



# Medical Specialties and Therapeutic Procedures

Carl Bess

Rylee Thomson

First Edition, 2012

ISBN 978-81-323-1413-4

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*Published by:*

**College Publishing House**  
4735/22 Prakashdeep Bldg,  
Ansari Road, Darya Ganj,  
Delhi - 110002  
Email: [info@wtbooks.com](mailto:info@wtbooks.com)

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# Chapter 1

## Specialty

A **specialty** in medicine is a branch of medical science. After completing medical school, physicians or surgeons usually further their medical education in a specific specialty of medicine by completing a multiple year residency. Medical practitioners who engage in a medical specialty are known as medical specialists.

### ***Medical specialties***

In this table, as in many healthcare arenas, medical specialties are organized into the following groups:

- Surgical specialties focus on manually operative and instrumental techniques to treat disease.
- Medical specialties that focus on the diagnosis and non-surgical treatment of disease.
- Diagnostic specialties focus more purely on diagnosis of disorders.

<b>Specialty</b>	<b>Code</b>	<b>Group</b>	<b>Subspecialties</b>	<b>Focus</b>
Allergy and Immunology				Allergic reactions and the immune system
Alternative Medicine			Acupuncture · Anthroposophic medicine · Ayurveda · Chiropractic · Herbalism · Homeopathy · Naturopathy · Osteopathy · Siddha medicine · Traditional medicine (Chinese · Tibetan) · Unani	
Andrology				Male health
Anesthesiology	AN, PAN	Surgery	Paediatrics, Pain management, Intensive Care, Critical Care, Obstetrics and gynaecology, Cardiothoracic anesthesiology, Trauma Care, Pre and Post Operative Assessment and	Anesthesia

Care, Generalist (covers all the sub-specialities)

Cardiology

Medicine

Disease of the cardiovascular system

Cardiovascular surgery

Surgery

The operation of heart and major blood vessels of the chest.

- Transfusion medicine is concerned with the transfusion of blood and blood component, including the maintenance of a "blood bank".
- Cellular pathology is concerned with diagnosis using samples from patients taken as tissues and cells using histology and cytology.
- Clinical chemistry is concerned with diagnosis by making biochemical analysis of blood, body fluids and tissues.
- Hematology is concerned with diagnosis by looking at changes in the cellular composition of the blood and bone marrow as well as the coagulation system in the blood.
- Clinical microbiology is concerned with the *in vitro* diagnosis of diseases caused by bacteria, viruses, fungi, and parasites.
- Clinical immunology is concerned with disorders of the immune

Clinical laboratory sciences

Diagnostic

Application of diagnostic techniques in medical laboratories such as assays, microscope analysis.

system and related body defenses. It also deals with diagnosis of allergy.

Dermatology	D, DS	Medicine	Dermatopathology, Mohs Surgery	Skin and its appendages (hair, nails, sweat glands etc.).
Dietetics				Food and nutrition
Emergency medicine	EM	Medicine	<ul style="list-style-type: none"> <li>• Palliative medicine</li> <li>• Medical toxicology</li> <li>• Pediatric emergency medicine</li> <li>• Sports medicine, undersea and hyperbaric medicine</li> </ul>	The initial management of emergent medical conditions, often in hospital emergency departments or the field.
Endocrinology		Medicine		The endocrine system (i.e. endocrine glands and hormones) and its diseases, including diabetes and thyroid diseases.
Family Medicine FM		Medicine	<ul style="list-style-type: none"> <li>• Adolescent Medicine</li> <li>• Geriatric Medicine</li> <li>• Hospice and Palliative Medicine</li> <li>• Sleep Medicine</li> <li>• Sports Medicine</li> </ul>	Continuing, comprehensive health care for the individual and family, integrating the biological, clinical and behavioral sciences to treat patients of all ages, sexes, organ systems, and diseases.
Forensic Medicine		Medicine		

Gastroenterology GI		Medicine		The alimentary tract
General surgery GS		Surgery	<ul style="list-style-type: none"> <li>• Colorectal surgery</li> <li>• Gastrointestinal surgery</li> <li>• Transplant surgery</li> <li>• Trauma surgery</li> </ul>	
Geriatrics	IMG	Medicine		Elderly patients
Gynecology				Female reproductive health
Hepatology		Medicine		The liver and biliary tract, usually a part of gastroenterology.
Infectious disease	ID	Medicine		Diseases caused by biological agents
Intensive care medicine		Medicine		Life support and management of critically ill patients, often in an ICU.
Maxillofacial surgery	Maxfac, OMFS	Surgery	<ul style="list-style-type: none"> <li>• Craniofacial surgery (Head and neck)</li> <li>• Facial cosmetic surgery</li> <li>• Craniomaxillofacial trauma</li> </ul>	Disease of the head, neck, face, jaws and the hard and soft tissues of the oral and maxillofacial region.
Medical research			Anatomy, Biochemistry, Embryology, Genetics, Pharmacology, Toxicology	
Nephrology		Medicine		Kidney diseases
Neurology	N	Medicine	<ul style="list-style-type: none"> <li>• Behavioral Neurology</li> <li>• Clinical Neurophysiology</li> <li>• Geriatric Neurology</li> <li>• Headache Medicine</li> <li>• Neuromuscular Medicine</li> <li>• Neurodevelopmental Disabilities</li> </ul>	Diseases involving the central, peripheral, and autonomic nervous systems

			<ul style="list-style-type: none"> <li>• Neuro-oncology</li> <li>• Neuroradiology</li> <li>• Vascular Neurology</li> <li>• Hospice and Palliative Medicine</li> <li>• Pain Medicine</li> <li>• Sleep Medicine</li> </ul>	
Neurosurgery	NS	Surgery		Disease of the central nervous system, peripheral nervous system, and spinal column.
Nursing				
Obstetrics and gynecology	OB/GYN	Surgery	<ul style="list-style-type: none"> <li>• Reproductive medicine</li> <li>• Fertility medicine</li> </ul>	
Oncology	ON	Medicine	<ul style="list-style-type: none"> <li>• Radiation oncology – pertains to the use of radiation therapy (the medical use of ionizing radiation) as part of cancer treatment to control malignant cells (not to be confused with radiology).</li> </ul>	Cancer and other malignant diseases, often grouped with hematology.
Ophthalmology	OPH	Surgery		Diseases of the visual pathways, including the eyes, brain, etc.
Orthopedic surgery	ORS	Surgery	hand surgery, surgical sports medicine, adult reconstruction, spine surgery, foot and ankle, musculoskeletal oncology, orthopaedic trauma surgery, paediatric orthopedic surgery	Injury and disease of the musculoskeletal system.
Otolaryngology, or ENT	ORL, ENT	Surgery	Head and neck, facial cosmetic surgery, Neurotology, Laryngology	Treatment of ear, nose, and throat disorders. The term head and neck surgery defines a closely

Palliative care    PLM    Medicine

related specialty which is concerned mainly with the surgical management of cancer of the same anatomical structures.

A relatively modern branch of clinical medicine that deals with pain and symptom relief and emotional support in patients with terminal illnesses including cancer and heart failure.

Pathology    PTH    Diagnostic

Understanding disease through examination of molecules, cells, tissues and organs. The term encompasses both the medical specialty which uses tissues and body fluids to obtain clinically useful information, as well as the related scientific study of disease processes.

Pediatrics    PD    Medicine

Children. Like internal medicine, pediatrics has many subspecialties for specific age ranges, organ systems, disease classes, and sites of care delivery. Most subspecialties

deals with the medical care of infants, children, and adolescents (from newborn to age 16-21,

			of adult medicine have a pediatric equivalent such as pediatric cardiology, pediatric endocrinology, pediatric gastroenterology, pediatric hematology, pediatric oncology, pediatric ophthalmology, and neonatology.	depending on the country).
Pediatric surgery		Surgery	Treats a wide variety of thoracic and abdominal (and sometimes urologic) diseases of childhood.	
Physical medicine and rehabilitation Or Physiatry	PM&R	Medicine		Concerned with functional improvement after injury, illness, or congenital disorders. Elective cosmetic surgery as well as reconstructive surgery after traumatic or operative mutilation.
Plastic surgery	PS	Surgery	<ul style="list-style-type: none"> <li>• Cosmetic surgery</li> <li>• Burn</li> <li>• Microsurgery</li> <li>• Hand surgery</li> <li>• Craniofacial surgery</li> </ul>	(or Colorectal Surgery) Treats disease in the rectum, anus, and colon.
Proctology	PRO	Medicine		
Psychiatry	P	Medicine	<ul style="list-style-type: none"> <li>• Child and adolescent psychiatry focuses on the care of children and adolescents with mental, emotional, and learning problems including ADHD, autism, and family conflicts.</li> <li>• Geriatric psychiatry focuses on the care of elderly people with mental illnesses</li> </ul>	The bio-psycho-social study of the etiology, diagnosis, treatment and prevention of cognitive, perceptual, emotional and behavioral disorders. Related non-

including dementias, post-stroke cognitive changes, and depression.

medical fields include psychotherapy and clinical psychology.

- Addiction psychiatry focuses on substance abuse and its treatment.
- Forensic psychiatry focuses on the interface of psychiatry and law.
- Neuropsychiatry focuses on affective, cognitive and behavioral disorders attributable to diseases of the nervous system
- Sleep medicine focuses on the diagnosis and treatment of sleep disorders.
- Psychosomatic medicine
- Hospice and Palliative Medicine
- Pain medicine

Pulmonology

Medicine

The lungs and respiratory system. *Pulmonology* is generally considered a branch of internal medicine, although it is closely related to intensive care medicine when dealing with patients requiring mechanical ventilation.

Radiology

R, DR

Diagnostic

- Interventional radiology is concerned with using

The use of radiation in

imaging of the human body, usually from CT, ultrasound, or fluoroscopy, to do biopsies, place certain tubes, and perform intravascular procedures.

- Nuclear Medicine uses radioactive substances for *in vivo* and *in vitro* diagnosis using either imaging of the location of radioactive substances placed into a patient, or using *in vitro* diagnostic tests utilizing radioactive substances.

Rheumatology	RHU	Medicine	Autoimmune and inflammatory diseases of the joints and other organ systems, such as arthritis and other rheumatic diseases.
Stomatology		Dentistry	Diseases of the mouth
Surgical oncology	SO	Surgery	Curative and palliative surgical approaches to cancer treatment.
Thoracic surgery	TS	Surgery	Surgery of the organs of the thoracic cavity: the heart, lungs, and great vessels.
Transplant surgery	TTS	Surgery	Transplantation of organs from one body to another

Urgent Care Medicine	UCM	Medicine	Immediate medical care offering outpatient care for the treatment of acute and chronic illness and injury
Urology	U	Surgery	Urinary tracts of males and females, and the male reproductive system. It is often practiced together with andrology ("men's health").
Vascular surgery	VS	Surgery	The peripheral blood vessels— those outside of the chest (usually operated on by cardiovascular surgeons) and of the central nervous system (treated by neurosurgery)

***Physician compensation***

The mean annual salary of a medical specialist is \$175,011 in the US, and \$272,000 for surgeons. However, because of commodity inflation, increasing negligent costs, steep price rise of rental, the annual salary range of a medical specialist varies and is not rising as fast as other professional pay.

The table below details the average range of salaries for physicians of selected specialties as of July 2010. Also given in the average number of hours worked per week for full time physicians (numbers are from 2003).

<b>Specialty</b>	<b>Median salary (USD)</b>	<b>Average hours work/week</b>	<b>Average salary/hour (USD)</b>
Anesthesiology	331,000 to \$423,507	61	
Dermatology	313,100 to \$480,088	45.5	103
Emergency medicine	239,000 to \$316,296	46	87
Cardiac Surgery	218,684 to \$500,000	55	
Family practice	175,000 to \$220,196	52.5	58
Internal medicine	184,200 to \$231,691	57	58
Neurology	213,000 to \$301,327	55.5	93
Obstetrics and Gynecology	251,500 to \$326,924	61	83
Ophthalmology	150,000 to \$351,000	47	
Orthopedic surgery	397,879 to \$600,000	58	
Otolaryngology	191,000 to \$393,000	53.5	
Pathology	239,000 to \$331,842	45.5	
Pediatrics	160,111 to \$228,750	54	69
Psychiatry	173,800 to \$248,198	48	72
Radiology (diagnostic)	377,300 to \$478,000	58	
Surgery (general)	284,642 to \$383,333	60	
Urology	331,192 to \$443,518	60.5	
Neurologic surgery			132
Plastic surgery			114
Gastroenterology			93
Pulmonary diseases			72

## ***Specialties by country***

### **Australia and New Zealand**

Specialty training in Australia and New Zealand is overseen by the specialty colleges:

- Royal Australasian College of Surgeons
- Royal Australasian College of Physicians

### **Canada**

Specialty training in Canada is overseen by the Royal College of Physicians and Surgeons of Canada

## India

Specialty training in India is overseen by the Medical Council of India which is responsible for recognition of post graduate training and by the National Board of Examinations. and education of Ayurveda in overseen by Central Council of Indian Medicine (CCIM), the council conducts u.g and p.g courses all over India, while Central Council of Homoeopathy does the same in the field of Homeopathy.

