may help the control of urination. These techniques teach the child to anticipate the need to urinate and prevent urination when away from a toilet. Techniques that may help nighttime incontinence include:

- Determining bladder capacity
- Stretching the bladder (delaying urinating)
- Drinking less fluid before sleeping
- Developing routines for waking up

Unfortunately, none of the above has demonstrated proven success.

Techniques that may help daytime incontinence include:

- Urinating on a schedule, such as every 2 hours (this is called timed voiding)
- Avoiding caffeine or other foods or drinks that may contribute to a child's incontinence
- Following suggestions for healthy urination, such as relaxing muscles and taking your time

Moisture alarms

At night, moisture alarms can awaken a person when he or she begins to urinate. These devices include a water-sensitive pad worn in pajamas, a wire connecting to a battery-driven control, and an alarm that sounds when moisture is first detected. For the alarm to be effective, the child must awaken or be awakened as soon as the alarm goes off. This may require having another person sleep in the same room to awaken the bedwetter.

Chapter 14

Hypertension

Hypertension

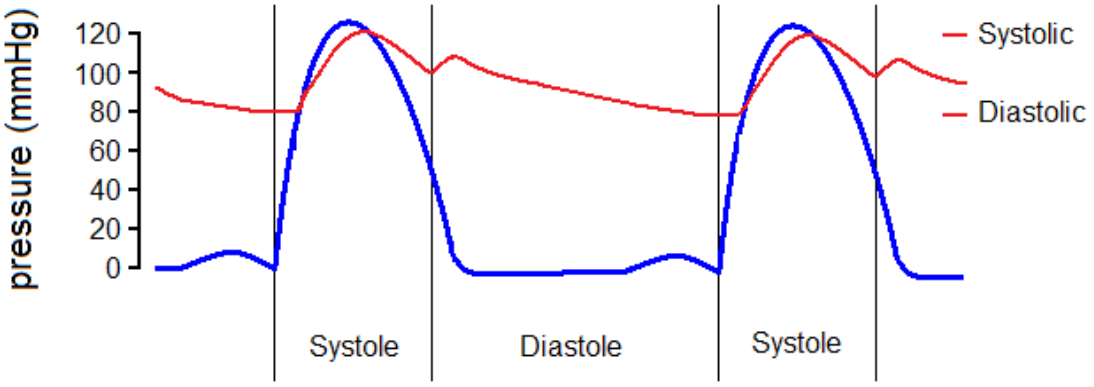
Automated arm blood pressure meter showing arterial hypertension (shown a systolic blood pressure 158 mmHg, diastolic blood pressure 99 mmHg and heart rate of 80 beats per minute).

ICD-10	I10.,I11.,I12., I13.,I15.
ICD-9	401
OMIM	145500
DiseasesDB	6330
MedlinePlus	000468
eMedicine	med/1106 ped/1097 emerg/267
MeSH	D006973

Hypertension (HTN) or **high blood pressure** is a cardiac chronic medical condition in which the systemic arterial blood pressure is elevated. It is the opposite of hypotension. Hypertension is classified as either primary (essential) or secondary. About 90–95% of cases are termed "primary hypertension", which refers to high blood pressure for which no medical cause can be found. The remaining 5–10% of cases (Secondary hypertension) are caused by other conditions that affect the kidneys, arteries, heart, or endocrine system.

Persistent hypertension is one of the risk factors for stroke, myocardial infarction, heart failure and arterial aneurysm, and is a leading cause of chronic kidney failure. Moderate elevation of arterial blood pressure leads to shortened life expectancy. Dietary and lifestyle changes can improve blood pressure control and decrease the risk of associated health complications, although drug treatment may prove necessary in patients for whom lifestyle changes prove ineffective or insufficient.

Classification



The variation in pressure in the left ventricle (blue line) and the aorta (red line) over two cardiac cycles ("heart beats"), showing the definitions of systolic and diastolic pressure

Classification	Systolic pressure		Diastolic pressure	
	mmHg	kPa	mmHg	kPa
Normal	90–119	12–15.9	60–79	8.0–10.5
Prehypertension	120–139	16.0–18.5	80–89	10.7–11.9
Stage 1	140–159	18.7–21.2	90–99	12.0–13.2
Stage 2	≥160	≥21.3	≥100	≥13.3
Isolated systolic hypertension	≥140	≥18.7	<90	<12.0

Blood pressure is usually classified based on the systolic and diastolic blood pressures. Systolic blood pressure is the blood pressure in vessels during a heart beat. Diastolic blood pressure is the pressure between heartbeats. A systolic or the diastolic blood pressure measurement higher than the accepted normal values for the age of the individual is classified as prehypertension or hypertension.

Hypertension has several sub-classifications including, hypertension stage I, hypertension stage II, and isolated systolic hypertension. Isolated systolic hypertension refers to elevated systolic pressure with normal diastolic pressure and is common in the elderly. These classifications are made after averaging a patient's resting blood pressure readings taken on two or more office visits. Individuals older than 50 years are classified as having hypertension if their blood pressure is consistently at least 140 mmHg systolic or

90 mmHg diastolic. Patients with blood pressures higher than 130/80 mmHg with concomitant presence of diabetes mellitus or kidney disease require further treatment.

Hypertension is also classified as resistant if medications do not reduce blood pressure to normal levels.

Exercise hypertension is an excessively high elevation in blood pressure during exercise. The range considered normal for systolic values during exercise is between 200 and 230 mm Hg. Exercise hypertension may indicate that an individual is at risk for developing hypertension at rest.

Signs and symptoms

Mild to moderate essential hypertension is usually asymptomatic.

Accelerated hypertension

Accelerated hypertension is associated with headache, drowsiness, confusion, vision disorders, nausea, and vomiting symptoms which are collectively referred to as hypertensive encephalopathy. Hypertensive encephalopathy is caused by severe small blood vessel congestion and brain swelling, which is reversible if blood pressure is lowered.

Children

Some signs and symptoms are especially important in newborns and infants such as failure to thrive, seizures, irritability, lack of energy, and difficulty breathing. In children, hypertension can cause headache, fatigue, blurred vision, nosebleeds, and facial paralysis.

Even with the above clinical symptoms, the true incidence of pediatric hypertension is not known. In adults, hypertension has been defined due to the adverse effects caused by hypertension. However, in children, similar studies have not been performed thoroughly to link any adverse effects with the increase in blood pressure. Therefore, the prevalence of pediatric hypertension remains unknown due to the lack of scientific knowledge.

Secondary hypertension

Some additional signs and symptoms suggest that the hypertension is caused by disorders in hormone regulation. Hypertension combined with obesity distributed on the trunk of the body, accumulated fat on the back of the neck ('buffalo hump'), wide purple marks on the abdomen (abdominal striae), or the recent onset of diabetes suggests that an individual has a hormone disorder known as Cushing's syndrome. Hypertension caused by other hormone disorders such as hyperthyroidism, hypothyroidism, or growth hormone excess will be accompanied by additional symptoms specific to these disorders. For example, hyperthyrodism can cause weight loss, tremors, heart rate abnormalities, reddening of the palms, and increased sweating. Signs and symptoms associated with

growth hormone excess include coarsening of facial features, protrusion of the lower jaw, enlargement of the tongue, excessive hair growth, darkening of the skin color, and excessive sweating. Other hormone disorders like hyperaldosteronism may cause less specific symptoms such as numbness, excessive urination, excessive sweating, electrolyte imbalances and dehydration, and elevated blood alkalinity and also cause of mental pressure.

Pregnancy

Hypertension in pregnant women is one symptom of pre-eclampsia. Pre-eclampsia can progress to a life-threatening condition called eclampsia, which is the development of protein in the urine, generalized swelling, and severe seizures. Other symptoms indicating that brain function is becoming impaired may precede these seizures such as nausea, vomiting, headaches, and vision loss.

In addition, the systemic vascular resistance and blood pressure decrease during pregnancy. The body must compensate by increasing cardiac output and blood volume to provide sufficient circulation in the utero-placental arterial bed.