## United States

There are three agencies or organizations in the United States which collectively oversee physician board certification of MD and DO (osteopathic) physicians in the 26 approved medical specialties recognized in the United States. These organizations are the American Board of Medical Specialties (ABMS) and the American Medical Association; the American Osteopathic Association Bureau of Osteopathic Specialists (AOABOS) and the American Osteopathic Association; the American Board of Physician Specialties (ABPS) and the American Association of Physician Specialists. Each of these agencies and their associated national medical organization functions as its various specialty academies, colleges and societies.

### **Certifying Board National Organization Physician Type**

ABMS	AMA	MD and DO
AOA-BOS	AOA	DO Only
ABPS	AAPS	MD and DO

All boards of certification now require that medical practitioners demonstrate, by examination, continuing mastery of the core knowledge and skills for a chosen specialty. Recertification varies by particular specialty between every seven and every ten years.

### ***Other uses***

In the U.S. Army, the term "medical specialist" refers to occupational therapists, physical therapists, dietitians and physician assistants, also known as allied health professionals. Also included in the term "medical specialist", but not in the term "allied health professional" are EMT/combat medics.

## Chapter 2

# Emergency Medicine



Emergency department entrance at the Toronto General Hospital

**Emergency medicine** is a medical specialty in which physicians care for patients with acute illnesses or injuries which require immediate medical attention. While not usually providing long-term or continuing care, emergency medicine physicians diagnose a variety of illnesses and undertake acute interventions to stabilize the patient. Emergency medicine physicians practice in hospital emergency departments, in pre-hospital settings via emergency medical services, other locations where initial medical treatment of illness

takes place, and recently the intensive-care unit. Just as clinicians operate by immediacy rules under large emergency systems, emergency practitioners aim to diagnose emergent conditions and stabilize the patient for definitive care.

Physicians specializing in emergency medicine in the US can enter fellowships to receive credentials in subspecialties. These are palliative medicine, medical toxicology, wilderness medicine, pediatric emergency medicine, sports medicine, and undersea and hyperbaric medicine.

## **Scope**

Emergency medicine has evolved to treat conditions that pose a threat to life, limb, or have a significant risk of morbidity. In the words of the International Federation for Emergency Medicine:

"Emergency medicine is a medical specialty—a field of practice based on the knowledge and skills required for the prevention, diagnosis and management of acute and urgent aspects of illness and injury affecting patients of all age groups with a full spectrum of undifferentiated physical and behavioral disorders. It further encompasses an understanding of the development of pre-hospital and in-hospital emergency medical systems and the skills necessary for this development."

Emergency Medicine encompasses a large amount of general medicine and surgery including the surgical sub-specialties. Emergency physicians are tasked with seeing a large number of patients, treating their illnesses and arranging for disposition—either admitting them to the hospital or releasing them after treatment as necessary. The emergency physician requires a broad field of knowledge and advanced procedural skills often including surgical procedures, trauma resuscitation, advanced cardiac life support and advanced airway management. Emergency physicians must have the skills of many specialists—the ability to resuscitate a patient (Critical Care Medicine), manage a difficult airway (Anesthesia), suture a complex laceration (Plastic Surgery), reduce (set) a fractured bone or dislocated joint (Orthopedic surgery), treat a heart attack (Cardiology), work-up a pregnant patient with vaginal bleeding (Obstetrics and Gynecology), stop a bad nosebleed (ENT), place a chest tube (Cardiothoracic Surgery), and to conduct and interpret ultrasounds (Radiology).

## **History**

During the French Revolution, after seeing the speed with which the carriages of the French flying artillery maneuvered across the battlefields, French military surgeon Dominique Jean Larrey applied the idea of ambulances, or "flying carriages", for rapid transport of wounded soldiers to a central place where medical care was more accessible and effective. Larrey manned ambulances with trained crews of drivers, corpsmen and litter-bearers and had them bring the wounded to centralized field hospitals, effectively creating a forerunner of the modern MASH units. Dominique Jean Larrey is sometimes called the father of emergency medicine for his strategies during the French wars.

Emergency medicine (EM) as a medical specialty is relatively young. Prior to the 1960s and 70s, hospital emergency departments were generally staffed by physicians on staff at the hospital on a rotating basis, among them general surgeons, internists, psychiatrists, and dermatologists. Physicians in training (interns and residents), foreign medical graduates and sometimes nurses also staffed the Emergency Department (ED). EM was born as a specialty in order to fill the time commitment required by physicians on staff to work in the increasingly chaotic emergency departments (EDs) of the time. During this period, groups of physicians began to emerge who had left their respective practices in order to devote their work completely to the ED. The first of such groups was headed by Dr. James DeWitt Mills who, along with four associate physicians; Dr. Chalmers A. Loughridge, Dr. William Weaver, Dr. John McDade, and Dr. Steven Bednar at Alexandria Hospital, VA established 24/7 year round emergency care which became known as the "Alexandria Plan". It was not until the establishment of American College of Emergency Physicians (ACEP), the recognition of emergency medicine training programs by the AMA and the AOA, and in 1979 a historical vote by the American Board of Medical Specialties that EM became a recognized medical specialty.

### **United Kingdom**

Emergency medicine traces its development as a specialty in UK to 1952 when Mr Maurice Ellis was appointed as the first consultant in Emergency Medicine in the UK at Leeds General Infirmary. In 1967 the Casualty Surgeons Association was established with Maurice Ellis as its first President. The name of the Association was changed twice, in 1990, to the British Association for Accident and Emergency Medicine, and later on in 2004, to British Association for Emergency Medicine (BAEM). In 1993, Intercollegiate Faculty of Accident and Emergency Medicine (FAEM) was formed at the Royal College of Surgeons of England, London. In 2005, the BAEM and the FAEM were merged to form College of Emergency Medicine. The College of Emergency Medicine is the single authoritative body for emergency medicine in the UK. It conducts its fellowship and membership exams, publishes guidelines and standards for the practise of emergency medicine, and has its own journal, called the *Emergency Medicine Journal* (EMJ).

### **Organizations around the world**

#### **Australia and New Zealand**

In Australia and New Zealand, advanced training in Emergency Medicine is overseen by the Australasian College for Emergency Medicine (ACEM).

#### **India**

In India, many private hospitals and institutes have been providing emergency medicine training for doctors, nurses & paramedics since 1994. The certification programs varied from 6 months to 3 years. Emergency medicine was recognized as a separate specialty by Medical Council of India (MCI) only from July 2009. After this many medical colleges

are about to start postgraduate training i.e. MD in Emergency Medicine. It will be at least a few years until the specialty gets streamlined in India..

## **Canada**

In Canada, there are two routes to certification in emergency medicine. The vast majority of full-time practicing ER physicians in Canada are certified via one of these routes. Most busy urban, sub-urban and larger rural hospitals are staffed primarily by full time, certified career emergency physicians. Smaller rural and community hospitals may still be staffed by family physicians who work in the emergency department on a part-time rotating basis. Basic experience in emergency medicine is a core component of family medicine training in Canada. The general trend in Canadian emergency departments over the last decade has been the gradual replacement of part-time, non-certified physicians (mostly family physicians) by full-time certified emergency physicians. This trend was first noted in larger academic centers but has gradually evolved to include most busy emergency departments.

The two routes to ER certification can be summarized as follows:

Route 1: A five year residency leading to the designation of FRCP(EM) through the Royal College of Physicians and Surgeons of Canada. Route 2: A 3 year residency leading to the designation of CCFP(EM) through the College of Family Physicians of Canada.

CCFP(EM) ER physicians outnumber FRCP(EM) physicians by about 3 to 1, and tend to work primarily as clinicians with a smaller focus on academic activities such as teaching and research. FRCP(EM) ER physicians tend to congregate in academic centers and tend to have more academically oriented careers, which emphasize administration, research and teaching. Furthermore the length of the FRCP(EM) residency allows more time for formal training in these areas.

As a consequence of the above, most Canadian medical students who wish to pursue an academic emergency medicine career, and/or work primarily in a major academic center, choose the FRCP route of certification. Conversely, those who wish to function primarily as clinical ER physicians choose the CCFP route of certification.

Although many in the Emergency Medicine community in Canada feel that a unified training process would be beneficial to the current 2 stream schism, this has yet to happen for a variety of complex reasons.

## **United Kingdom and Ireland**

In the United Kingdom and Ireland, the College of Emergency Medicine sets the examinations that trainees in Emergency Medicine take in order to become consultants (fully-trained emergency physicians).

## United States

In the United States, there are many member organizations for emergency clinicians:

- The American College of Emergency Physicians (ACEP) is the oldest and largest professional organization. Originally founded in 1968, it now has over 25,000 members, although many are not board certified.
- The American College of Osteopathic Emergency Physicians (ACOEP) was founded in 1975 and is open only to D.O. emergency physicians.
- The Association of Emergency Physicians (AEP) offers membership to any practicing emergency physician regardless of training.
- The American Academy of Emergency Medicine (AAEM) restricts its membership to board certified specialists in emergency medicine, and as of 2009 has over 6000 members. It promotes the independence of emergency physicians and seeks to limit the interference of corporations and other outside groups in the doctor-patient relationship.
- The Emergency Department Practice Management Association (EDPMA) is a trade association that offers membership to physician groups and staffing companies, billing companies, and emergency department supporting organizations.

In the United States and Canada, there are four ways to become board certified in emergency medicine:

- The American Board of Emergency Medicine (ABEM) is primarily for MD's, and is under the authority of the American Board of Medical Specialties.
- The American Osteopathic Board of Emergency Medicine (AOBEM) certifies only emergency physicians with a D.O. degree. It is under the authority of the American Osteopathic Association.
- The Royal College of Physicians and Surgeons of Canada.
- There is now an alternative route for those physicians who are either unable or unwilling to take the ABEM, AOBEM, or RCPCSC exams, which is the Board of Certification in Emergency Medicine (BCEM). The BCEM is the newest certifying body in emergency medicine, and since 1988 the only organization in the United States that will grant board certification in emergency medicine to a physician who has not completed an emergency medicine residency (but did complete another residency, such as one of the primary care residencies). Many of the Legacy physicians that practice Emergency Medicine in the United States are certified by the BCEM. It is under the authority of the American Board of Physician Specialists/American Association of Physician Specialists.

## **Education**

### **Canada**

In Canada there are a few different ways to become certified as an emergency physician. For all methods one has to first complete a medical degree. The next most common step is to complete two years of family medicine residency offered by the College of Family Physicians Canada (CFPC) followed by a further one year residency in emergency medicine. There is also a 5 year residency offer by the Royal College of Physicians and Surgeons of Canada that may be completed instead of the above. The CFPC also allows those who have worked a minimum of 4 years at a minimum of 400 hours per year in emergency medicine to challenge the examination of special competence in emergency medicine and thus become specialized.

### **United States**

Emergency medicine is a moderately competitive specialty for medical graduates to enter, ranking 7 of 16 specialties in terms of percentage of U.S. graduates whose applications are successful. However, over 90% of applicants from U.S. medical schools to U.S. Emergency Medicine residencies are successful. Emergency medicine residencies can be three or four years in length, depending on the training institution. In addition to the didactic exposure, much of an emergency medicine residency involves rotating through other specialties. By the end of their training, emergency physicians are expected to handle a vast field of medical, surgical, and psychiatric emergencies, and are considered specialists in the stabilization and treatment of emergent condition.

A number of fellowships are available for emergency medicine graduates including prehospital medicine (emergency medical services), research, hyperbaric medicine, sports medicine, ultrasound, pediatric emergency medicine, and Critical Care Medicine.

### **United Kingdom**

Emergency medical trainees enter specialty training after five years of medical school and two years of foundation training.

During the two year core training programme (Acute Care Common Stem), doctors complete training in anaesthesia, acute medicine, intensive care, and emergency medicine. In the third year the trainee learns about emergency medicine (paediatric focus) and musculo-skeletal emergency medicine. They must also pass the Membership of the College of Emergency Medicine (MCEM) examination. Trainees will then go onto Higher Training, lasting a further 3 years. Before the end of higher training, the final examination—the Fellowship of the College of Emergency Medicine (FCEM) must be passed. Upon completion of training the doctor will be eligible for entry on the GMC Specialist Register and allowed to apply for a post as a Consultant in Emergency Medicine.

Emergency Medicine training in the UK is emerging. Historically emergency specialists were drawn from anaesthesia, medicine and surgery. Many established EM consultants were surgically trained; some hold the Fellowship of Royal College of Surgeons of Edinburgh in Accident and Emergency—FRCSEd(A&E). Some of these consultants will be referred to as 'Mister' whilst others choose either not to change from 'Doctor' or to change back to 'Doctor' after passing the FCEM exam. Others used the MRCP or the FRCA as their primary examination (now replaced by MCEM). Trainees in emergency medicine may dual accredit in Intensive Care Medicine or seek sub-specialisation in Paediatric emergency medicine.

## ***Work***

The employment arrangement of emergency physician practices are either private (a democratic group of EPs staff an ED under contract), institutional (EPs with an independent contractor relationship with the hospital), corporate (EPs with an independent contractor relationship with a third party staffing company that services multiple emergency departments) or governmental (employed by the US armed forces, the US public health service, the Veteran's Administration or other government agency).

Most emergency physicians staff hospital emergency departments in shifts, a job structure necessitated by the 24/7 nature of the emergency department. In the United States, emergency medicine practitioners are expected to be competent in treating, diagnosing and managing a wide array of illnesses and conditions, both chronic and acute. Contrary to popular belief, emergency physicians do not treat a disproportionate number of, nor do they provide primary care to, the uninsured. In Massachusetts, when health insurance became mandatory, emergency department usage actually rose. Overall, more than half of emergency physicians report high levels of career satisfaction. Although career satisfaction has remained high among emergency physicians, concern about burnout is substantial.

In the United Kingdom all Consultants in Emergency Medicine work in the NHS. There is little scope for private emergency practice.

According to the American College of Emergency Physicians, the US will likely face a shortage of physicians in the near future, leading to increased employment opportunities.

## ***Epidemiology***

A U.S. government report found there were 119 million emergency department visits in 2006, an increase of 36% from 1996. During this same ten year period of increased usage, the number of emergency departments decreased, from 4,019 to 3,833 and the rate of emergency department visits per 100 people in the U.S. rose from 34.2 to 40.5.

## Chapter 3

# Family Medicine

**Family medicine (FM)** is a medical specialty devoted to comprehensive health care to people of all ages. It is a form of primary care that provides continuing, comprehensive health care for the individual and family across all ages, sexes, diseases, and parts of the body. It is based on knowledge of the patient in the context of the family and the community, emphasizing disease prevention and health promotion. According to the World Organization of Family Doctors (Wonca), the aim of family medicine is to provide personal, comprehensive and continuing care for the individual in the context of the family and the community.

### ***Scope of practice***

Family physicians in the United States may hold either an M.D. or a D.O. degree. Physicians who specialize in family medicine must successfully complete an accredited three-year family medicine residency in the United States in addition to their medical degree. They are then eligible to sit for a board certification examination now required by most hospitals and health plans. The American Board of Family Medicine requires its Diplomates to maintain certification through an ongoing process of continuing medical education, medical knowledge review, patient care oversight through chart audits, practice-based learning through quality improvement projects and retaking the board certification examination every 7 to 10 years.

The term "family medicine" is used in Canada and many European and Asian countries, instead of "general medicine" or "general practice". In Sweden, certification in family medicine requires five years working with a tutor, after the medical degree. In India, those who want to specialize in family medicine must complete a three-year family medicine residency, after their medical degree (MBBS). They are awarded either a DNB or an MD in family medicine. Similar systems exist in other countries.

Family physicians deliver a range of acute, chronic and preventive medical care services. In addition to diagnosing and treating illness, they also provide preventive care, including routine checkups, health-risk assessments, immunization and screening tests, and personalized counseling on maintaining a healthy lifestyle. Family physicians also manage chronic illness, often coordinating care provided by other subspecialists. Many American family physicians deliver babies and provide prenatal care.

Family medicine and family physicians play a very important role in the healthcare system of a country. In USA, for example, nearly one in four of all office visits are made to family physicians. That is 208 million office visits each year — nearly 83 million more than the next largest medical specialty. Today, family physicians provide more care for America's underserved and rural populations than any other medical specialty.

## ***Family medicine in USA***

Following World War II, two events shaped the advent of family medicine. First, medical specialties and subspecialties increased in popularity, having an adverse affect on the number of physicians in general practice. At the same time, many medical advances were being made and there was concern within the "general practitioner" or "GP" population that four years of medical school plus a one-year internship was no longer adequate preparation for the breadth of medical knowledge required of the profession. Many of these doctors wanted to see a residency program added to their training; this would not only give them additional training, knowledge, and prestige, but would allow for board certification, which was increasingly required to gain hospital privileges. In 1969, family medicine (then known as family practice) was recognized as a distinct specialty in the U.S.

Family physicians complete undergraduate school, medical school, and three more years of specialized medical residency training in family medicine. Their residency training includes rotations in internal medicine, pediatrics, obstetrics-gynecology, psychiatry, and geriatrics. The specialty focuses on treating the whole person—acknowledging the effects of all outside influences—through all life stages. Family physicians will see anyone with any problem, but are experts in common problems. Many family physicians deliver babies in addition to taking care of patients of all ages.

In order to become board certified, family physicians must complete a residency in family medicine, possess a full and unrestricted medical license, and take a written cognitive examination. Between 2003 and 2009, the process for maintenance of board certification in family medicine is being changed (as well as all other American Specialty Boards) to a series of yearly tests on differing areas. The American Board of Family Medicine, as well as other specialty boards, are requiring additional participation in continuous learning and self-assessment to enhance clinical knowledge, expertise and skills. The Board has created a program called the "Maintenance of Certification Program for Family Physicians" (MC-FP) which will require family physicians to continuously demonstrate proficiency in four areas of clinical practice: professionalism, self assessment/lifelong learning, cognitive expertise, and performance in practice. Three hundred hours of continuing medical education within the prior six years is also required to be eligible to sit for the exam.

Family physicians may pursue fellowships in diverse topics including adolescent medicine, geriatric medicine, sports medicine, sleep medicine, and hospice and palliative medicine. The American Board of Family Medicine offers Certificates of Added Qualifications (CAQs) in each of these topics. Recently, new fellowships in International

Family Medicine have emerged. These fellowships are designed to train family physicians working in resource poor environments.

The family medicine (FM) paradigm is bolstered by primary care physicians trained in internal medicine (IM); although these physicians are trained in internal medicine only, adult patients provide the majority of the patient base of many family medicine practices. In the United States, there is a rising contingent of physicians dually trained in internal medicine and pediatrics, which can be completed in four years, instead of the three years each for IM and pediatrics. A significant number of family medicine practices (especially in suburban and urban areas) do not provide obstetric services anymore (due to litigation issues and provider preference), and as such, this blurs the line between the FM and IM/Peds difference. One suggested difference is that the IM/Peds-trained physicians are more geared towards subspecialty training or hospital-based practice. Even so, there are groups with FM-trained and IM/Peds-trained physicians working in seamless harmony.

While many sources cite a shortage of family physicians (and also other primary care providers, i.e. internists, pediatricians, and general practitioners), the per capita supply of primary care physicians has actually increased about 1 percent per year since 1998. Additionally, a recent decrease in the number of M.D. graduates pursuing a residency in primary care, has been offset by the number of D.O graduates and graduates of international medical schools who enter primary care residencies. Still, projections indicate that by 2020 the demand for family physicians will exceed their supply.

The number of students entering family medicine residency training has fallen from a high of 3,293 in 1998 to 1,172 in 2008, according to National Residency Matching Program data. Fifty-five family medicine residency programs have closed since 2000, while only 28 programs have opened.

In 2006, when the nation had 100,431 family physicians, a workforce report by the American Academy of Family Physicians indicated the United States would need 139,531 family physicians by 2020 to meet the need for primary medical care. To reach that figure 4,439 family physicians must complete their residencies each year, but currently the nation is attracting only half the number of future family physicians that we will need.

The waning interest in family medicine is likely due to several factors, including the lesser prestige associated with the specialty, the lesser pay, and the increasingly frustrating practice environment in the U.S. Salaries for family physicians in the United States are respectable but lower than average for physicians, with the average being \$129,295 and ranging from \$110,000 to \$204,000, but when faced with debt from medical school, most medical students are opting for the higher paying specialties. Family physicians are trained to manage acute and chronic health issues for an individual simultaneously, yet their appointment slots may average only ten minutes. Physicians are increasingly forced to do more administrative work, and to shoulder higher malpractice premiums, thus forcing doctors to spend less and less time with patient care due to the current payor model stressing patient volume vs. quality of care. Things are starting to

change as more insurance carriers consolidate. They are not stressing performance but more and more volume, thus increasing insurance company profit margins. Physicians are starting to shun insurance carriers to lessen the paperwork in order to focus more on patient care as they are originally trained to do.

Most family physicians in the US practice in solo or small-group private practices or as hospital employees in practices of similar sizes owned by hospitals. However, the specialty is broad and allows for a variety of career options including education, emergency medicine or urgent care, inpatient medicine, international or wilderness medicine, public health, sports medicine, and research. Others choose to practice as consultants to various medical institutions, including insurance companies.

There is a current trend among family physicians to adopt a practice model called the micro practice, or "Ideal Medical Practice". These practices focus on reducing their overhead and increase their utilization of technology. Because the overhead is reduced, the need to see a high volume of patients to generate more revenue is diminished. This allows the doctor to spend more time with their patients, which results in higher satisfaction for the patient and the physician.

### ***Family medicine in India***

Family Medicine (FM) came to be recognized as a medical specialty in India only in the late 1990s. According to the National Health Policy - 2002, there is an acute shortage of specialists in family medicine. As family physicians play very important role in providing affordable and universal health care to people, the Government of India is now prompting family medicine. There are lot of poverty and bad law and order situation in India which further make difficult for family medicine.

Although family medicine is sometimes called general practice, they are not identical in India. A medical graduate who has successfully completed the MBBS (Bachelor of Medicine and Bachelor of Surgery) course and has been registered with Indian Medical Council or any state medical council is considered a general practitioner. A family physician, however, is a primary care physician who has done specialist training in the discipline of family medicine.

The Medical Council of India requires three-year residency for family medicine specialty, leading to the award of Doctor of Medicine (MD) in Family Medicine or Diplomate of National Board (DNB) in Family Medicine.

The National Board of Examinations conducts family medicine residency programme at teaching hospitals accredited by it. On successful completion of their three-year residency, candidates are awarded Diplomate of National Board (Family Medicine). The curriculum of DNB (FM) comprises: (1) medicine and allied sciences; (2) surgery and allied sciences; (3) maternal and child health; (4) basic sciences and community health. During their three-year residency, candidates receive integrated inpatient and outpatient learning. They also receive field training at community health centres and clinics.

The Medical Council of India permits accredited medical colleges (medical schools) to conduct a similar residency programme in family medicine. On successful completion of three-year residency, candidates are awarded Doctor of Medicine (Family Medicine). However, medical colleges are yet to start this MD (FM) course, even though there is an acute shortage of qualified family physicians in India.

Indian Medical Association's College of General Practitioners, conducts one-year Diploma in Family Medicine (DFM), a distance education programme of the Postgraduate Institute of Medicine, University of Colombo, Sri Lanka, for doctors with minimum five years of experience in general practice. An institution at the forefront of promoting family medicine, Christian Medical College, Vellore, conducts Postgraduate Diploma in Family Medicine (PGDFM), a two-year distance education programme. Since the Medical Council of India requires three-year residency for family medicine specialty, these diplomas are not recognized qualifications in India.

Perhaps the first of its kind in India, Herbertpur Christian Hospital, Herbertpur, started Family Medicine Department in 2006, to support its family medicine programme. Most teaching institutions, however, do not have a Department of Family Medicine. It is mostly the Department of Internal Medicine that caters to family medicine residents. This may soon change, as more specialists in family medicine will be available in the near future.

As India's need for primary and secondary levels of health care is enormous, medical educationalists call for some systemic changes to include family medicine in the undergraduate medical curriculum as well.

Recently the residency trained family physicians have formed their association, called "Academy of Family Physicians of India." Currently there are about two hundred family medicine residency training sites accredited by National Board of Examination India providing around 700 training posts annually. However there are various issues like academic acceptance, accreditation, curriculum development, uniform training standards, faculty development, research in primary care etc which need urgent attention for family medicine to flourish as an academic specialty in India. Government of India has declared Family Medicine as focus area of human resource development in health sector in the National Health Policy 2002. There is discussion ongoing to employ multiskilled doctors with DNB family medicine qualification against specialist posts in NRHM.

Regarding how family physicians will practise their specialty in India, one can only speculate now. Possibly, three models might evolve, namely (1) private practice, (2) practising at primary care clinics/hospitals, (3) practising as consultants at secondary/tertiary care hospitals.

## Chapter 4

# General Surgery



A surgeon operating

**General surgery**, despite its name, is a surgical specialty that focuses on abdominal organs, e.g., intestines including esophagus, stomach, small bowel, colon, liver, pancreas, gallbladder and bile ducts, and often the thyroid gland (depending on the availability of head and neck surgery specialists). They also deal with diseases involving the skin, breast, and hernias. These surgeons deal mainly in the Torso.

### **Scope**

With the prevalent trend for increasing sub-specialization in today's medical practice, General Surgery has lost most of its former glory and scope. Nonetheless, it continues to be a somewhat competitive, rewarding and demanding specialty in its own right. Until recently, all surgeons in the United States were required to be board certified by the American Board of Surgery in order to progress into further sub-specialty training. However, recently, board certification has been delegated into separate sub-branches, whereby successful completion of a Residency in General Surgery is not necessarily required, but may well be desired - depending on the country and area of practice, as well as the individual sub-specialty.