Causes

Essential hypertension

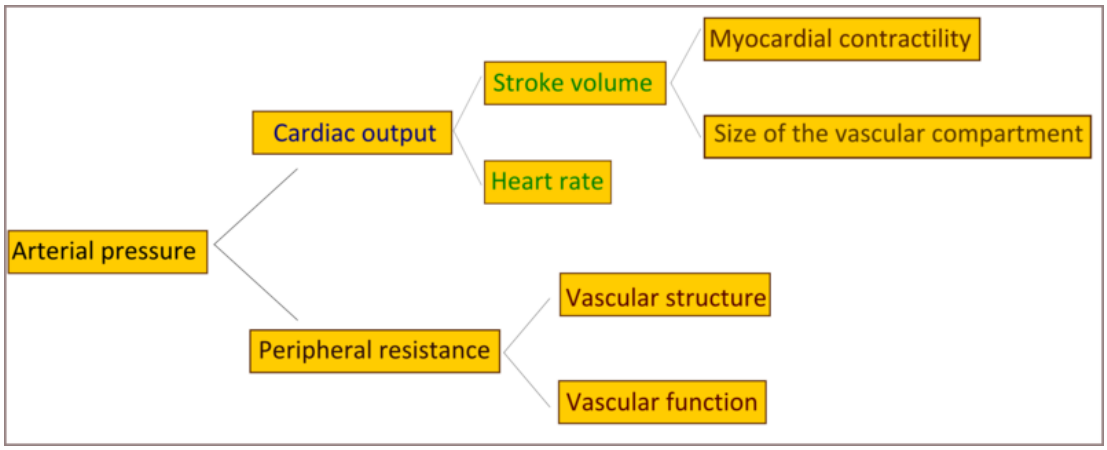
Essential hypertension is the most prevalent hypertension type, affecting 90–95% of hypertensive patients. Although no direct cause has been identified, there are many factors such as sedentary lifestyle, smoking, stress, visceral obesity, potassium deficiency (hypokalemia), obesity (more than 85% of cases occur in those with a body mass index greater than 25), salt (sodium) sensitivity, alcohol intake, and vitamin D deficiency that increase the risk of developing hypertension. Risk also increases with aging, some inherited genetic mutations, and having a family history of hypertension. An elevated level of renin, a hormone secreted by the kidney, is another risk factor, as is sympathetic nervous system overactivity. Insulin resistance, which is a component of syndrome X (or the metabolic syndrome), is also thought to contribute to hypertension. Recent studies have implicated low birth weight as a risk factor for adult essential hypertension.

Secondary hypertension

Secondary hypertension by definition results from an identifiable cause. This type is important to recognize since it's treated differently to essential hypertension, by treating the underlying cause of the elevated blood pressure. Hypertension results in the compromise or imbalance of the pathophysiological mechanisms, such as the hormone-regulating endocrine system, that regulate blood plasma volume and heart function. Many conditions cause hypertension, some are common and well recognized secondary causes such as Cushing's syndrome, which is a condition where the adrenal glands overproduce the hormone cortisol. In addition, hypertension is caused by other conditions that cause hormone changes such as hyperthyroidism, hypothyroidism, and certain tumors of the

adrenal medulla (e.g., pheochromocytoma). Other common causes of secondary hypertension include kidney disease, obesity/metabolic disorder, pre-eclampsia during pregnancy, the congenital defect known as coarctation of the aorta, and certain prescription and illegal drugs.

Pathophysiology



A diagram explaining factors affecting arterial pressure

Most of the mechanisms associated with secondary hypertension are generally fully understood. However, those associated with essential (primary) hypertension are far less understood. What is known is that cardiac output is raised early in the disease course, with total peripheral resistance (TPR) normal; over time cardiac output drops to normal levels but TPR is increased. Three theories have been proposed to explain this:

- Inability of the kidneys to excrete sodium, resulting in natriuretic factors such as Atrial Natriuretic Factor being secreted to promote salt excretion with the side effect of raising total peripheral resistance.
- An overactive Renin-angiotensin system leads to vasoconstriction and retention of sodium and water. The increase in blood volume plus vasoconstriction leads to hypertension.
- An overactive sympathetic nervous system, leading to increased stress responses.

It is also known that hypertension is highly heritable and polygenic (caused by more than one gene) and a few candidate genes have been postulated in the etiology of this condition.

Recently, work related to the association between essential hypertension and sustained endothelial damage has gained popularity among hypertension scientists. It remains unclear however whether endothelial changes precede the development of hypertension or whether such changes are mainly due to long standing elevated blood pressures.

Diagnosis

Hypertension is generally diagnosed on the basis of a persistently high blood pressure. Usually this requires three separate sphygmomanometer measurements at least one week apart. Often, this entails three separate visits to the physician's office. Initial assessment of the hypertensive patient should include a complete history and physical examination. Exceptionally, if the elevation is extreme, or if symptoms of organ damage are present then the diagnosis may be given and treatment started immediately.

Once the diagnosis of hypertension has been made, physicians will attempt to identify the underlying cause based on risk factors and other symptoms, if present. Secondary hypertension is more common in preadolescent children, with most cases caused by renal disease. Primary or essential hypertension is more common in adolescents and has multiple risk factors, including obesity and a family history of hypertension. Laboratory tests can also be performed to identify possible causes of secondary hypertension, and determine if hypertension has caused damage to the heart, eyes, and kidneys. Additional tests for Diabetes and high cholesterol levels are also usually performed because they are additional risk factors for the development of heart disease require treatment. Tests typically performed are classified as follows:

System	Tests
Renal	Microscopic urinalysis, proteinuria, serum BUN (blood urea nitrogen) and/or creatinine
Endocrine	Serum sodium, potassium, calcium, TSH (thyroid-stimulating hormone).
Metabolic	Fasting blood glucose, total cholesterol, HDL and LDL cholesterol, triglycerides
Other	Hematocrit, electrocardiogram, and chest radiograph

Creatinine (renal function) testing is done to determine if kidney disease is present, which can be either the cause or result of hypertension. In addition, it provides a baseline measurement of kidney function that can be used to monitor for side-effects of certain antihypertensive drugs on kidney function. Additionally, testing of urine samples for protein is used as a secondary indicator of kidney disease. Glucose testing is done to determine if diabetes mellitus is present. Electrocardiogram (EKG/ECG) testing is done to check for evidence of the heart being under strain from high blood pressure. It may also show if there is thickening of the heart muscle (left ventricular hypertrophy) or has experienced a prior minor heart distubance such as a silent heart attack. A chest X-ray may be performed to look for signs of heart enlargement or damage to heart tissue.

Prevention

The degree to which hypertension can be prevented depends on a number of features including current blood pressure level, sodium/potassium balance, detection and omission of environmental toxins, changes in end/target organs (retina, kidney, heart, among

others), risk factors for cardiovascular diseases and the age at diagnosis of prehypertension or at risk for hypertension. A prolonged assessment in which repeated measurements of blood pressure are taken provides the most accurate assessment of blood pressure levels. Following this, lifestyle changes are recommended to lower blood pressure, before the initiation of prescription drug therapy. The process of managing prehypertension according the guidelines of the British Hypertension Society suggest the following lifestyle changes:

- Weight reduction and regular aerobic exercise (e.g., walking): Regular exercise improves blood flow and helps to reduce the resting heart rate and blood pressure.
- Reducing dietary sugar.
- Reducing sodium (salt) in the body by disuse of condiment sodium and the adoption of a high potassium diet which rids the renal system of excess sodium. Many people use potassium chloride salt substitute to reduce their salt intake.
- Additional dietary changes beneficial to reducing blood pressure include the DASH diet (**d**ietary **a**pproaches to **s**top **h**ypertension) which is rich in fruits and vegetables and low-fat or fat-free dairy products. This diet has been shown to be effective based on research sponsored by the National Heart, Lung, and Blood Institute. In addition, an increase in dietary potassium, which offsets the effect of sodium has been shown to be highly effective in reducing blood pressure.
- Discontinuing tobacco use and alcohol consumption has been shown to lower blood pressure. The exact mechanisms are not fully understood, but blood pressure (especially systolic) always transiently increases following alcohol or nicotine consumption. Abstaining from cigarette smoking reduces the risk of stroke and heart attack which are associated with hypertension.

Limiting alcohol intake to less than 2 standard drinks per day can reduce systolic blood pressure by between 2-4mmHg.

- Reducing stress, for example with relaxation therapy, such as meditation and other mindbody relaxation techniques, by reducing environmental stress such as high sound levels and over-illumination can also lower blood pressure. Jacobson's Progressive Muscle Relaxation and biofeedback are also beneficial, such as device-guided paced breathing, although meta-analysis suggests it is not effective unless combined with other relaxation techniques.

Increasing omega 3 fatty acids can help lower hypertension. Fish oil is shown to lower blood pressure in hypertensive individuals. The fish oil may increase sodium and water excretion.

Treatment

Lifestyle modifications

The first line of treatment for hypertension is the same as the recommended preventative lifestyle changes such as the dietary changes, physical exercise, and weight loss, which

have all been shown to significantly reduce blood pressure in people with hypertension. If hypertension is high enough to justify immediate use of medications, lifestyle changes are still recommended in conjunction with medication. Drug prescription should take into account the patient's absolute cardiovascular risk (including risk of myocardial infarction and stroke) as well as blood pressure readings, in order to gain a more accurate picture of the patient's cardiovascular profile. Different programs aimed to reduce psychological stress such as biofeedback, relaxation or meditation are advertised to reduce hypertension. However, in general claims of efficacy are not supported by scientific studies, which have been in general of low quality.

Regarding dietary changes, a low sodium diet is beneficial; A Cochrane review published in 2008 concluded that a long term (more than 4 weeks) low sodium diet in Caucasians has a useful effect to reduce blood pressure, both in people with hypertension and in people with normal blood pressure. Also, the DASH diet (Dietary Approaches to Stop Hypertension) is a diet promoted by the National Heart, Lung, and Blood Institute (part of the NIH, a United States government organization) to control hypertension. A major feature of the plan is limiting intake of sodium, and it also generally encourages the consumption of nuts, whole grains, fish, poultry, fruits and vegetables while lowering the consumption of red meats, sweets, and sugar. It is also "rich in potassium, magnesium, and calcium, as well as protein".