Many sub-specialties are still part of the General Surgical training program. That is, General Surgeons may sub-specialize into one or more of the following disciplines:

### **Trauma surgery**

In the United States and Canada, the overall responsibility for trauma care falls under the auspices of general surgery. Some general surgeons obtain advanced training and specialty certification in this field alone. General surgeons must be able to deal initially with almost any surgical emergency. Often they are the first port of call to critically ill or gravely injured patients, and must perform a variety of procedures to stabilise such patients, such as intubation, burr hole, cricothyroidotomy, and emergency laparotomy or thoracotomy to stanch bleeding.

All General Surgeons are trained in emergency surgery. Bleeding, infections, bowel obstructions and organ perforations are the main problems they deal with. Cholecystectomy, the surgical removal of the gallbladder, is one of the most common surgical procedures done worldwide. This is most often done electively, but the gallbladder can become acutely inflamed and require an emergency operation. Ruptures of the appendix and small bowel obstructions are other common emergencies.

### **Laparoscopic surgery**

Is a relatively new specialty dealing with minimal access techniques using cameras and small instruments inserted through 0.5 to 1 cm incisions. Robotic surgery is now evolving from this concept (see below). Gallbladders, appendices, and colons can all be removed with this technique. Hernias are now repaired mostly laparoscopically. Most bariatric surgery is performed laparoscopically. General surgeons that are trained today are expected to be proficient in laparoscopic procedures.

### **Colorectal surgery**

General Surgeons treat a wide variety of minor colon and rectal diseases ranging from inflammatory bowel diseases (such as ulcerative colitis or Crohn's disease) to diverticulitis, gastrointestinal bleeding, hemorrhoids, etc.

### **Breast surgery**

General surgeons perform a majority of all non-cosmetic breast surgery from lumpectomy to mastectomy, especially pertaining to the evaluation and diagnosis, of breast cancer

### **Vascular surgery**

General Surgeons can perform vascular surgery if they receive special training and certification in vascular surgery. Otherwise, these procedures are performed by vascular

surgery specialists. However, general surgeons are capable of treating minor vascular disorders.

## **Endocrine surgery**

General Surgeons are trained to remove all or part of the thyroid and parathyroid glands in the neck and the adrenal glands just above each kidney in the abdomen. In many communities, they are the only surgeon trained to do this. In communities that have a number of subspecialists other subspecialty surgeons may assume responsibility for these procedures.

## **Dermatological Surgery**

General Surgeons perform a wide variety of skin-related surgeries ranging from removing suspicious moles to treating major burns. General Surgeons also remove tumors that often grow just below the skin such as fatty tumors or tumors that arise in muscles or other soft tissues. General Surgeons also treat more complex skin or subcutaneous infections including necrotizing fasciitis and will often employ skin grafts to cover defects in the skin resulting from burns, trauma, or infections.

## **Trends**

In the last few years minimally invasive surgery has become more prevalent. Considerable enthusiasm has built around robotic surgery (also known as *robotic-assisted surgery*), despite a lack of data suggesting it has significant benefits that justify its cost.

## **Training**

In Canada, Australia, New Zealand, and the United States general surgery is a five to seven year residency and follows completion of medical school, either MD, MBBS, MBChB, or DO degrees. In Australia and New Zealand, a residency leads to eligibility for Fellowship of the Royal Australasian College of Surgeons. In Canada, residency leads to eligibility for Certification by and Fellowship of the Royal College of Physicians and Surgeons of Canada, while in the United States, completion of a residency in general surgery leads to eligibility for board certification by the American Board of Surgery which is also required upon completion of training for a general surgeon to have operating privileges at most hospitals in the United States.

In the United Kingdom, surgical trainees enter training after five years of medical school and two years of the Foundation Programme. During the two to three-year core training programme, doctors will sit the Membership of the Royal College of Surgeons (MRCS) examination. On award of the MRCS examination, surgeons may hold the title 'Mister' or 'Miss/Ms' rather than doctor. This is a tradition dating back hundreds of years in the United Kingdom that is still in use today. Trainees will then go onto Higher Surgical Training (HST), lasting a further four to five years. During this time they may choose to subspecialise. Before the end of HST, the examination of Fellow of the Royal College of

Surgeons (FRCS) must be taken in General Surgery plus the subspeciality. Upon completion of training the surgeon will become a Consultant Surgeon and will be eligible for entry on the GMC Specialist Register and may work both in the NHS and independent sector as a Consultant General Surgeon. However, with the implementation of the European Working Time Directive limiting UK surgical residents to a 48-hour working week there are concerns that upon completion of training UK surgeons will not be confident enough to work independently. The introduction of a sub-consultant grade to enable those who have recently received a UK Certificate of Completion of Training may be necessary.

## **Subspecialization**

In many countries general surgery is a prerequisite for subspecialization in:

- vascular surgery
- thoracic surgery
- cardiac surgery
- plastic surgery
- Surgical Critical Care

## Chapter 5

# Dermatology

### Dermatologist

#### Occupation

<b>Names</b>	Doctor, Medical Specialist
<b>Type</b>	Specialty
<b>Activity sectors</b>	Medicine

#### Description

<b>Education required</b>	Doctor of Medicine
<b>Fields of employment</b>	Hospitals, Clinics

**Dermatology** is the branch of medicine dealing with the skin and its diseases, a unique specialty with both medical and surgical aspects. A dermatologist takes care of diseases, in the widest sense, and some cosmetic problems of the skin, scalp, hair, and nails.

### ***Etymology***

Coined in English 1819, the word *dermatology* originated in the form of the words *dermologie* (in French, 1764) and, a little later, *dermatologia* (in Latin, 1777). The term derives from the Greek "δέρματος" (*dermatos*), genitive of "δέρμα" (*derma*), "skin" (from "δέρω" – *dero*, "to flay") + "-logy, "the study of", a suffix derived from "λόγος" (*logos*), amongst others meaning "speech, oration, discourse, quote, study, calculation, reason", in turn from "λέγω" – *lego*, "to say", "to speak".

### ***History***

Readily visible alterations of the skin surface have been recognized since the dawn of history, with some being treated, and some not. In 1801 the first great school of dermatology became a reality at the famous Hôpital Saint-Louis in Paris, while the first textbooks (Willan's, 1798–1808) and atlases (Alibert's, 1806–1814) appeared in print during the same period of time. In 1952, Dermatology was greatly advanced by Dr. Norman Orentreich's pioneering work in hair transplantation.

## ***Training***

After earning a medical degree (M.D. or D.O.), the length of training for a general dermatologist in the United States is a total of four years. This training consists of an initial medical or surgical intern year followed by a three-year dermatology residency. Following this training, one- or two- year post-residency fellowships are available in immunodermatology, phototherapy, laser medicine, Mohs micrographic surgery, cosmetic surgery or dermatopathology. For the past several years, dermatology residency positions in the United States have been the most competitive to obtain.

## ***Subspecialties***

### **Cosmetic dermatology**

Dermatologists have been leaders in the field of cosmetic surgery. Some dermatologists complete fellowships in surgical dermatology. Many are trained in their residency on the use of botox, fillers, and laser surgery. Some dermatologists perform cosmetic procedures including liposuction, blepharoplasty, and face lifts. Most dermatologists limit their cosmetic practice to minimally invasive procedures. Despite an absence of formal guidelines from the American Board of Dermatology, many cosmetic fellowships are offered in both surgery and laser medicine.

### **Dermatopathology**

A dermatopathologist is a pathologist or dermatologist who specializes in the pathology of the skin. This field is shared by dermatologists and pathologists. Usually a dermatologist or pathologist will complete one year of dermatopathology fellowship. This usually includes six months of general pathology, and six months of dermatopathology. Alumni of both specialties can qualify as dermatopathologists. At the completion of a standard residency in dermatology, many dermatologists are also competent at dermatopathology. Some dermatopathologists qualify to sit for their examinations by completing a residency in dermatology and one in pathology.

### **Immunodermatology**

This field specializes in the treatment of immune-mediated skin diseases such as lupus, bullous pemphigoid, pemphigus vulgaris, and other immune-mediated skin disorders. Specialists in this field often run their own immunopathology labs.

### **Mohs surgery**

The dermatologic subspecialty called Mohs surgery focuses on the excision of skin cancers using a tissue-sparing technique that allows intraoperative assessment of 100% of the peripheral and deep tumor margins developed in the 1930s by Dr. Frederic E. Mohs. The procedure is defined as a type of CCPDMA processing. Physicians trained in this technique must be comfortable with both pathology and surgery, and dermatologists

receive extensive training in both during their residency. Physicians who perform Mohs surgery can receive training in this specialized technique during their dermatology residency, but many will seek additional training either through preceptorships to join the American Society for Mohs Surgery or through formal one- to two-year Mohs surgery fellowship training programs administered by the American College of Mohs Surgery.

## **Pediatric dermatology**

Physicians can qualify for this specialization by completing both a pediatric residency and a dermatology residency. Or they might elect to complete a post-residency fellowship. This field encompasses the complex diseases of the neonates, hereditary skin diseases or genodermatoses, and the many difficulties of working with the pediatric population.

## **Teledermatology**

Teledermatology is a form of dermatology where telecommunication technologies are used to exchange medical information via all kinds of media (audio, visual and also data communication, but typically photos of dermatologic conditions) usually made by non-dermatologists for evaluation off-site by dermatologists). This subspecialty deals with options to view skin conditions over a large distance to provide knowledge exchange, to establish second-opinion services for experts or to use this for follow-up of individuals with chronic skin conditions.

## **Therapies**

Therapies provided by dermatologists include, but not restricted to:

- Cosmetic filler injections
- Hair removal with laser or other modalities
- Hair transplantation – a cosmetic procedure practiced by many dermatologists.
- Intralesional treatment – with steroid or chemotherapy.
- Laser therapy – for both the management of birth marks, skin disorders (like vitiligo), tattoo removal, and cosmetic resurfacing and rejuvenation.
- Photodynamic therapy – for the treatment of skin cancer and precancerous growths.
- Phototherapy – including the use of narrowband UVB, broadband UVB, psoralen and UVB.
- Tattoo removal with laser
- Tumescent liposuction – liposuction was invented by a gynecologist. A dermatologist (Dr. Jeffrey A. Klein) adapted the procedure to local infusion of dilute anesthetic called tumescent liposuction. This method is now widely practiced by dermatologists, plastic surgeons and gynecologists.
- Cryosurgery – for the treatment of warts, skin cancers, and other dermatosis.
- Radiation therapy – although rarely practiced by dermatologists, many dermatologist continue to provide radiation therapy in their office.

- Vitiligo surgery – Including procedures like autologous melanocyte transplant, suction blister grafting and punch grafting.
- Allergy testing – 'Patch testing' for contact dermatitis.
- Systemic therapies – including antibiotics, immunomodulators, and novel injectable products.
- Topical therapies – dermatologists have the best understanding of the numerous products and compounds used topically in medicine.

Most dermatologic pharmacology can be categorized based on the Anatomical Therapeutic Chemical Classification System, specifically the ATC code D.

## Chapter 6

# 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 subspecialty 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 to 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 person. 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 7

# Gynaecology

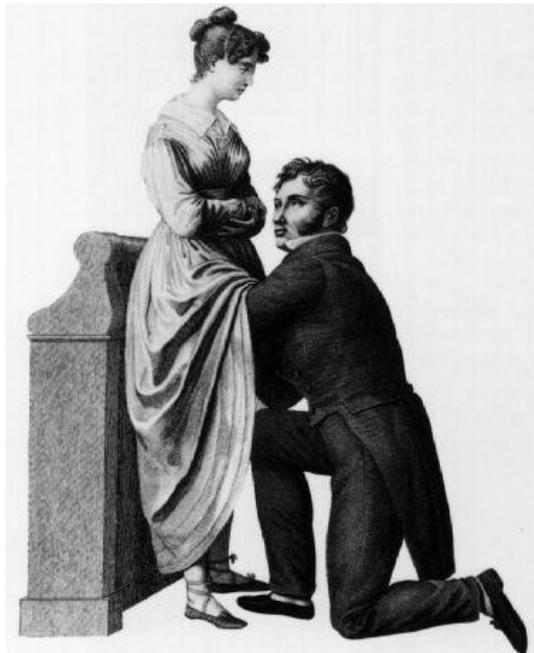
### Gynaecologist

#### Occupation

<b>Names</b>	Doctor, Medical Specialist
<b>Type</b>	Specialty
<b>Activity sectors</b>	Medicine

#### Description

<b>Education required</b>	Doctor of Medicine, Doctor of Osteopathic Medicine
<b>Fields of employment</b>	Hospitals, Clinics



The historic taboo associated with the examination of female genitalia has long inhibited the science of gynaecology. This 1822 drawing by Jacques-Pierre Maygnier shows a

"compromise" procedure, in which the physician is kneeling before the woman but cannot see her genitalia. Modern gynaecology has shed these inhibitions.

**Gynaecology** or **gynecology**, from the Greek, gynaika (γυναικᾶ) meaning woman, is the medical practice dealing with the health of the female reproductive system (uterus, vagina, and ovaries). Literally, outside medicine, it means "the science of women". It is the counterpart to andrology, which deals with medical issues specific to the male reproductive system.

Almost all modern gynaecologists are also obstetricians. In many areas, the specialties of gynaecology and obstetrics overlap. Gynaecology has been considered to end at 28 weeks gestation, but practically there is no clear cut-off. Since 1st October 1992, this cut-off may be considered to occur at 24 weeks gestation in the United States, since the law and definition of abortion changed to bring it closer to the gestation at which a foetus becomes viable.

## ***Etymology***

The word "gynecology" comes from the Greek ancient Greek gyne, γυνή, modern Greek gynaika, γυναικᾶ, meaning woman + logia meaning study, so gynecology literally is the study of women.

## ***History***

The Kahun Gynaecological Papyrus is the oldest known medical text of any kind. Dated to about 1800 B.C., it deals with women's complaints—gynaecological diseases, fertility, pregnancy, contraception, etc. The text is divided into thirty-four sections, each section dealing with a specific problem and containing diagnosis and treatment, no prognosis is suggested. Treatments are non surgical, comprising applying medicines to the affected body part or swallowing them. The womb is at times seen as the source of complaints manifesting themselves in other body parts.

According to the Suda, the ancient Greek physician Soranus of Ephesus practised in Alexandria and subsequently Rome. He was the chief representative of the school of physicians known as the "Methodists". His treatise *Gynaikeia* is extant (together with a 6th-century Latin paraphrase by Muscio, a physician of the same school).

In the United States, J. Marion Sims is considered the father of American gynaecology.

## ***Examination***

Gynaecology is typically considered a consultant specialty. In some countries, women must first see a general practitioner (GP; also known as a family practitioner (FP)) prior to seeing a gynaecologist. If their condition requires training, knowledge, surgical technique, or equipment unavailable to the GP, the patient is then referred to a gynaecologist. In the United States, however, law and many health insurance plans

allow/force gynaecologists to provide primary care in addition to aspects of their own specialty. With this option available, some women opt to see a gynaecological surgeon for non-gynaecological problems without another physician's referral.

As in all of medicine, the main tools of diagnosis are clinical history and examination. Gynaecological examination is quite intimate, more so than a routine physical exam. It also requires unique instrumentation such as the speculum. The speculum consists of two hinged blades of concave metal or plastic which are used to retract the tissues of the vagina and permit examination of the cervix, the lower part of the uterus located within the upper portion of the vagina. Gynaecologists typically do a bimanual examination (one hand on the abdomen and one or two fingers in the vagina) to palpate the cervix, uterus, ovaries and bony pelvis. It is not uncommon to do a rectovaginal examination for complete evaluation of the pelvis, particularly if any suspicious masses are appreciated. Male gynaecologists may have a female chaperone for their examination. An abdominal and/or vaginal ultrasound can be used to confirm any abnormalities appreciated with the bimanual examination or when indicated by the patient's history.

## ***Diseases***

The main conditions dealt with by a gynaecologist are:

1. Cancer and pre-cancerous diseases of the reproductive organs including ovaries, fallopian tubes, uterus, cervix, vagina, and vulva
2. Incontinence of urine.
3. Amenorrhoea (absent menstrual periods)
4. Dysmenorrhoea (painful menstrual periods)
5. Infertility
6. Menorrhagia (heavy menstrual periods). This is a common indication for hysterectomy.
7. Prolapse of pelvic organs
8. Infections of the vagina, cervix and uterus (including fungal, bacterial, viral, and protozoal)

There is some crossover in these areas. For example, a woman with urinary incontinence may be referred to a urologist.

## ***Therapies***

As with all surgical specialties, gynaecologists may employ medical or surgical therapies (or many times, both), depending on the exact nature of the problem that they are treating. Pre- and post-operative medical management will often employ many standard drug therapies, such as antibiotics, diuretics, antihypertensives, and antiemetics. Additionally, gynaecologists make frequent use of specialized hormone-modulating therapies (such as Clomifene citrate and hormonal contraception) to treat disorders of the female genital tract that are responsive to pituitary and/or gonadal signals.

Surgery, however, is the mainstay of gynaecological therapy. For historical and political reasons, gynaecologists were previously not considered "surgeons", although this point has always been the source of some controversy. Modern advancements in both general surgery and gynaecology, however, have blurred many of the once rigid lines of distinction. The rise of sub-specialties within gynaecology which are primarily surgical in nature (for example urogynaecology and gynaecological oncology) have strengthened the reputations of gynaecologists as surgical practitioners, and many surgeons and surgical societies have come to view gynaecologists as comrades of sorts. As proof of this changing attitude, gynaecologists are now eligible for fellowship in both the American College of Surgeons and Royal Colleges of Surgeons, and many newer surgical textbooks include chapters on (at least basic) gynaecological surgery.

Some of the more common operations that gynaecologists perform include:

1. Dilation and curettage (removal of the uterine contents for various reasons, including completing a partial miscarriage and diagnostic sampling for dysfunctional uterine bleeding refractive to medical therapy)
2. Hysterectomy (removal of the uterus)
3. Oophorectomy (removal of the ovaries)
4. Tubal ligation
5. Hysteroscopy
6. Diagnostic laparoscopy – used to diagnose and treat sources of pelvic and abdominal pain; perhaps most famously used to provide definitive diagnosis of endometriosis.
7. Exploratory laparotomy – may be used to investigate the level of progression of benign or malignant disease, or to assess and repair damage to the pelvic organs.
8. Various surgical treatments for urinary incontinence, including cystoscopy and sub-urethral slings.
9. Surgical treatment of pelvic organ prolapse, including correction of cystocele and rectocele.
10. Appendectomy – often performed to remove site of painful endometriosis implantation and/or prophylactically (against future acute appendicitis) at the time of hysterectomy or Caesarean section. May also be performed as part of a staging operation for ovarian cancer.
11. Cervical Excision Procedures (including cryosurgery) – removal of the surface of the cervix containing pre-cancerous cells which have been previously identified on Pap smear.

### ***Specialist training***

In the UK the Royal College of Obstetricians and Gynaecologists, based in London, encourages the study and advancement of the science and practice of obstetrics and gynaecology. This is done through postgraduate medical education and training development, and the publication of clinical guidelines and reports on aspects of the speciality and service provision. The RCOG International Office works with other

international organisations to help lower maternal morbidity and mortality in under-resourced countries.

## Chapter 8

# Neurology

### Neurologist

#### Occupation

<b>Names</b>	Physician, Medical Practitioner
<b>Type</b>	Profession
<b>Activity sectors</b>	Medicine

#### Description

**Education required** M.D. or D.O. (US) MBBS (UK)

**Fields of employment** Hospitals, Clinics

**Neurology** (from Greek νεῦρον, *neuron*, "nerve"; and -λογία, '-logia', "'study of'") is a medical specialty dealing with disorders of the nervous system. Specifically, it deals with the diagnosis and treatment of all categories of disease involving the central, peripheral, and autonomic nervous systems, including their coverings, blood vessels, and all effector tissue, such as muscle. The corresponding surgical specialty is neurosurgery. A neurologist is a physician who specializes in neurology, and is trained to investigate, or diagnose and treat neurological disorders. Pediatric neurologists treat neurological disease in children. Neurologists may also be involved in clinical research, clinical trials, as well as basic research and translational research.

Neurology is the medical application of neuroscience which is the scientific study of the nervous system.

### **Field of work**

A large number of Neurological disorders have been described. These can affect the central nervous system (brain and spinal cord), the peripheral nervous system, or the autonomic nervous system.

## ***Qualifications***

In the United States and Canada, neurologists are physicians who have completed postgraduate training in neurology after graduation from medical school. Neurologists complete, on average, at least 10–12 years of college education and clinical training. This training includes obtaining a four-year undergraduate degree, a medical degree, which is an additional four years, and then completing a three or four-year residency in neurology. The four-year residency consists of one year of internal medicine training followed by three years of training in neurology. One and two year fellowships are available following completion of the neurology residency if desired.

Many neurologists also have additional subspecialty training (fellowships) after completing their residency in one area of neurology such as stroke or vascular neurology, interventional neurology, epilepsy, neuromuscular, neurorehabilitation, behavioral neurology, sleep medicine, pain management, neuroimmunology, clinical neurophysiology, or movement disorders.

In Germany, a compulsory year of psychiatry must be done to complete a residency of neurology.

In the United Kingdom and Ireland, neurology is a subspecialty of general (internal) medicine. After five to nine years of medical school and a year as a pre-registration house officer (or two years on the Foundation Programme) a neurologist must pass the examination for Membership of the Royal College of Physicians (or the Irish equivalent) before entering specialist training in neurology. A generation ago some neurologists would also spend a couple of years working in psychiatric units and obtain a Diploma in Psychological Medicine, but that became uncommon and now that a basic psychiatric qualification takes three years to obtain it is no longer practical. A period of research is essential, and obtaining a higher degree aids career progression: many found it was eased after an attachment to the Institute of Neurology at Queen Square in London. Some neurologists enter the field of rehabilitation medicine (known as physiatry in the US) to specialise in neurological rehabilitation, which may include stroke medicine as well as brain injuries.

## ***Testing examinations***

During a neurological examination, the neurologist reviews the patient's health history with special attention to the current condition. The patient then takes a neurological exam. Typically, the exam tests mental status, function of the cranial nerves (including vision), strength, coordination, reflexes and sensation. This information helps the neurologist determine if the problem exists in the nervous system and the clinical localization. Localization of the pathology is the key process by which neurologists develop their differential diagnosis. Further tests may be needed to confirm a diagnosis and ultimately guide therapy and appropriate management.

## ***Clinical tasks***

### **General caseload**

Neurologists are responsible for the diagnosis, treatment, and management of all the above conditions. When surgical intervention is required, the neurologist may refer the patient to a neurosurgeon. In some countries, additional legal responsibilities of a neurologist may include making a finding of brain death when it is suspected that a patient is deceased. Neurologists frequently care for people with hereditary (genetic) diseases when the major manifestations are neurological, as is frequently the case. Lumbar punctures are frequently performed by neurologists. Some neurologists may develop an interest in particular subfields, such as dementia, movement disorders, headaches, epilepsy, sleep disorders, chronic pain management, multiple sclerosis or neuromuscular diseases.

### **Overlapping areas**

There is some overlap with other specialties, varying from country to country and even within a local geographic area. Acute head trauma is most often treated by neurosurgeons, whereas sequelae of head trauma may be treated by neurologists or specialists in rehabilitation medicine. Although stroke cases have been traditionally managed by internal medicine or hospitalists, the emergence of vascular neurology and interventional neurologists has created a demand for stroke specialists. The establishment of JCAHO certified stroke centers has increased the role of neurologists in stroke care in many primary as well as tertiary hospitals. Some cases of nervous system infectious diseases are treated by infectious disease specialists. Most cases of headache are diagnosed and treated primarily by general practitioners, at least the less severe cases. Similarly, most cases of sciatica and other mechanical radiculopathies are treated by general practitioners, though they may be referred to neurologists or a surgeon (neurosurgeons or orthopedic surgeons). Sleep disorders are also treated by pulmonologists and psychiatrists. Cerebral palsy is initially treated by pediatricians, but care may be transferred to an adult neurologist after the patient reaches a certain age. In the United Kingdom and other countries, many of the conditions encountered by older patients such as movement disorders including Parkinson's Disease, stroke, dementia or gait disorders are managed predominantly by specialists in geriatric medicine.

Clinical neuropsychologists are often called upon to evaluate brain-behavior relationships for the purpose of assisting with differential diagnosis, planning rehabilitation strategies, documenting cognitive strengths and weaknesses, and measuring change over time (e.g., for identifying abnormal aging or tracking the progression of a dementia).

### **Relationship to clinical neurophysiology**

In some countries, e.g. USA and Germany, neurologists may specialize in clinical neurophysiology, the field responsible for EEG, nerve conduction studies, EMG and

evoked potentials. In other countries, this is an autonomous specialty (e.g. United Kingdom, Sweden).

## **Overlap with psychiatry**

Although many mental illnesses are believed to be neurological disorders affecting the central nervous system, traditionally they are classified separately, and treated by psychiatrists. In a 2002 review article in the American Journal of Psychiatry, Professor Joseph B. Martin, Dean of Harvard Medical School and a neurologist by training, wrote that *the separation of the two categories is arbitrary, often influenced by beliefs rather than proven scientific observations. And the fact that the brain and mind are one makes the separation artificial anyway.*

There are strong indications that neurochemical mechanisms play an important role in the development of, for instance, bipolar disorder and schizophrenia. Also, "neurological" diseases often have "psychiatric" manifestations, such as post-stroke depression, depression and dementia associated with Parkinson's disease, mood and cognitive dysfunctions in Alzheimer's disease and Huntington disease, to name a few. Hence, there is no sharp distinction between neurology and psychiatry on a biological basis – this distinction has mainly practical reasoning and strong historical roots (such as the dominance of Freud's psychoanalytic theory in the first three quarters of the 20th century – which has since then been largely replaced by the focus on neurosciences – aided by the tremendous advances in genetics and neuroimaging.)