Medications

Several classes of medications, collectively referred to as antihypertensive drugs, are currently available for treating hypertension. Agents within a particular class generally share a similar pharmacologic mechanism of action, and in many cases have an affinity for similar cellular receptors. An exception to this rule is the diuretics, which are grouped together for the sake of simplicity but actually exert their effects by a number of different mechanisms.

Reduction of the blood pressure by 5 mmHg can decrease the risk of stroke by 34%, of ischaemic heart disease by 21%, and reduce the likelihood of dementia, heart failure, and mortality from cardiovascular disease. The aim of treatment should be reduce blood pressure to <140/90 mmHg for most individuals, and lower for individuals with diabetes or kidney disease (some medical professionals recommend keeping levels below 120/80 mmHg). If the blood pressure goal is not met, a change in treatment should be made as therapeutic inertia is a clear impediment to blood pressure control. Comorbidity also plays a role in determining target blood pressure, with lower BP targets applying to patients with end-organ damage or proteinuria.

Often multiple drugs are combined to achieve the goal blood pressure. Commonly used prescription drugs include:

- ACE inhibitors (e.g., captopril)
- Alpha blockers (e.g., prazosin)
- Angiotensin II receptor antagonists (e.g., losartan)

- Beta blockers (e.g., propranolol)
- Calcium channel blockers (e.g., verapamil)
- Diuretics (e.g. hydrochlorothiazide)
- Direct renin inhibitors (e.g., aliskiren)

Some examples of common combined prescription drug treatments include:

- A fixed combination of an ACE inhibitor and a calcium channel blocker. One example of this is the combination of perindopril and amlodipine, the efficacy of which has been demonstrated in individuals with glucose intolerance or metabolic syndrome.
- A fixed combination of a diuretic and an ARB.

Combinations of an ACE inhibitor or angiotensin II–receptor antagonist, a diuretic and an NSAID (including selective COX-2 inhibitors and non-prescribed drugs such as ibuprofen) should be avoided whenever possible due to a high documented risk of acute renal failure. The combination is known colloquially as a "triple whammy" in the Australian health industry.

In the elderly

Treating moderate to severe high blood pressure with prescription medications decreases death rates in those under 80 years of age however there is no decrease in those over 80 years old. Even though there was no decrease in total mortality, the results showed similarities between cardiovascular mortality and morbidity.

Resistant

Guidelines for treating resistant hypertension have been published in the UK and US.

Complications

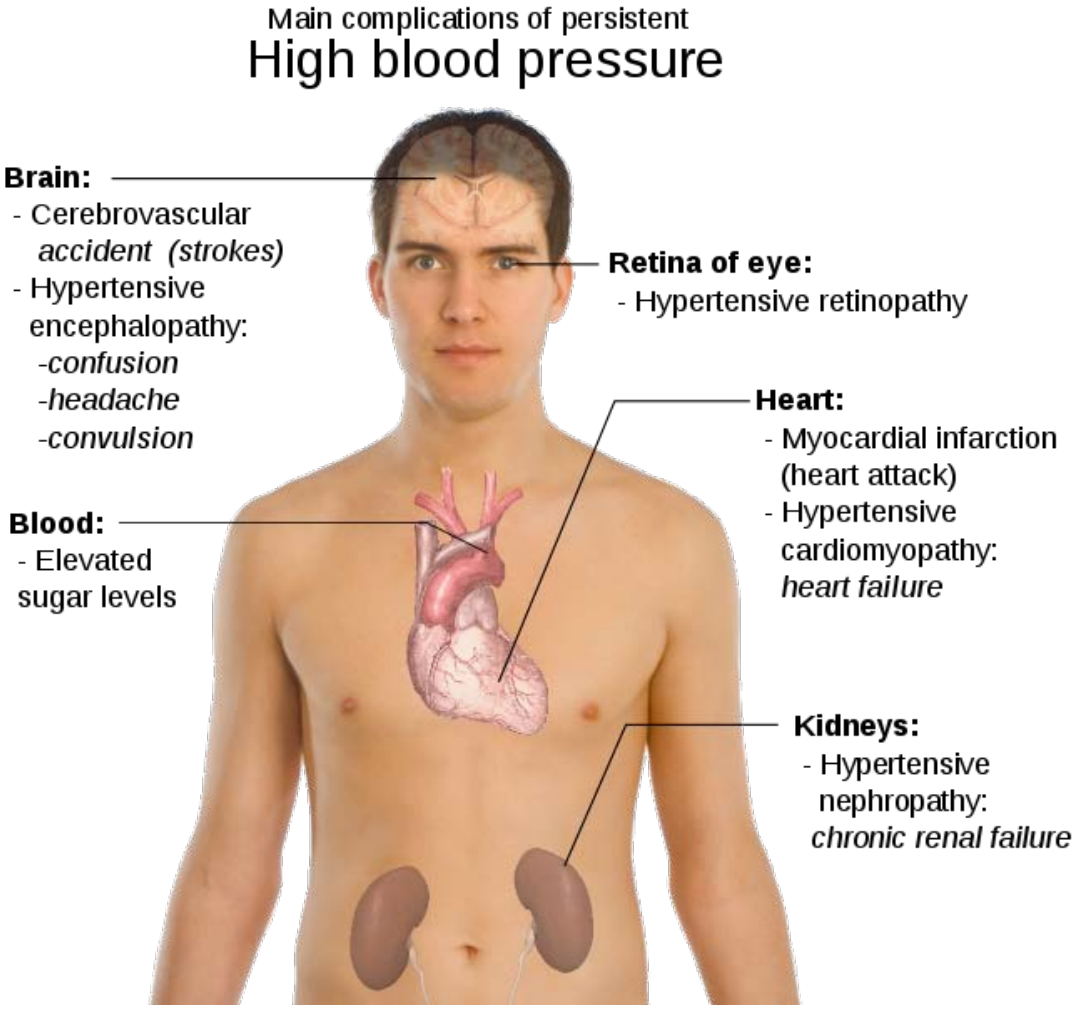


Diagram illustrating the main complications of persistent high blood pressure

Hypertension is the most important risk factor for death in industrialized countries. It increases hardening of the arteries thus predisposes individuals to heart disease, peripheral vascular disease, and strokes. Types of heart disease that may occur include: myocardial infarction, heart failure, and left ventricular hypertrophy Other complications include:

- Hypertensive retinopathy
- Hypertensive nephropathy
- If blood pressure is very high hypertensive encephalopathy may result.

Epidemiology

In the year 2000 it is estimated that nearly one billion people or ~26% of the adult population have hypertension worldwide. It was common in both developed (333 million) and undeveloped (639 million) countries. However rates vary markedly in different

regions with rates as low as 3.4% (men) and 6.8% (women) in rural India and as high as 68.9% (men) and 72.5% (women) in Poland.

In 1995 it is estimated that 43 million people in the United States had hypertension or were taking antihypertensive medication, almost 24% of the adult population. The prevalence of hypertension in the United States is increasing and reached 29% in 2004. It is more common in blacks and native Americans and less in whites and Mexican Americans, rates increase with age, and is greater in the southeastern United States. Hypertension is more prevalent in men (though menopause tends to decrease this difference) and those of low socioeconomic status.

Over 90–95% of adult hypertension is essential hypertension. The most common cause of secondary hypertension is primary aldosteronism. The incidence of exercise hypertension is reported to range from 1–10%.

Pediatrics

The prevalence of high blood pressure in the young is increasing. Most childhood hypertension, particularly in preadolescents, is secondary to an underlying disorder. Kidney disease is the most common (60–70%) cause of hypertension in children. Adolescents usually have primary or essential hypertension, which accounts for 85–95% of cases.