## **Cosmetic Neurology**

The emerging field of cosmetic neurology highlights the potential of therapies to improve such things as workplace efficacy, attention in school, and overall happiness in personal lives. However, this field has also given rise to questions about neuroethics and the psychopharmacology of "lifestyle drugs".

## Chapter 9

# Obstetrics

### Obstetrician

#### Occupation

<b>Names</b>	Doctor, consultant, medical specialist
<b>Type</b>	Specialty
<b>Activity sectors</b>	Medicine and surgery

#### Description

<b>Education required</b>	Medical training and specialised postgraduate training
<b>Fields of employment</b>	Hospitals, clinics

**Obstetrics** (from the Latin *obstare*, "to stand by") is the surgical specialty dealing with the care of women and their children during pregnancy (prenatal period), childbirth and the postnatal period. Midwifery is the non-surgical equivalent. Veterinary obstetrics is the same concept for veterinary medicine. Almost all modern obstetricians are also gynaecologists.

### ***Prenatal care***

Prenatal care is important in screening for various complications of pregnancy. This includes routine office visits with physical exams and routine lab tests:



3D ultrasound of 3-inch (76 mm) fetus (about 14 weeks gestational age)



Fetus at 17 weeks



Fetus at 20 weeks

### First trimester

- Complete blood count (CBC)
- Blood type
- General antibody screen (indirect Coombs test) for HDN
  - Rh D negative antenatal patients should receive RhoGam at 28 weeks to prevent Rh disease.
- Rapid plasma reagent (RPR) which screens for syphilis
- Rubella antibody screen
- Hepatitis B surface antigen
- Gonorrhea and Chlamydia culture
- PPD for tuberculosis
- Pap smear
- Urinalysis and culture
- HIV screen
- Group B Streptococcus screen – will receive IV penicillin or ampicillin (it is much cheaper and has a wider coverage) if positive (if mother is allergic, alternative therapies include IV clindamycin or IV vancomycin)

genetic screening for downs syndrome (trisomy 21) and trisomy 18 the national standard in the United States is rapidly evolving away from the AFP-Quad screen for downs syndrome- done typically in the second trimester at 16–18 weeks. The newer integrated screen (formerly called F.A.S.T.E.R for First And Second Trimester Early Results) can be done at 10 plus weeks to 13 plus weeks with an ultrasound of the fetal neck (thick skin is bad) and two chemicals (analytes) Papp-a and bhcg (pregnancy hormone level itself). It gives an accurate risk profile very early. There is a second blood screen at 15 to 20 weeks which refines the risk more accurately. The cost is higher than an "AFP-quad" screen due

to the ultrasound and second blood test but it is quoted to have a 93% pick up rate as opposed to 88% for the standard AFP/QS. This is an evolving standard of care in the United States.

### **Second trimester**

- MSAFP/quad. screen (four simultaneous blood tests) (maternal serum alpha-fetoprotein; inhibin; estriol; bhcg or free bhcg) - elevations, low numbers or odd patterns correlate with neural tube defect risk and increased risks of trisomy 18 or trisomy 21
- Ultrasound either abdominal or transvaginal to assess cervix, placenta, fluid and baby
- Amniocentesis is the national standard for women over 35 or who reach 35 by mid pregnancy or who are at increased risk by family history or prior birth history

### **Third trimester**

- Hematocrit (if low, mother will receive iron supplementation)
- Glucose loading test (GLT) - screens for gestational diabetes; if  $> 140$  mg/dL, a glucose tolerance test (GTT) is administered; a fasting glucose  $> 105$  mg/dL suggests gestational diabetes.

Most doctors do a sugar load in a drink form of 50 grams of glucose in cola, lime or orange and draw blood an hour later (plus or minus 5 minutes) ; the standard modified criteria have been lowered to 135 since the late 1980s

### **Antenatal record**

On the first visit to her obstetrician or midwife, the pregnant woman is asked to carry out the antenatal record, which constitutes a medical history and physical examination. On subsequent visits, the gestational age (GA) is rechecked with each visit.

Symphysis-fundal height (SFH; in cm) should equal gestational age after 20 weeks of gestation, and the fetal growth should be plotted on a curve during the antenatal visits. The fetus is palpated by the midwife or obstetrician using Leopold maneuver to determine the position of the baby. Blood pressure should also be monitored, and may be up to 140/90 in normal pregnancies. High blood pressure indicates hypertension and possibly pre-eclampsia, if severe swelling (edema) and spilled protein in the urine are also present.

Fetal screening is also used to help assess the viability of the fetus, as well as congenital problems. Genetic counseling is often offered for families who may be at an increased risk to have a child with a genetic condition. Amniocentesis at around the 20th week is sometimes done for women 35 or older to check for Down's Syndrome and other chromosome abnormalities in the fetus.

Even earlier than amniocentesis is performed, the mother may undergo the triple test, nuchal screening, nasal bone, alpha-fetoprotein screening and Chorionic villus sampling, also to check for disorders such as Down Syndrome. Amniocentesis is a prenatal genetic screening of the fetus, which involves inserting a needle through the mother's abdominal wall and uterine wall, to extract fetal DNA from the amniotic fluid. There is a risk of miscarriage and fetal injury with amniocentesis because it involves penetrating the uterus with the baby still in utero.

## Imaging



A dating scan at 12 weeks

Imaging is another important way to monitor a pregnancy. The mother and fetus are also usually imaged in the first trimester of pregnancy. This is done to predict problems with the mother; confirm that a pregnancy is present inside the uterus; estimate the gestational age; determine the number of fetuses and placentae; evaluate for an ectopic pregnancy and first trimester bleeding; and assess for early signs of anomalies.

X-rays and computerized tomography (CT) are not used, especially in the first trimester, due to the ionizing radiation, which has teratogenic effects on the fetus. No effects of magnetic resonance imaging (MRI) on the fetus have been demonstrated, but this technique is too expensive for routine observation. Instead, ultrasound is the imaging

method of choice in the first trimester and throughout the pregnancy, because it emits no radiation, is portable, and allows for realtime imaging.

Ultrasound imaging may be done at any time throughout the pregnancy, but usually happens at the 12th week (dating scan) and the 20th week (detailed scan).

A normal gestation would reveal a gestational sac, yolk sac, and fetal pole. The gestational age can be assessed by evaluating the mean gestational sac diameter (MGD) before week 6, and the crown-rump length after week 6. Multiple gestation is evaluated by the number of placentae and amniotic sacs present.

## **Complications and emergencies**

The main emergencies include:

- Ectopic pregnancy is when an embryo implants in the Fallopian tube or (rarely) on the ovary or inside the peritoneal cavity. This may cause massive internal bleeding.
- Pre-eclampsia is a disease which is defined by a combination of signs and symptoms that are related to maternal hypertension. The cause is unknown, and markers are being sought to predict its development from the earliest stages of pregnancy. Some unknown factors cause vascular damage in the endothelium, causing hypertension. If severe, it progresses to *eclampsia*, where a convulsions occur, which can be fatal. Preeclamptic patients with the HELLP syndrome show liver failure and Disseminated intravascular coagulation (DIC).
- Placental abruption where the patient can bleed to death if not managed appropriately.
- Fetal distress where the fetus is getting compromised in the uterine environment.
- Shoulder dystocia where one of the fetus' shoulders becomes stuck during vaginal birth, especially in macrosomic babies of diabetic mothers.
- Uterine rupture can occur during obstructed labor and endangered fetal and maternal life.
- Prolapsed cord refers to the prolapse of the fetal cord during labor with the risk of fetal suffocation.
- Obstetrical hemorrhage may be due to a number of factors such as placenta previa, uterine rupture of tears, uterine atony, retained placenta or placental fragments, or bleeding disorders.
- Puerperal sepsis is a progressed infection of the uterus during or after labor.

## **Fetal assessments**

Ultrasound is routinely used for dating the gestational age of a pregnancy from the size of the fetus, the most accurate dating being in first trimester before the growth of the fetus has been significantly influenced by other factors. Ultrasound is also used for detecting congenital anomalies (or other fetal anomalies) and determining the biophysical profiles (BPP), which are generally easier to detect in the second trimester when the fetal

structures are larger and more developed. Specialised ultrasound equipment can also evaluate the blood flow velocity in the umbilical cord, looking to detect a decrease/absence/reversal or diastolic blood flow in the umbilical artery.

Other tools used for assessment include:

- Fetal karyotype can be used for the screening of genetic diseases. This can be obtained via amniocentesis or chorionic villus sampling (CVS)
- Fetal hematocrit for the assessment of fetal anemia, Rh isoimmunization, or hydrops can be determined by percutaneous umbilical blood sampling (PUBS) which is done by placing a needle through the abdomen into the uterus and taking a portion of the umbilical cord.
- Fetal lung maturity is associated with how much surfactant the fetus is producing. Reduced production of surfactant indicates decreased lung maturity and is a high risk factor for infant respiratory distress syndrome. Typically a lecithin:sphingomyelin ratio greater than 1.5 is associated with increased lung maturity.
- Nonstress test (NST) for fetal heart rate
- Oxytocin challenge test

## **Childbirth**

### **Induction**

Induction is a method of artificially or prematurely stimulating labour in a woman. Reasons to induce can include pre-eclampsia, placental malfunction, intrauterine growth retardation, and other various general medical conditions, such as renal disease. Induction may occur any time after 34 weeks of gestation if the risk to the fetus or mother is greater than the risk of delivering a premature fetus regardless of lung maturity.

Induction may be achieved via several methods:

- Pessary of *Prostin* cream, prostaglandin E<sub>2</sub>
- Intravaginal or oral administration of misoprostol
- Cervical insertion of a 30-mL Foley catheter
- Rupturing the amniotic membranes
- Intravenous infusion of synthetic oxytocin (Pitocin or Syntocinon)

### **Labor**

During labor itself, the obstetrician/doctor/intern/medical student under supervision may be called on to do a number of tasks. These tasks can include:

- Monitor the progress of labor, by reviewing the nursing chart, performing vaginal examination, and assessing the trace produced by a fetal monitoring device (the cardiotocograph)

- Accelerate the progress of labor by infusion of the hormone oxytocin
- Provide pain relief, either by nitrous oxide, opiates, or by epidural anesthesia done by anaesthetists, an anesthesiologist, or a nurse anesthetist.
- Surgically assisting labor, by forceps or the Ventouse (a suction cap applied to the fetus' head)
- Caesarean section, if there is an associated risk with vaginal delivery, as such fetal or maternal compromise supported by evidence and literature. Caesarean section can either be elective, that is, arranged before labor, or decided during labor as an alternative to hours of waiting. True "emergency" Cesarean sections include abruptio placenta, and are more common in multigravid patients, or patients attempting a Vaginal Birth After Caesarean section (VBAC).

## ***Postnatal***

A woman in the Western world who is delivering in a hospital may leave the hospital as soon as she is medically stable and chooses to leave, which can be as early as a few hours postpartum, though the average for spontaneous vaginal delivery (SVD) is 1–2 days, and the average caesarean section postnatal stay is 3–4 days. During this time the mother is monitored for bleeding, bowel and bladder function, and baby care. The infant's health is also monitored.

## ***Post-Natal Care***

Care provided to the mother following parturition. Certain things must be kept in mind as the physician proceeds with the post-natal care.

1. General Condition of the patient.
2. Check for Vital Signs (Pulse, Blood Pressure, Temperature, Respiratory Rate, (Pain) at times)
3. Palor?
4. Edema?
5. Dehydration?
6. Fundus (height following parturition, and the feel of the fundus) (Per Abdominal Examination)
7. If an Episiotomy or a C-Section was performed, check for the dressing. Intact, pus, oozing, haematomas?
8. Lochia (colour, amount, odour)?
9. Bladder (keep the patient catheterized for 12 hours following local anaesthesia and 24-48 hours after general anaesthesia) ? (check for bladder function)
10. Bowel Movements?
11. Follow up with the neonate to check if they're healthy.

## Chapter 10

# Oncology

### Oncologist

#### Occupation

<b>Names</b>	Doctor, Medical Specialist
<b>Type</b>	Specialty
<b>Activity sectors</b>	Medicine

#### Description

Doctor of Medicine

#### Education required

Medical residency Fellowship  
(medicine)

#### Fields of employment

Hospitals, Clinics

**Oncology** (from the Ancient Greek *onkos* (ὄγκος), meaning bulk, mass, or tumor, and the suffix *-logy* (-λογία), meaning "study of") is a branch of medicine that deals with tumors (cancer). A medical professional who practices oncology is an *oncologist*.

Oncology is concerned with:

- The diagnosis of any cancer in a person
- Therapy (e.g., surgery, chemotherapy, radiotherapy and other modalities)
- Follow-up of cancer patients after successful treatment
- Palliative care of patients with terminal malignancies
- Ethical questions surrounding cancer care
- Screening efforts:
  - of populations, or
  - of the relatives of patients (in types of cancer that are thought to have a hereditary basis, such as breast cancer)

## ***Diagnosis***

The most important diagnostic tool remains the medical history: the character of the complaints and any specific symptoms (fatigue, weight loss, unexplained anemia, fever of unknown origin, paraneoplastic phenomena and other signs). Often a physical examination will reveal the location of a malignancy.

Diagnostic methods include:

- Biopsy, either incisional or excisional;
- Endoscopy, either upper or lower gastrointestinal, bronchoscopy, or nasendoscopy;
- X-rays, CT scanning, MRI scanning, ultrasound and other radiological techniques;
- Scintigraphy, Single Photon Emission Computed Tomography, Positron emission tomography and other methods of nuclear medicine;
- Blood tests, including Tumor markers, which can increase the suspicion of certain types of tumors or even be pathognomonic of a particular disease.

Apart from in diagnosis, these modalities (especially imaging by CT scanning) are often used to determine operability, i.e. whether it is surgically possible to remove a tumor in its entirety.

Generally, a "tissue diagnosis" (from a biopsy) is considered essential for the proper identification of cancer. When this is not possible, "empirical therapy" (without an exact diagnosis) may be given, based on the available evidence (e.g. history, x-rays and scans.)

Occasionally, a metastatic lump or pathological lymph node is found (typically in the neck) for which a primary tumor cannot be found. This situation is referred to as "carcinoma of unknown primary", and again, treatment is empirical based on past experience of the most likely origin.

## ***Therapy***

It completely depends on the nature of the tumor identified what kind of therapeutical intervention will be necessary. Certain disorders will require immediate admission and chemotherapy (such as ALL or AML), while others will be followed up with regular physical examination and blood tests.

Often, surgery is attempted to remove a tumor entirely. This is only feasible when there is some degree of certainty that the tumor can in fact be removed. When it is certain that parts will remain, curative surgery is often impossible, e.g. when there are metastases elsewhere, or when the tumor has invaded a structure that cannot be operated upon without risking the patient's life. Occasionally surgery can improve survival even if not all tumour tissue has been removed; the procedure is referred to as "debulking" (i.e. reducing the overall amount of tumour tissue). Surgery is also used for the palliative

treatment of some of cancers, e.g. to relieve biliary obstruction, or to relieve the problems associated with some cerebral tumors. The risks of surgery must be weighed up against the benefits.

Chemotherapy and radiotherapy are used as a first-line radical therapy in a number of malignancies. They are also used for adjuvant therapy, i.e. when the macroscopic tumor has already been completely removed surgically but there is a reasonable statistical risk that it will recur. Chemotherapy and radiotherapy are commonly used for palliation, where disease is clearly incurable: in this situation the aim is to improve the quality of and prolong life.

Hormone manipulation is well established, particularly in the treatment of breast and prostate cancer.

There is currently a rapid expansion in the use of monoclonal antibody treatments, notably for lymphoma (Rituximab), and breast cancer (Trastuzumab).

Vaccine and other immunotherapies are the subject of intensive research.

### ***Palliative care***

Approximately 50% of all cancer cases in the Western world can be treated to remission with radical treatment. For paediatric patients, that number is much higher. A large number of cancer patients will die from the disease, and a significant proportion of patients with incurable cancer will die of other causes. There may be ongoing issues with symptom control associated with progressive cancer, and also with the treatment of the disease. These problems may include pain, nausea, anorexia, fatigue, immobility, and depression. Not all issues are strictly physical: personal dignity may be affected. Moral and spiritual issues are also important.

While many of these problems fall within the remit of the oncologist, palliative care has matured into a separate, closely allied speciality to address the problems associated with advanced disease. Palliative care is an essential part of the multidisciplinary cancer care team. Palliative care services may be less hospital-based than oncology, with nurses and doctors who are able to visit the patient at home.

### ***Ethical issues***

There are a number of recurring *ethical questions* and *dilemmas* in oncological practice. These include:

- What information to give the patient regarding disease extent/progression/prognosis.
- Entry into clinical trials, especially in the face of terminal illness.
- Withdrawal of active treatment.
- "Do Not Resuscitate" orders and other end of life issues.

These issues are closely related to the patients' personality, religion, culture, personal, and family life. The answers are rarely black and white. It requires a degree of sensitivity and very good communication on the part of the oncology team to address these problems properly.

## ***Progress and research***

There is a tremendous amount of research being conducted on all frontiers of oncology, ranging from cancer cell biology to chemotherapy treatment regimens and optimal palliative care and pain relief. This makes oncology a continuously changing field.

Therapeutic trials often involve patients from many different hospitals in a particular region. In the UK, patients are often enrolled in large studies coordinated by Cancer Research UK (CRUK), Medical Research Council (MRC), the European Organisation for Research and Treatment of Cancer (EORTC) or the National Cancer Research Network (NCRN).

## ***Specialties***

There are several sub-specialties within oncology. Moreover, oncologists often develop an interest and expertise in the management of particular types of cancer.

Oncologists may be divided on the basis of the type of treatment provided.

- Radiation oncology: treatment primarily with radiation, a process called radiotherapy.
- Surgical oncology: surgeons who specialize in tumor removal.
- Medical oncology: treatment primarily with drugs, e.g. chemotherapy
- Interventional oncology: interventional radiologists who specialize in minimally invasive image guided tumor therapies.
- Gynecologic oncology: focuses on cancers of the female reproductive system.
- Pediatric oncology: concerned with the diagnosis and treatment of cancer in children

In the United Kingdom and several other countries, oncologists may be either *clinical* or *medical oncologists*. The main difference is that clinical oncologists deliver radiotherapy, while medical oncologists do not. (This difference does not apply in North America: the terms, *clinical oncologist* and *medical oncologist* are used interchangeably.)

In most countries it is now common that patients are treated by a multidisciplinary team. These teams will meet on regular basis and discuss the patients under their care. These teams consist of the medical oncologist, a clinical oncologist or radiotherapist, a surgeon (sometimes there is a second reconstructive surgeon), a radiologist, a pathologist, an organ specific specialist such as a gynecologist or dermatologist, and sometimes the general practitioner is also involved. These disease oriented teams are sometimes in conflict with the general organisation and operation in hospitals. Historically hospitals are

organised in an organ or technique specific manner. Multidisciplinary teams operate over these borders and it is sometimes difficult to define who is in charge.

## Chapter 11

# Ophthalmology



Slit lamp examination of eyes in an Ophthalmology Clinic



A phoropter in use

**Ophthalmology** is the branch of medicine which deals with the anatomy, physiology and diseases of the eye. The term **ophthalmologist** refers to a specialist in medical and surgical eye problems. Since ophthalmologists perform operations on eyes, they are considered to be both surgical and medical specialists.

The word *ophthalmology* comes from the Greek roots *ophthalmos* meaning *eye* and *logos* meaning *word, thought, or discourse*; ophthalmology literally means "the science of eyes". "Optomology" is a common mis-hearing or mis-remembering of the term. As a discipline, it applies to animal eyes also, since the differences from human practice are surprisingly minor and are related mainly to differences in anatomy or prevalence, not differences in disease processes. However, veterinary medicine is regulated separately in many countries and states/provinces resulting in few ophthalmologists treating both humans and animals.

### ***Early Developments***

#### **Sushruta**

Sushruta wrote *Sushruta Samhita* in Sanskrit in about 800 BC He described 76 ocular diseases (of these 51 surgical) as well as several ophthalmological surgical instruments and techniques. His description of cataract surgery was more akin to extracapsular lens

extraction than to couching. The Indian surgeon Sushruta has been described as the first cataract surgeon.

## **Pre-Hippocrates**

The pre-Hippocratics largely based their anatomical conceptions of the eye on speculation, rather than empiricism. They recognized the sclera and transparent cornea running flushly as the outer coating of the eye, with an inner layer with pupil, and a fluid at the centre. It was believed, by Alcamaeon and others, that this fluid was the medium of vision and flowed from the eye to the brain via a tube. Aristotle advanced such ideas with empiricism. He dissected the eyes of animals, and discovering three layers (not two), found that the fluid was of a constant consistency with the lens forming (or congealing) after death, and the surrounding layers were seen to be juxtaposed. He, and his contemporaries, further put forth the existence of three tubes leading from the eye, not one. One tube from each eye met within the skull.

## **Rufus**

Rufus recognised a more modern eye, with conjunctiva, extending as a fourth epithelial layer over the eye. Rufus was the first to recognise a two chambered eye; with one chamber from cornea to lens (filled with water), the other from lens to retina (filled with an egg-white-like substance). Galen remedied some mistakes including the curvature of the cornea and lens, the nature of the optic nerve, and the existence of a posterior chamber. Though this model was roughly a correct but simplistic modern model of the eye, it contained errors. Yet it was not advanced upon again until after Vesalius. A ciliary body was then discovered and the sclera, retina, choroid and cornea were seen to meet at the same point. The two chambers were seen to hold the same fluid as well as the lens being attached to the choroid. Galen continued the notion of a central canal, though he dissected the optic nerve, and saw it was solid, He mistakenly counted seven optical muscles, one too many. He also knew of the tear ducts.

## **Middle Eastern ophthalmology**

Medieval Islamic physicians are considered founders of ophthalmology as an independent discipline. One of the pioneers of ophthalmology was the Persian physician Rhazes. Innovations from this period include “injection syringe”, invented by the Iraqi physician Ammar ibn Ali of Mosul, which was used for the extraction by suction of soft cataracts. In cataract surgery, Ammar ibn Ali attempted the earliest extraction of cataracts using suction. He introduced a hollow metallic syringe hypodermic needle through the sclera and successfully extracted the cataracts through suction.

Ibn al-Haytham (Alhazen) wrote extensively on optics and the anatomy of the eye in his *Book of Optics* (1021). He was the first to hint at the retina being involved in the process of image formation.

Ibn al-Nafis, in *The Polished Book on Experimental Ophthalmology*, discovered that the muscle behind the eyeball does not support the ophthalmic nerve, and that the optic nerves transect but do not get in touch with each other. He also discovered new treatments for glaucoma and the weakness of vision in one eye when the other eye is affected by disease. Salah-ud-din bin Youssef al-Kalal bi Hama (i.e. the eye doctor of Hama) was a Syrian oculist who flourished in Hama in 1296. He wrote an elaborate treatise of ophthalmology entitled *Nur al-Uyun wa Jami al-Funun* (light of the eyes and collection of rules).

## **Seventeenth and eighteenth century**

The seventeenth and eighteenth century saw the use of hand lenses (by Malpighi), microscopes (van Leeuwenhoek), preparations for fixing the eye for study (Ruysch) and later the freezing of the eye (Petit). This allowed for detailed study of the eye and an advanced model. Some mistakes persisted such as: why the pupil changed size (seen to be vessels of the iris filling with blood), the existence of the posterior chamber, and of course the nature of the retina. In 1722 Leeuwenhoek noted the existence of rods and cones though they were not properly discovered until Gottfried Reinhold Treviranus in 1834 by use of a microscope.

## **Ophthalmic surgery in Great Britain**

The first ophthalmic surgeon in Great Britain was John Freke, appointed to the position by the Governors of St Bartholomew's Hospital in 1727, but the establishment of the first dedicated ophthalmic hospital in 1805; now called Moorfields Eye Hospital in London, England was a transforming event in modern ophthalmology. Clinical developments at Moorfields and the founding of the Institute of Ophthalmology (now part of the University College London) by Sir Stewart Duke Elder established the site as the largest eye hospital in the world and a nexus for ophthalmic research.

## ***Professional requirements***

Ophthalmologists are medical doctors (MD/MBBS or D.O., not OD or BOptom) who have completed a college degree, medical school, and residency in ophthalmology. In many countries, ophthalmologists also undergo additional specialized training in one of the many subspecialties. Ophthalmology was the first branch of medicine to offer board certification, now a standard practice among all specialties.

## **Australia and New Zealand**

In Australia and New Zealand, the FRACO/Franzco is the equivalent postgraduate specialist qualification. It is a very competitive speciality to enter training and has a closely monitored and structured training system in place over the five years of postgraduate training. Overseas-trained Ophthalmologists are assessed using the pathway published on the RANZCO website. Those who have completed their formal training in the UK and have the CCST/CCT are usually deemed to be comparable.

## **Canada**

In Canada, an Ophthalmology residency after medical school is undertaken. The residency lasts a minimum of five years after the MD degree although subspecialty training is undertaken by about 30% of fellows (FRCSC). There are about 30 vacancies per year for ophthalmology training in all of Canada.

## **Finland**

In Finland, physicians willing to become Ophthalmologists must undergo a five year specialization which includes practical training and theoretical studies.

## **Germany**

In Germany, physicians willing to become Ophthalmologists must undergo a five year specialization of practical training.