History

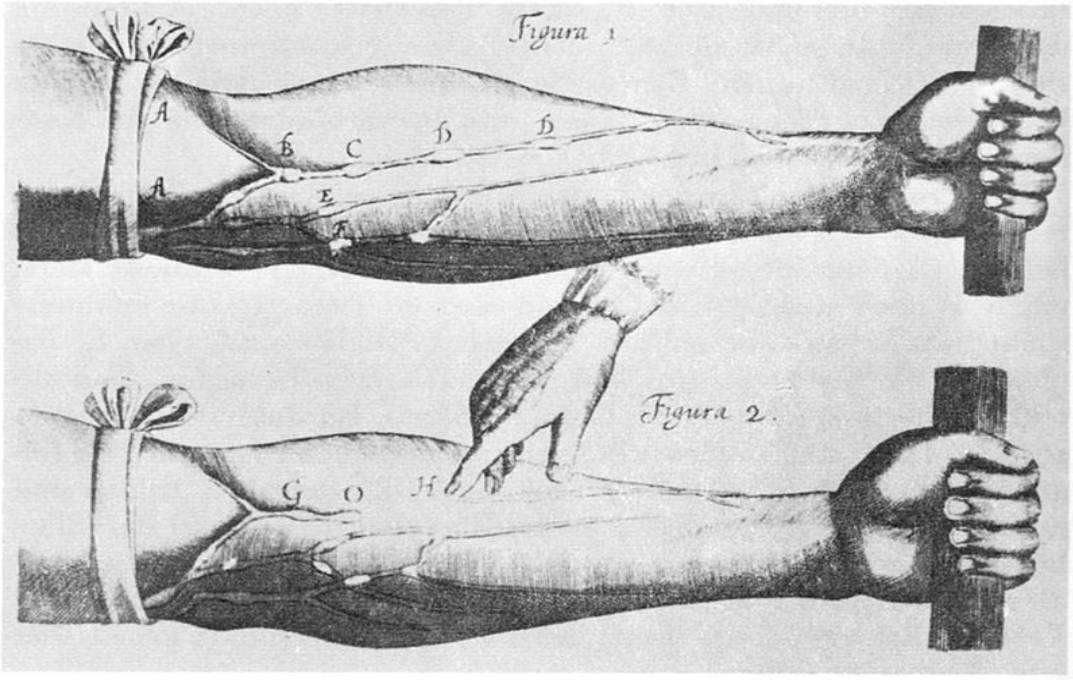


Image of veins from Harvey's *Exercitatio Anatomica de Motu Cordis et Sanguinis in Animalibus*

Some cite the writings of Sushruta in the 6th century BC as being the first mention of symptoms like those of hypertension. Others propose even earlier descriptions dating as far as 2600 BCE. Main treatment for what was called the "hard pulse disease" consisted in reducing the quantity of blood in a subject by the sectioning of veins or the application of leeches. Well known individuals such as The Yellow Emperor of China, Cornelius Celsus, Galen, and Hipocrates advocated such treatments.

Our modern understanding of hypertension began with the work of physician William Harvey (1578–1657), who was the first to describe correctly the systemic circulation of blood being pumped around the body by the heart in his book "*De motu cordis*". The basis for measuring blood pressure were established by Stephen Hales in 1733. Initial descriptions of hypertension as a disease came among others from Thomas Young in 1808 and specially Richard Bright in 1836. The first ever elevated blood pressure in a patient without kidney disease was reported by Frederick Mahomed (1849–1884). It was not until 1904 that sodium restriction was advocated while a rice diet was popularized around 1940.

Studies in the 1920s demonstrated the public health impact of untreated high blood pressure; treatment options were limited at the time, and deaths from malignant hypertension and its complications were common. A prominent victim of severe hypertension leading to cerebral hemorrhage was Franklin D. Roosevelt (1882–1945). The Framingham Heart Study added to the epidemiological understanding of hypertension and its relationship with coronary artery disease. The National Institutes of Health also sponsored other population studies, which additionally showed that African Americans had a higher burden of hypertension and its complications. Before pharmacological treatment for hypertension became possible, three treatment modalities were used, all with numerous side-effects: strict sodium restriction, sympathectomy (surgical ablation of parts of the sympathetic nervous system), and pyrogen therapy (injection of substances that caused a fever, indirectly reducing blood pressure).

The first chemical for hypertension, sodium thiocyanate, was used in 1900 but had many side effects and was unpopular. Several other agents were developed after the Second World War, the most popular and reasonably effective of which were tetramethylammonium chloride and its derivative hexamethonium, hydralazine and reserpine (derived from the medicinal plant *Rauwolfia serpentina*). A randomized controlled trial sponsored by the Veterans Administration using these drugs had to be stopped early because those not receiving treatment were developing more complications and it was deemed unethical to withhold treatment from them. These studies prompted public health campaigns to increase public awareness of hypertension and the advice to get blood pressure measured and treated. These measures appear to have contributed at least in part of the observed 50% fall in stroke and ischemic heart disease between 1972 and 1994.

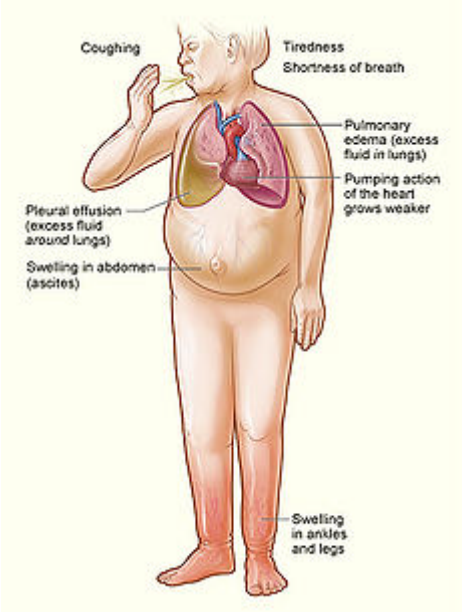
A major breakthrough was achieved with the discovery of the first well-tolerated orally available agents. The first was chlorothiazide, the first thiazide and developed from the antibiotic sulfanilamide, which became available in 1958; it increased salt excretion

while preventing fluid accumulation. In 1975, the Lasker Special Public Health Award was awarded to the team that developed chlorothiazide. The British physician James W. Black developed beta blockers in the early 1960s; these were initially used for angina, but turned out to lower blood pressure. Black received the 1976 Lasker Award and in 1988 the Nobel Prize in Physiology or Medicine for his discovery. The next class of antihypertensives to be discovered was that of the calcium channel blockers. The first member was verapamil, a derivative of papaverine that was initially thought to be a beta blocker and used for angina, but then turned out to have a different mode of action and was shown to lower blood pressure. ACE inhibitors were developed through rational drug design; the renin-angiotensin system was known to play an important role in blood pressure regulation, and snake venom from *Bothrops jararaca* could lower blood pressure through inhibition of ACE. In 1977 captopril, an orally active agent, was described; this led to the development of a number of other ACE inhibitors.

Chapter 15

Heart Failure

Heart failure



The major signs and symptoms of heart failure.

ICD-10	I50.
ICD-9	428.0
DiseasesDB	16209
MedlinePlus	000158
eMedicine	med/3552 emerg/108 radio/189 med/1367150 ped/2636
MeSH	D006333

Heart failure (**HF**) is generally defined as inability of the heart to supply sufficient blood flow to meet the body's needs. It has various diagnostic criteria, and the term *heart failure* is often incorrectly used to describe other cardiac-related illnesses, such as myocardial infarction (heart attack) or cardiac arrest.

Common causes of heart failure include myocardial infarction (heart attacks) and other forms of ischemic heart disease, hypertension, valvular heart disease, and cardiomyopathy. Heart failure can cause a number of symptoms including shortness of breath (typically worse when lying flat, which is called orthopnea), coughing, chronic venous congestion, ankle swelling, and exercise intolerance. Heart failure is often undiagnosed due to a lack of a universally agreed definition and challenges in definitive diagnosis. Treatment commonly consists of lifestyle measures (such as smoking cessation, light exercise including breathing protocols, decreased salt intake and other dietary changes) and medications, and sometimes devices or even surgery.

Heart failure is a common, costly, disabling, and potentially deadly condition. In developed countries, around 2% of adults suffer from heart failure, but in those over the age of 65, this increases to 6–10%. Mostly due to costs of hospitalization it is associated with a high health expenditure; costs have been estimated to amount to 2% of the total budget of the National Health Service in the United Kingdom, and more than $35 billion in the United States. Heart failure is associated with significantly reduced physical and mental health, resulting in a markedly decreased quality of life. With the exception of heart failure caused by reversible conditions, the condition usually worsens with time. Although some people survive many years, progressive disease is associated with an overall annual mortality rate of 10%.

Terminology

Heart failure is a global term for the physiological state in which cardiac output is insufficient in meeting the needs of the body and lungs.

This occurs most commonly when the cardiac output is low (often termed "congestive heart failure" or CHF, because the body becomes congested with fluid).

It may also occur when the body's requirements for oxygen and nutrients are increased and demand outstrips what the heart can provide, (termed "high output cardiac failure"). This can occur from severe anemia, Gram negative septicaemia, beriberi (vitamin B_1/thiamine deficiency), thyrotoxicosis, Paget's disease, arteriovenous fistulae, or arteriovenous malformations.

Fluid overload is a common problem for people with heart failure but is not synonymous with it. Patients with treated heart failure will often be euvolaemic (a term for normal fluid status), or more rarely, dehydrated.

Medical professionals use the words "acute" to mean of rapid onset and "chronic" of long duration. Chronic heart failure is therefore a long term situation, usually with stable treated symptomatology.

Acute decompensated heart failure is a term used to describe exacerbated or decompensated heart failure, referring to episodes in which a patient can be characterized

as having a change in heart failure signs and symptoms resulting in a need for urgent therapy or hospitalization.

There are several terms which are closely related to heart failure, and may be the cause of heart failure, but should not be confused with it:

- Cardiac arrest and asystole refer to situations in which there is *no* cardiac output at all. Without urgent treatment these result in sudden death.
- Myocardial infarction ("Heart attack") refers to heart muscle damage due to insufficient blood supply, usually as a result of a blocked coronary artery.
- Cardiomyopathy refers specifically to problems within the heart muscle, and these problems usually result in heart failure. Ischemic cardiomyopathy implies that the cause of muscle damage is coronary artery disease. Dilated cardiomyopathy implies that the muscle damage has resulted in enlargement of the heart. Hypertrophic cardiomyopathy involves enlargement and *thickening* of the heart muscle.

Classification

There are many different ways to categorize heart failure, including:

- the side of the heart involved, (left heart failure versus right heart failure) Left heart failure compromises aortic flow to the body and brain. Right heart failure compromises pulmonic flow to the lungs. Mixed presentations are common, especially when the cardiac septum is involved.
- whether the abnormality is due to insufficient contraction and/or relaxation of the heart (systolic dysfunction vs. diastolic dysfunction)
- whether the problem is primarily increased venous back pressure (behind) the heart Afterload, or failure to supply adequate arterial perfusion (in front of) the heart Preload (backward vs. forward failure)
- whether the abnormality is due to low cardiac output with high systemic vascular resistance or high cardiac output with low vascular resistance (low-output heart failure vs. high-output heart failure)
- the degree of functional impairment conferred by the abnormality (as in the NYHA functional classification)
- the degree of coexisting illness: i.e. heart failure/systemic hypertension, heart failure/pulmonary hypertension, heart failure/diabetes, heart failure/renal failure, etc.

Functional classification generally relies on the New York Heart Association Functional Classification. The classes (I-IV) are:

- Class I: no limitation is experienced in any activities; there are no symptoms from ordinary activities.
- Class II: slight, mild limitation of activity; the patient is comfortable at rest or with mild exertion.

- Class III: marked limitation of any activity; the patient is comfortable only at rest.
- Class IV: any physical activity brings on discomfort and symptoms occur at rest.

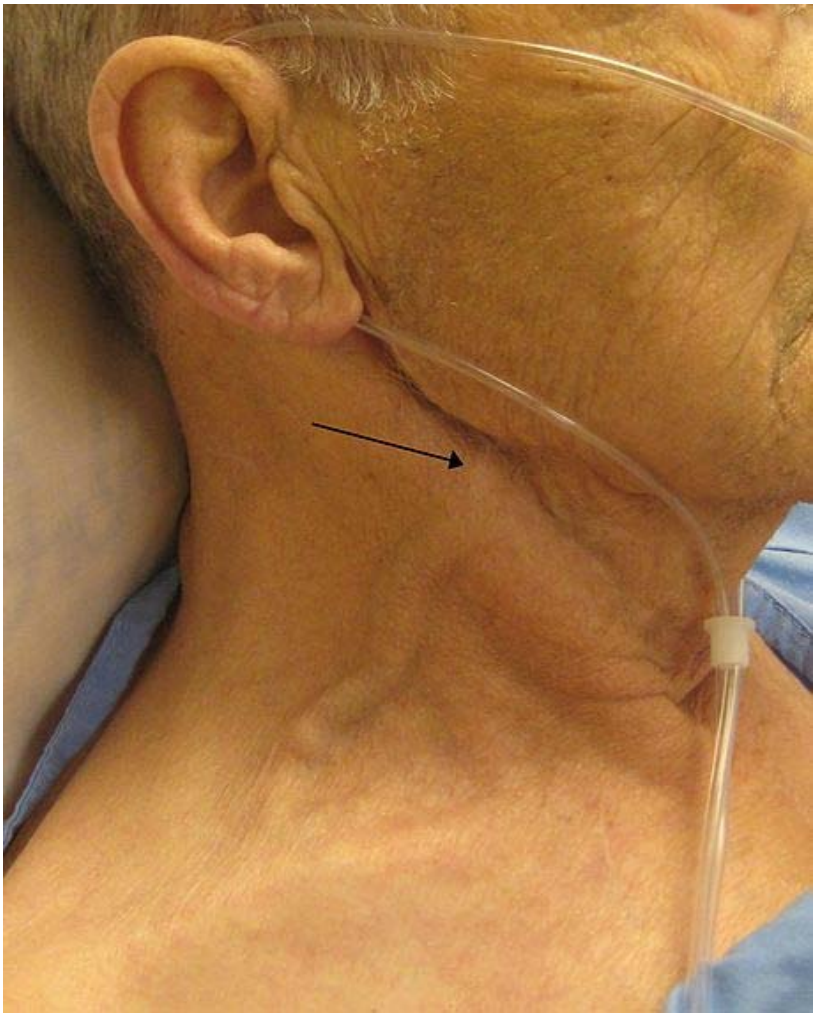
This score documents severity of symptoms, and can be used to assess response to treatment. While its use is widespread, the NYHA score is not very reproducible and doesn't reliably predict the walking distance or exercise tolerance on formal testing.

In its 2001 guidelines the American College of Cardiology/American Heart Association working group introduced four stages of heart failure:

- Stage A: Patients at high risk for developing HF in the future but no functional or structural heart disorder;
- Stage B: a structural heart disorder but no symptoms at any stage;
- Stage C: previous or current symptoms of heart failure in the context of an underlying structural heart problem, but managed with medical treatment;
- Stage D: advanced disease requiring hospital-based support, a heart transplant or palliative care.

The ACC staging system is useful in that Stage A encompasses "pre-heart failure" - a stage where intervention with treatment can presumably prevent progression to overt symptoms. ACC stage A does not have a corresponding NYHA class. ACC Stage B would correspond to NYHA Class I. ACC Stage C corresponds to NYHA Class II and III, while ACC Stage D overlaps with NYHA Class IV.

Signs and symptoms



A man with congestive heart failure and marked jugular venous distension. External jugular vein marked by an arrow.

Signs

Left-sided failure

Common respiratory signs are tachypnea (increased *rate* of breathing) and increased *work* of breathing (non-specific signs of respiratory distress). Rales or crackles, heard initially in the lung bases, and when severe, throughout the lung fields suggest the development of pulmonary edema (fluid in the alveoli). Cyanosis which suggests severe hypoxemia, is a late sign of extremely severe pulmonary edema.

Additional signs indicating left ventricular failure include a laterally displaced apex beat (which occurs if the heart is enlarged) and a gallop rhythm (additional heart sounds) may be heard as a marker of increased blood flow, or increased intra-cardiac pressure. Heart

murmurs may indicate the presence of valvular heart disease, either as a cause (e.g. aortic stenosis) or as a result (e.g., mitral regurgitation) of the heart failure.

Right-sided failure

Physical examination can reveal pitting peripheral edema, ascites, and hepatomegaly. Jugular venous pressure is frequently assessed as a marker of fluid status, which can be accentuated by the hepatojugular reflux. If the right ventricular pressure is increased, a parasternal heave may be present, signifying the compensatory increase in contraction strength.

Biventricular failure

Dullness of the lung fields to finger percussion and reduced breath sounds at the bases of the lung may suggest the development of a pleural effusion (fluid collection in between the lung and the chest wall). Though it can occur in isolated left- or right-sided heart failure, it is more common in biventricular failure because pleural veins drain both into the systemic and pulmonary venous system. When unilateral, effusions are often right sided.

Symptoms

Heart failure symptoms are traditionally and somewhat arbitrarily divided into "left" and "right" sided, recognizing that the left and right ventricles of the heart supply different portions of the circulation. However, heart failure is not exclusively *backward failure* (in the part of the circulation which drains to the ventricle).

There are several other exceptions to a simple left-right division of heart failure symptoms. Left sided *forward* failure overlaps with right sided *backward* failure. Additionally, the most common cause of right-sided heart failure is left-sided heart failure. The result is that patients commonly present with both sets of signs and symptoms.

Left-sided failure

Backward failure of the left ventricle causes congestion of the pulmonary vasculature, and so the symptoms are predominantly respiratory in nature. Backward failure can be subdivided into failure of the left atrium, the left ventricle or both within the left circuit. The patient will have dyspnea (shortness of breath) on exertion (*dyspnée d'effort*) and in severe cases, dyspnea at rest. Increasing breathlessness on lying flat, called orthopnea, occurs. It is often measured in the number of pillows required to lie comfortably, and in severe cases, the patient may resort to sleeping while sitting up. Another symptom of heart failure is paroxysmal nocturnal dyspnea a sudden nighttime attack of severe breathlessness, usually several hours after going to sleep. Easy fatigueability and exercise intolerance are also common complaints related to respiratory compromise.

"Cardiac asthma" or wheezing may occur.

Compromise of left ventricular *forward* function may result in symptoms of poor systemic circulation such as dizziness, confusion and cool extremities at rest.

Right-sided failure

Backward failure of the right ventricle leads to congestion of systemic capillaries. This generates excess fluid accumulation in the body. This causes swelling under the skin (termed peripheral edema or anasarca) and usually affects the dependent parts of the body first (causing foot and ankle swelling in people who are standing up, and sacral edema in people who are predominantly lying down). Nocturia (frequent nighttime urination) may occur when fluid from the legs is returned to the bloodstream while lying down at night. In progressively severe cases, ascites (fluid accumulation in the abdominal cavity causing swelling) and hepatomegaly (enlargement of the liver) may develop. Significant liver congestion may result in impaired liver function, and jaundice and even coagulopathy (problems of decreased blood clotting) may occur.

Causes

Chronic heart failure

The predominance of causes of heart failure are difficult to analyze due to challenges in diagnosis, differences in populations, and changing prevalence of causes with age.

A 19 year study of 13000 healthy adults in the United States (the National Health and Nutrition Examination Survey (NHANES I) found the following causes ranked by Population Attributable Risk score:

1. Ischaemic heart disease 62%
2. Cigarette smoking 16%
3. Hypertension (high blood pressure)10%
4. Obesity 8%
5. Diabetes 3%
6. Valvular heart disease 2% (much higher in older populations)

An Italian registry of over 6200 patients with heart failure showed the following underlying causes:

1. Ischaemic heart disease 40%
2. Dilated cardiomyopathy 32%
3. Valvular heart disease 12%
4. Hypertension 11%
5. Other 5%

Rarer causes of heart failure include:

- Viral myocarditis (an infection of the heart muscle)
- Infiltrations of the muscle such as amyloidosis
- HIV cardiomyopathy (caused by human immunodeficiency virus)
- Connective tissue diseases such as systemic lupus erythematosus
- Abuse of drugs such as alcohol and cocaine
- Pharmaceutical drugs such as chemotherapeutic agents
- Arrhythmias

Obstructive sleep apnea a condition of sleep disordered breathing overlaps with obesity, hypertension, and diabetes and is regarded as an independent cause of heart failure.

Acute decompensated heart failure

Chronic stable heart failure may easily decompensate. This most commonly results from an intercurrent illness (such as pneumonia), myocardial infarction (a heart attack), arrhythmias, uncontrolled hypertension, or a patient's failure to maintain a fluid restriction, diet, or medication. Other well recognized precipitating factors include anemia and hyperthyroidism which place additional strain on the heart muscle. Excessive fluid or salt intake, and medication that causes fluid retention such as NSAIDs and thiazolidinediones, may also precipitate decompensation.

Pathophysiology

Heart failure is caused by any condition which reduces the efficiency of the myocardium, or heart muscle, through damage or overloading. As such, it can be caused by as diverse an array of conditions as myocardial infarction (in which the heart muscle is starved of oxygen and dies), hypertension (which increases the force of contraction needed to pump blood) and amyloidosis (in which protein is deposited in the heart muscle, causing it to stiffen). Over time these increases in workload will produce changes to the heart itself:

- Reduced force of contraction, due to overloading of the ventricle. In health, increased filling of the ventricle results in increased force of contraction (by the Frank–Starling law of the heart) and thus a rise in cardiac output. In heart failure this mechanism fails, as the ventricle is loaded with blood to the point where heart muscle contraction becomes less efficient. This is due to reduced ability to cross-link actin and myosin filaments in over-stretched heart muscle.
- A reduced stroke volume, as a result of a failure of systole, diastole or both. Increased end systolic volume is usually caused by reduced contractility. Decreased end diastolic volume results from impaired ventricular filling – as occurs when the compliance of the ventricle falls (i.e. when the walls stiffen).
- Reduced spare capacity. As the heart works harder to meet normal metabolic demands, the amount cardiac output can increase in times of increased oxygen demand (e.g. exercise) is reduced. This contributes to the exercise intolerance commonly seen in heart failure. This translates to the loss of one's cardiac reserve.

The cardiac reserve refers to the ability of the heart to work harder during exercise or strenuous activity. Since the heart has to work harder to meet the normal metabolic demands, it is incapable of meeting the metabolic demands of the body during exercise.

- Increased heart rate, stimulated by increased sympathetic activity in order to maintain cardiac output. Initially, this helps compensate for heart failure by maintaining blood pressure and perfusion, but places further strain on the myocardium, increasing coronary perfusion requirements, which can lead to worsening of ischemic heart disease. Sympathetic activity may also cause potentially fatal arrhythmias.
- Hypertrophy (an increase in physical size) of the myocardium, caused by the terminally differentiated heart muscle fibres increasing in size in an attempt to improve contractility. This may contribute to the increased stiffness and decreased ability to relax during diastole.
- Enlargement of the ventricles, contributing to the enlargement and spherical shape of the failing heart. The increase in ventricular volume also causes a reduction in stroke volume due to mechanical and contractile inefficiency.

The general effect is one of reduced cardiac output and increased strain on the heart. This increases the risk of cardiac arrest (specifically due to ventricular dysrhythmias), and reduces blood supply to the rest of the body. In chronic disease the reduced cardiac output causes a number of changes in the rest of the body, some of which are physiological compensations, some of which are part of the disease process:

- Arterial blood pressure falls. This destimulates baroreceptors in the carotid sinus and aortic arch which link to the nucleus tractus solitarius. This center in the brain increases sympathetic activity, releasing catecholamines into the blood stream. Binding to alpha-1 receptors results in systemic arterial vasoconstriction. This helps restore blood pressure but also increases the total peripheral resistance, increasing the workload of the heart. Binding to beta-1 receptors in the myocardium increases the heart rate and make contractions more forceful, in an attempt to increase cardiac output. This also, however, increases the amount of work the heart has to perform.
- Increased sympathetic stimulation also causes the hypothalamus to secrete vasopressin (also known as antidiuretic hormone or ADH), which causes fluid retention at the kidneys. This increases the blood volume and blood pressure.
- Reduced perfusion (blood flow) to the kidneys stimulates the release of renin – an enzyme which catalyses the production of the potent vasopressor angiotensin. Angiotensin and its metabolites cause further vasocontriction, and stimulate increased secretion of the steroid aldosterone from the adrenal glands. This promotes salt and fluid retention at the kidneys, also increasing the blood volume.
- The chronically high levels of circulating neuroendocrine hormones such as catecholamines, renin, angiotensin, and aldosterone affects the myocardium directly, causing structural remodelling of the heart over the long term. Many of these remodelling effects seem to be mediated by transforming growth factor beta (TGF-beta), which is a common downstream target of the signal transduction

cascade initiated by catecholamines and angiotensin II, and also by epidermal growth factor (EGF), which is a target of the signaling pathway activated by aldosterone
- Reduced perfusion of skeletal muscle causes atrophy of the muscle fibres. This can result in weakness, increased fatigueability and decreased peak strength - all contributing to exercise intolerance.

The increased peripheral resistance and greater blood volume place further strain on the heart and accelerates the process of damage to the myocardium. Vasoconstriction and fluid retention produce an increased hydrostatic pressure in the capillaries. This shifts the balance of forces in favour of interstitial fluid formation as the increased pressure forces additional fluid out of the blood, into the tissue. This results in edema (fluid build-up) in the tissues. In right-sided heart failure this commonly starts in the ankles where venous pressure is high due to the effects of gravity (although if the patient is bed-ridden, fluid accumulation may begin in the sacral region.) It may also occur in the abdominal cavity, where the fluid build-up is called ascites. In left-sided heart failure edema can occur in the lungs - this is called cardiogenic pulmonary edema. This reduces spare capacity for ventilation, causes stiffening of the lungs and reduces the efficiency of gas exchange by increasing the distance between the air and the blood. The consequences of this are shortness of breath, orthopnea and paroxysmal nocturnal dyspnea.

The symptoms of heart failure are largely determined by which side of the heart fails. The left side pumps blood into the systemic circulation, whilst the right side pumps blood into the pulmonary circulation. Whilst left-sided heart failure will reduce cardiac output to the systemic circulation, the initial symptoms often manifest due to effects on the pulmonary circulation. In systolic dysfunction, the ejection fraction is decreased, leaving an abnormally elevated volume of blood in the left ventricle. In diastolic dysfunction, end-diastolic ventricular pressure will be high. This increase in volume or pressure backs up to the left atrium and then to the pulmonary veins. Increased volume or pressure in the pulmonary veins impairs the normal drainage of the alveoli and favors the flow of fluid from the capillaries to the lung parenchyma, causing pulmonary edema. This impairs gas exchange. Thus, left-sided heart failure often presents with respiratory symptoms: shortness of breath, orthopnea and paroxysmal nocturnal dyspnea.

In severe cardiomyopathy, the effects of decreased cardiac output and poor perfusion become more apparent, and patients will manifest with cold and clammy extremities, cyanosis, claudication, generalized weakness, dizziness, and syncope

The resultant hypoxia caused by pulmonary edema causes vasoconstriction in the pulmonary circulation, which results in pulmonary hypertension. Since the right ventricle generates far lower pressures than the left ventricle (approximately 20 mmHg versus around 120 mmHg, respectively, in the healthy individual) but nonetheless generates cardiac output exactly equal to the left ventricle, this means that a small increase in pulmonary vascular resistance causes a large increase in amount of work the right ventricle must perform. However, the main mechanism by which left-sided heart failure causes right-sided heart failure is actually not well understood. Some theories invoke

mechanisms that are mediated by neurohormonal activation. Mechanical effects may also contribute. As the left ventricle distends, the intraventricular septum bows into the right ventricle, decreasing the capacity of the right ventricle.

Systolic dysfunction

Heart failure caused by systolic dysfunction is more readily recognized. It can be simplistically described as failure of the pump function of the heart. It is characterized by a decreased ejection fraction (less than 45%). The strength of ventricular contraction is attenuated and inadequate for creating an adequate stroke volume, resulting in inadequate cardiac output. In general, this is caused by dysfunction or destruction of cardiac myocytes or their molecular components. In congenital diseases such as Duchenne muscular dystrophy, the molecular structure of individual myocytes is affected. Myocytes and their components can be damaged by inflammation (such as in myocarditis) or by infiltration (such as in amyloidosis). Toxins and pharmacological agents (such as ethanol, cocaine, and amphetamines) cause intracellular damage and oxidative stress. The most common mechanism of damage is ischemia causing infarction and scar formation. After myocardial infarction, dead myocytes are replaced by scar tissue, deleteriously affecting the function of the myocardium. On echocardiogram, this is manifest by abnormal or absent wall motion.

Because the ventricle is inadequately emptied, ventricular end-diastolic pressure and volumes increase. This is transmitted to the atrium. On the left side of the heart, the increased pressure is transmitted to the pulmonary vasculature, and the resultant hydrostatic pressure favors extravassation of fluid into the lung parenchyma, causing pulmonary edema. On the right side of the heart, the increased pressure is transmitted to the systemic venous circulation and systemic capillary beds, favoring extravassation of fluid into the tissues of target organs and extremities, resulting in dependent peripheral edema.

Diastolic dysfunction

Heart failure caused by diastolic dysfunction is generally described as the failure of the ventricle to adequately relax and typically denotes a stiffer ventricular wall. This causes inadequate filling of the ventricle, and therefore results in an inadequate stroke volume. The failure of ventricular relaxation also results in elevated end-diastolic pressures, and the end result is identical to the case of systolic dysfunction (pulmonary edema in left heart failure, peripheral edema in right heart failure.)

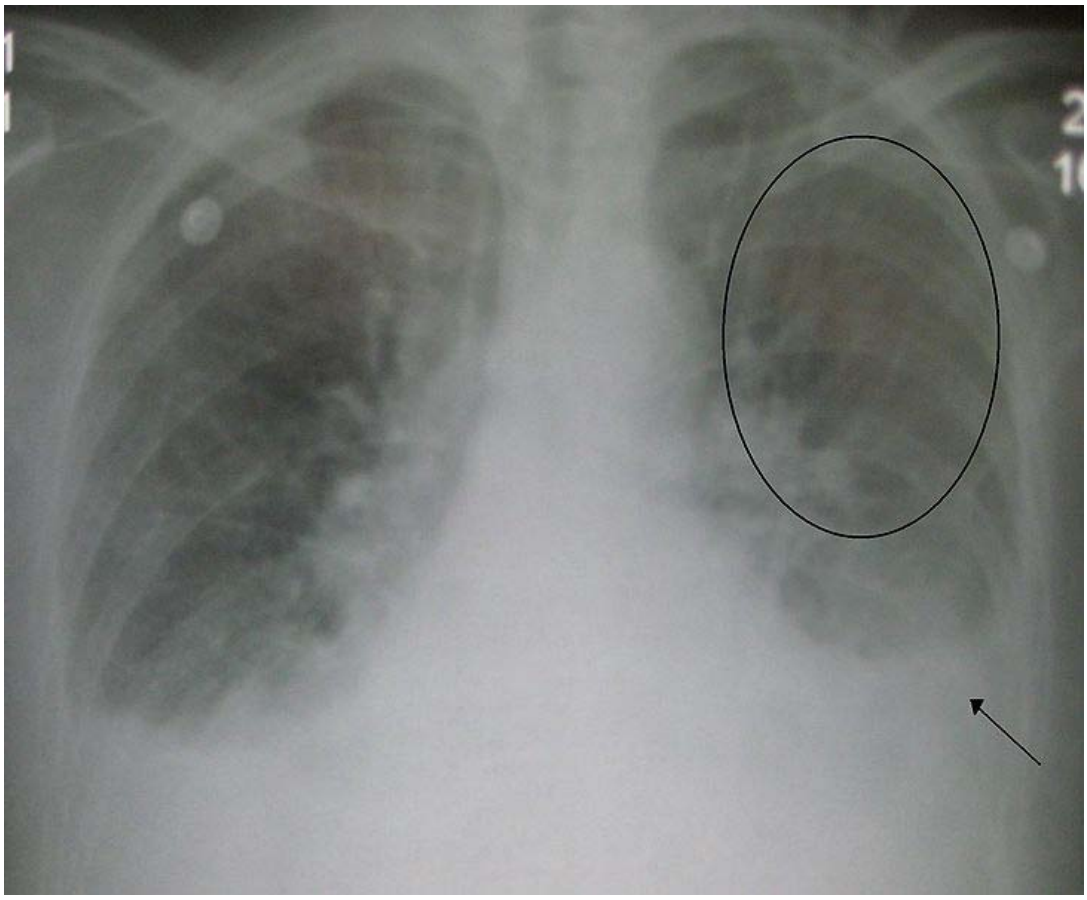
Diastolic dysfunction can be caused by processes similar to those that cause systolic dysfunction, particularly causes that affect cardiac remodeling.

Diastolic dysfunction may not manifest itself except in physiologic extremes if systolic function is preserved. The patient may be completely asymptomatic at rest. However, they are exquisitely sensitive to increases in heart rate, and sudden bouts of tachycardia (which can be caused simply by physiological responses to exertion, fever, or

dehydration, or by pathological tachyarrhythmias such as atrial fibrillation with rapid ventricular response) may result in flash pulmonary edema. Adequate rate control (usually with a pharmacological agent that slows down AV conduction such as a calcium channel blocker or a beta-blocker) is therefore key to preventing decompensation.

Left ventricular diastolic function can be determined through echocardiography by measurement of various parameters such as the E/A ratio (early-to-atrial left ventricular filling ratio), the E (early left ventricular filling) deceleration time, and the isovolumic relaxation time.

Diagnosis



Acute pulmonary edema. Note enlarged heart size, apical vascular redistribution (circle), and small bilateral pleural effusions (arrow).

No system of diagnostic criteria has been agreed as the gold standard for heart failure. Commonly used systems are the "Framingham criteria" (derived from the Framingham Heart Study), the "Boston criteria", the "Duke criteria", and (in the setting of acute myocardial infarction) the "Killip class".

Imaging

Echocardiography is commonly used to support a clinical diagnosis of heart failure. This modality uses ultrasound to determine the stroke volume (SV, the amount of blood in the heart that exits the ventricles with each beat), the end-diastolic volume (EDV, the total amount of blood at the end of diastole), and the SV in proportion to the EDV, a value known as the *ejection fraction* (EF). In pediatrics, the shortening fraction is the preferred measure of systolic function. Normally, the EF should be between 50% and 70%; in systolic heart failure, it drops below 40%. Echocardiography can also identify valvular heart disease and assess the state of the pericardium (the connective tissue sac surrounding the heart). Echocardiography may also aid in deciding what treatments will help the patient, such as medication, insertion of an implantable cardioverter-defibrillator or cardiac resynchronization therapy. Echocardiography can also help determine if acute myocardial ischemia is the precipitating cause, and may manifest as regional wall motion abnormalities on echo.

Chest X-rays are frequently used to aid in the diagnosis of CHF. In the compensated patient, this may show cardiomegaly (visible enlargement of the heart), quantified as the *cardiothoracic ratio* (proportion of the heart size to the chest). In left ventricular failure, there may be evidence of vascular redistribution ("upper lobe blood diversion" or "cephalization"), Kerley lines, cuffing of the areas around the bronchi, and interstitial edema.

Electrophysiology

An electrocardiogram (ECG/EKG) may be used to identify arrhythmias, ischemic heart disease, right and left ventricular hypertrophy, and presence of conduction delay or abnormalities (e.g. left bundle branch block). Although these findings are not specific to the diagnosis of heart failure a normal ECG virtually excludes left ventricular systolic dysfunction.

Blood tests

Blood tests routinely performed include electrolytes (sodium, potassium), measures of renal function, liver function tests, thyroid function tests, a complete blood count, and often C-reactive protein if infection is suspected. An elevated B-type natriuretic peptide (BNP) is a specific test indicative of heart failure. Additionally, BNP can be used to differentiate between causes of dyspnea due to heart failure from other causes of dyspnea. If myocardial infarction is suspected, various cardiac markers may be used.

According to a meta-analysis comparing BNP and N-terminal pro-BNP (NTproBNP) in the diagnosis of heart failure, BNP is a better indicator for heart failure and left ventricular systolic dysfunction. In groups of symptomatic patients, a diagnostic odds ratio of 27 for BNP compares with a sensitivity of 85% and specificity of 84% in detecting heart failure.

Angiography

Heart failure may be the result of coronary artery disease, and its prognosis depends in part on the ability of the coronary arteries to supply blood to the myocardium (heart muscle). As a result, coronary catheterization may be used to identify possibilities for revascularisation through percutaneous coronary intervention or bypass surgery.

Monitoring

Various measures are often used to assess the progress of patients being treated for heart failure. These include fluid balance (calculation of fluid intake and excretion), monitoring body weight (which in the shorter term reflects fluid shifts).

Algorithms

There are various algorithms for the diagnosis of heart failure. For example, the algorithm used by the Framingham Heart Study adds together criteria mainly from physical examination. In contrast, the more extensive algorithm by the European Society of Cardiology (ESC) weights the difference between supporting and opposing parameters from the medical history, physical examination, further medical tests as well as response to therapy.

Framingham criteria

By the Framingham criteria, diagnosis of congestive heart failure (heart failure with impaired pumping capability) requires the simultaneous presence of at least 2 of the following major criteria or 1 major criterion in conjunction with 2 of the following minor criteria:

Major criteria:

- Cardiomegaly on chest radiography
- S3 gallop (a third heart sound)
- Acute pulmonary edema
- Paroxysmal nocturnal dyspnea
- Crackles on lung auscultation
- Central venous pressure of more than 16 cm H2O at the right atrium
- Jugular vein distension
- Positive abdominojugular test
- Weight loss of more than 4.5 kg in 5 days in response to treatment (sometimes classified as a minor criterium)

Minor criteria:

- Tachycardia of more than 120 beats per minute
- Nocturnal cough

- Dyspnea on ordinary exertion
- Pleural effusion
- Decrease in vital capacity by one third from maximum recorded
- Hepatomegaly
- Bilateral ankle edema

Minor criteria are acceptable only if they can not be attributed to another medical condition such as pulmonary hypertension, chronic lung disease, cirrhosis, ascites, or the nephrotic syndrome. The Framingham Heart Study criteria are 100% sensitive and 78% specific for identifying persons with definite congestive heart failure.

ESC algorithm

The ESC algorithm weights the following parameters in establishing the diagnosis of heart failure:

Parameter	Influence + - to some degree ++ - to intermediate degree +++ - to high degree	Supports if present	Opposes if normal or absent
Compatible symptoms		++	++
Compatible signs		++	+
Cardiac dysfunction on echocardiography		+++	+++
Response of symptoms or signs to therapy		+++	++
ECG			
Normal			++
Abnormal		++	+
Dysrhythmia		+++	+
Laboratory			
BNP > 400 pg/mL and/or NT-proBNP > 2000 pg/mL		+++	+
BNP < 100 pg/mL and NT-proBNP < 400 pg/mL		+	+++
Hyponatraemia		+	+
Renal dysfunction		+	+
Mild elevations of troponin		+	+
Chest X-ray			
Pulmonary congestion		+++	+
Reduced exercise capacity		+++	++

Abnormal pulmonary function tests	+	+
Abnormal haemodynamics at rest	+++	++

Management

Treatment focuses on improving the symptoms and preventing the progression of the disease. Reversible causes of the heart failure also need to be addressed: (e.g. infection, alcohol ingestion, anemia, thyrotoxicosis, arrhythmia, hypertension). Treatments include lifestyle and pharmacological modalities.

Acute decompensation

In acute decompensated heart failure (ADHF), the immediate goal is to re-establish adequate perfusion and oxygen delivery to end organs. This entails ensuring that airway, breathing, and circulation are adequate. Immediated treatments usually involve some combination of vasodilators such as nitroglycerin, diuretics such as furosemide, and possibly non invasive positive pressure ventilation (NIPPV).

Chronic management

The goal is to prevent the development of acute decompensated heart failure, to counteract the deleterious effects of cardiac remodeling, and to minimize the symptoms that the patient suffers. First-line therapy for all heart failure patients is angiotensin-converting enzyme (ACE) inhibition. ACE inhibitors (i.e., enalapril, captopril, lisinopril, ramipril) improve survival and quality of life in heart failure patients, and have been shown to reduce mortality in patients with left ventricular dysfunction in numerous randomized trials. In addition to pharmacologic agents (oral loop diuretics, beta-blockers, ACE inhibitors or angiotensin receptor blockers, vasodilators, and in severe cardiomyopathy aldosterone receptor antagonists), behavioral modification should be pursued, specifically with regards to dietary guidelines regarding salt and fluid intake. Exercise should be encouraged as tolerated, as sufficient conditioning can significantly improve quality-of-life.

In patients with severe cardiomyopathy, implantation of an automatic implantable cardioverter defibrillator (AICD) should be considered. A select population will also probably benefit from ventricular resynchronization.

In select cases, cardiac transplantation can be considered. While this may resolve the problems associated with heart failure, the patient generally must remain on an immunosuppressive regimen to prevent rejection, which has its own significant downsides.

Palliative care and hospice

Without transplantation, heart failure caused by ischemic heart disease is not reversible, and cardiac function typically deteriorates with time. (In particular, diastolic function

worsens as a function of age even in individuals without ischemic heart disease.) The growing number of patients with Stage D heart failure (intractable symptoms of fatigue, shortness of breath or chest pain at rest despite optimal medical therapy) should be considered for palliative care or hospice, according to American College of Cardiology/American Heart Association guidelines.

Prognosis

Prognosis in heart failure can be assessed in multiple ways including clinical prediction rules and cardiopulmonary exercise testing. Clinical prediction rules use a composite of clinical factors such as lab tests and blood pressure to estimate prognosis. Among several clinical prediction rules for prognosing acute heart failure, the 'EFFECT rule' slightly outperformed other rules in stratifying patients and identifying those at low risk of death during hospitalization or within 30 days. Easy methods for identifying low risk patients are:

- ADHERE Tree rule indicates that patients with blood urea nitrogen < 43 mg/dl and systolic blood pressure at least 115 mm Hg have less than 10% chance of inpatient death or complications.
- BWH rule indicates that patients with systolic blood pressure over 90 mm Hg, respiratory rate of 30 or less breaths per minute, serum sodium over 135 mmol/L, no new ST-T wave changes have less than 10% chance of inpatient death or complications.

A very important method for assessing prognosis in advanced heart failure patients is cardiopulmonary exercise testing (CPX testing). CPX testing is usually required prior to heart transplantation as an indicator of prognosis. Cardiopulmonary exercise testing involves measurement of exhaled oxygen and carbon dioxide during exercise. The peak oxygen consumption (VO2 max) is used as an indicator of prognosis. As a general rule, a VO2 max less than 12-14 cc/kg/min indicates a poor survival and suggests that the patient may be a candidate for a heart transplant. Patients with a VO2 max<10 cc/kg/min have clearly poorer prognosis. The most recent International Society for Heart and Lung Transplantation (ISHLT) guidelines also suggest two other parameters that can be used for evaluation of prognosis in advanced heart failure, the heart failure survival score and the use of a criterion of VE/VCO2 slope > 35 from the CPX test. The heart failure survival score is a score calculated using a combination of clinical predictors and the VO2 max from the cardiopulmonary exercise test.

Epidemiology

Heart failure is the leading cause of hospitalization in people older than 65. In developed countries, the mean age of patients with heart failure is 75 years old. In developing countries, two to three percent of the population suffers from heart failure, but in those 70 to 80 years old, it occurs in 20—30 percent.

Heart failure affects close to 5 million people in the USA and each year close to 500,000 new cases are diagnosed. What is of more concern is that more than 50% of patients seek re-admission within 6 months after treatment and the average duration of hospital stay is 6 days.

In tropical countries, the most common cause of HF is valvular heart disease or some type of cardiomyopathy. Moreover as underdeveloped countries become more affluent, there has also been an increase in diabetes, hypertension and obesity which has resulted in heart failure.

In USA, HF is much higher in African Americans, Hispanics, Native Americans and recent immigrants from the eastern bloc countries like Russia. This high prevalence in these ethnic populations has been linked to high incidence of diabetes and hypertension. In many new immigrants to the USA the high prevalence of heart failure has largely been attributed to lack of preventive health care or substandard treatment.

Gender

Both men and women have similar incidence of HF. However, there are distinct differences between the two genders.

- Women generally develop heart failure after menopause.
- Women tend to become more depressed than men following diagnosis.
- Women have similar symptoms but the intensity is more pronounced.
- Women usually survive a lot longer with heart failure than men.

Race

New information suggests that elements of heart failure in African Americans and Caucasians may be different and therapy for heart failure has different efficacies depending on racial, ethnic, and genetic backgrounds.

Age

Heart failure basically means that the heart muscles have become weak and do not function as normal. Heart failure is a progressive medical disorder. As the heart gets weaker, symptoms and signs become prominent. Heart failure can affect the entire heart or only the right or left side. In the majority of cases, both sides of the heart are affected. HF can occur at any age depending on the cause. In general heart failure does increase with age.