## **India**

In India, after completing MBBS degree, post-graduation in Ophthalmology is required. The degrees are Doctor of Medicine (MD), Master of Surgery (MS), Diploma in Ophthalmic Medicine and Surgery (DOMS) or Diplomate of National Board (DNB). The concurrent training and work experience is in the form of a Junior Residency at a Medical College, Eye Hospital or Institution under the supervision of experienced faculty. Further work experience in form of fellowship, registrar or senior resident refines the skills of these eye surgeons. All India Ophthalmological Society (AIOS) and various state level Ophthalmological Societies (like DOS) hold regular conferences and actively promote continuing medical education. Royal colleges of the united kingdom, mainly Royal college of surgeons of Edinburgh (RCSEd), Royal College of ophthalmologists (RCOphth) and Royal college of physicians and Surgeons of Glasgow (RCPSG) have conducted their fellowship and membership examinations since the mid-1990s and awarding fellowships and memberships to the successful candidates.

## **Pakistan**

In Pakistan, after MBBS, a 4 year full time residency programme leads to FCPS in Ophthalmology. Moreover, a two and a half years residency programme leads to MCPS while 2 years training of DOMS is also being offered. M.S.(Ophthalmology) is also one of the specialty programmes. In addition to programmes for Doctors, various diplomas and degrees for Opticians are also being offered to produce competent Optic technicians in this field. These programmes are being offered notably by Punjab Institute of Preventive Ophthalmology (PIPO) Lahore, Pakistan. Sub-specialty Fellowships are also being offered in the field of Pediatric Ophthalmology and Vitreo-Retinal Ophthalmology.

## **Philippines**

Ophthalmology is considered a medical specialty that uses medicine and surgery to treat diseases of the eye. To become a general ophthalmologist, a candidate must have completed a Doctor of Medicine degree or its equivalent (e.g. MBBS), have passed the physician licensure exam, completed an internship in medicine, and completed residency at any Philippine Academy of Ophthalmology (PAO) accredited program. Attainment of board certification in ophthalmology from PBO is optional, but is preferred and required to gain privileges in most major health institutions. Graduates of residency programs can receive further training in subspecialties of ophthalmology such as neuro-ophthalmology, etc. by completing a fellowship program which varies in length depending on each program's requirements. The leading professional organization in the country is the Philippine Academy of Ophthalmology which also regulates ophthalmology residency programs and board certification through its accrediting agency, the Philippine Board of Ophthalmology.

## **United Kingdom and Republic of Ireland**

In the United Kingdom, there are three colleges that grant postgraduate degrees in ophthalmology. The Royal College of Ophthalmologists grants MRCOphth and FRCOphth (postgraduate exams), the Royal College of Edinburgh grants MRCSEd, the Royal College of Glasgow grants FRCS. In Ireland the Royal College of Ireland grants FRCOI. Work experience as a specialist registrar and one of these degrees is required for specialisation in eye diseases. There are only 2.3 ophthalmologists per 100,000 population in the UK -fewer pro rata than in any other nation in the European Union

## **United States**

In the United States, four years of residency training after medical school are required, with the first year being an internship in surgery, internal medicine, pediatrics, or a general transition year. Optional fellowships in advanced topics may be pursued for several years after residency. Most currently practicing ophthalmologists train in medical residency programs accredited by the Accreditation Council for Graduate Medical Education (ACGME) and are board certified by the American Board of Ophthalmology. Some physicians that train in osteopathic medical schools may hold a Doctor of Osteopathy ("DO") degree rather than an MD. The same residency and certification requirements for ophthalmology training must be fulfilled by osteopathic physicians. Completing the requirements of continuing medical education is mandatory for continuing licensure and re-certification. Professional bodies like the AAO and ASCRS organize conferences and help members through continuing medical education programs to maintain certification, in addition to political advocacy and peer support.

## ***Sub-specialities***

Ophthalmology includes sub-specialities which deal either with certain diseases or diseases of certain parts of the eye. Some of them are:

- Anterior segment surgery
- Cataract — not usually considered a subspecialty *per se*, since most general ophthalmologists perform cataract surgery
- Cornea, ocular surface, and external disease
- Glaucoma
- Medical retina, deals with treatment of retinal problems through non-surgical means.
- Neuro-ophthalmology
- Ocular oncology
- Oculoplastics & Orbit surgery
- Ophthalmic pathology
- Pediatric ophthalmology/Strabismus (mis-alignment of the eyes)
- Refractive surgery
- Uveitis/Immunology
- Veterinary Formal specialty training programs in veterinary ophthalmology now exist in some countries.
- Vitreo-retinal surgery, deals with surgical management of retinal and posterior segment diseases and disorders. Medical retina and vitreo-retinal surgery sometimes together called posterior segment subspecialisation.

## **Ophthalmic surgery**

### ***Notable ophthalmologists***

#### **18th-19th century**

- Sir William Adams (UK) Founder of Exeter's West of England Eye Infirmary.
- Carl Ferdinand von Arlt (1812–1887), the elder (Austrian) proved that myopia is largely due to an excessive axial length, published influential textbooks on eye disease, and ran annual eye clinics in needy areas long before the concept of volunteer eye camps became popular. His name is still attached to some disease signs, e.g., von Arlt's line in trachoma. His son Ferdinand Ritter von Arlt, the younger, was also an ophthalmologist.
- Jacques Daviel (France) claimed to be the 'father' of modern cataract surgery in that he performed extracapsular extraction instead of needling the cataract or pushing it back into the vitreous. It is said that he carried out the technique on 206 patients in 1752-3, out of which 182 were reported to be successful. These figures are not very credible, given the total lack of both anaesthesia and aseptic technique at that time.
- Frans Cornelis Donders (1818–1889) (Dutch) published pioneering analyses of ocular biomechanics, intraocular pressure, glaucoma, and physiological optics. Made possible the prescribing of combinations of spherical and cylindrical lenses to treat astigmatism.
- Albrecht von Graefe (1828–1870) (Germany) Along with Helmholtz and Donders, one of the 'founding fathers' of ophthalmology as a specialty. A brilliant clinician and charismatic teacher who had an international influence on the

- development of ophthalmology. A pioneer in mapping visual field defects and diagnosis and treatment of glaucoma. Introduced a cataract extraction technique that remained the standard for over 100 years, and many other important surgical techniques such as iridectomy. Rationalised the use of many ophthalmically important drugs, including mydriatics & miotics. The founder of the one of the earliest ophthalmic societies (German Ophthalmological Society, 1857) and one of the earliest ophthalmic journals (Graefe's Archives of Ophthalmology). The most important ophthalmologist of the nineteenth century.
- Allvar Gullstrand (Sweden), Nobel Prize winner in 1911 for his research on the eye as a light-refracting apparatus. Described the *schematic eye* a mathematical model of the human eye based on his measurements known as the *optical constants* of the eye. His measurements are still used today.
  - Hermann von Helmholtz, great German polymath, invented the ophthalmoscope (1851) and published important work on physiological optics, including colour vision (1850s).
  - Sir Arthur Conan Doyle (United Kingdom). English writer, primarily of the Sherlock Holmes stories. Trained in but apparently never practiced Ophthalmology.
  - Jose Rizal (Philippines). The Philippines National Hero was an Ophthalmologist, One of his works was operation of his mother's eye for twice from cataract.

## 20th-21st century

- William Horatio Bates (1860–1931) (United States) Creator of the unorthodox Bates Method, credited for being the founder of the Natural Vision Improvement movement.
- Vladimir Petrovich Filatov (1875–1956) (Ukraine) His contributions to the medical world include the tube flap grafting method, corneal transplantation and preservation of grafts from cadaver eyes and tissue therapy. He founded The Filatov Institute of Eye Diseases & Tissue Therapy, Odessa, one of the leading eye care institutes in the world.
- Ignacio Barraquer (1884–1965) (Spain) In 1917, invented the first motorized vacuum instrument (erisophake) for intracapsular cataract extraction. Founded of the Barraquer Clinic in 1941 and the Barraquer Institute in 1947 in Barcelona, Spain.
- Tsutomu Sato (Japan) Pioneer in incisional refractive surgery, including techniques for astigmatism and the invention of radial keratotomy for myopia.
- Jules Gonin (1870–1935) (Switzerland) "Father of retinal detachment surgery".
- Sir Harold Ridley (United Kingdom) In 1949, may have been the first to successfully implant an artificial intraocular lens after observing that plastic fragments in the eyes of wartime pilots were well tolerated. He fought for decades against strong reactionary opinions to have the concept accepted as feasible and useful.
- Charles Schepens (Belgium) "Father of modern retinal surgery". Developer of the Schepens indirect binocular ophthalmoscope whilst at Moorfields Eye Hospital. Founder of the Schepens Eye Research Institute in Boston, Massachusetts. This

premier research institute is associated with Harvard Medical School and Massachusetts Eye & Ear Infirmary.

- Marshall M. Parks "Father of pediatric ophthalmology".
- José Ignacio Barraquer (1916–1998) (Spain) "Father of modern refractive surgery". In the 1960s, developed lamellar techniques including keratomileusis and keratophakia, as well as the first microkeratome and corneal microlathe.
- Tadeusz Krwawicz (Poland) In 1961, developed the first cryoprobe for intracapsular cataract extraction.
- Svyatoslav Fyodorov (Russia) Popularizer of radial keratotomy.
- Charles Kelman (United States) Developed the ultrasound and mechanized irrigation and aspiration system for phacoemulsification, first allowing cataract extraction through a small incision.
- Ioannis Pallikaris (Greece) Performed the first laser-assisted intrastromal keratomileusis or LASIK surgery.
- Fred Hollows (New Zealand/Australia) Pioneered programs in Nepal, Eritrea, and Vietnam, and among Australian aborigines, including the establishment of cheap laboratory production of intraocular lenses in Nepal and Eritrea.
- Ian Constable (Australia) Founded the Lions Eye Institute in Perth, Western Australia, the largest eye research institute in the southern hemisphere and home to ten ophthalmologists.
- Rand Paul (United States) is a current member of The United States Senate from Kentucky. His father is U.S. Representative Ron Paul.
- L. L. Zamenhof (Poland) Creator of the Esperanto language.
- Bashar al-Assad (Syria) The President of Syria. He did his ophthalmology residency in a hospital in London.
- Wallace Foulds (United Kingdom) Founder president of the Royal College of Ophthalmologists, founder of the Scottish Ophthalmic Oncology Service, and provided support for the founding of the Singapore Eye Research Institute.

## Chapter 12

# Plastic Surgery

### Plastic surgeon

#### Occupation

<b>Names</b>	Doctor, Medical Specialist
<b>Type</b>	Specialty
<b>Activity sectors</b>	Surgery

#### Description

**Education required** MD or MBBS or DO-US

**Fields of employment** Hospitals, Clinics

**Plastic Surgery** is a medical specialty concerned with the correction or restoration of form and function. While famous *Italic text* for aesthetic surgery, plastic surgery also includes many types of reconstructive surgery, hand surgery, microsurgery, and the treatment of burns. The word "plastic" derives from the Greek *plastikos* (πλαστικός) meaning to mold or to shape, thus plastic surgery means "molding or shaping surgery" – its use here has no connection with plastics in the sense of synthetic polymer material. While the majority of cosmetic surgery comes under plastic surgery, most plastic surgery is not cosmetic surgery.

## History



Walter Yeo, a British soldier, is often cited as the first known person to have benefited from plastic surgery. The photograph shows him before the procedure (left) and after (right) receiving a skin graft performed by Sir Harold Gillies in 1917.

Reconstructive surgery techniques were being carried out in India by 800 BC. Sushruta, the father of Indian surgery, made important contributions to the field of plastic and cataract surgery in 6th century BC. The medical works of both Sushruta and Charak originally in Sanskrit were translated into Arabic language during the Abbasid Caliphate in 750 AD. The Arabic translations made their way into Europe via intermediaries. In Italy the Branca family of Sicily and Gaspare Tagliacozzi (Bologna) became familiar with the techniques of Sushruta.

British physicians traveled to India to see rhinoplasties being performed by native methods. Reports on Indian rhinoplasty performed by a Kumhar vaidya were published in the *Gentleman's Magazine* by 1794. Joseph Constantine Carpue spent 20 years in India studying local plastic surgery methods. Carpue was able to perform the first major surgery in the Western world by 1815. Instruments described in the *Sushruta Samhita* were further modified in the Western world.



Aulus Cornelius Celsus, who lived in the first century AD, described plastic surgery of the face, using skin from other parts of the body.

The ancient Egyptians and Romans also performed plastic cosmetic surgery. The Romans were able to perform simple techniques, such as repairing damaged ears from around the 1st century BC. For religious reasons, they did not dissect either human beings or animals, thus their knowledge was based in its entirety on the texts of their Greek predecessors. Notwithstanding, Aulus Cornelius Celsus left some surprisingly accurate anatomical descriptions, some of which — for instance, his studies on the genitalia and the skeleton — are of special interest to plastic surgery.

In 1465, Sabuncuoglu's book, description, and classification of hypospadias was more informative and up to date. Localization of urethral meatus was described in detail. Sabuncuoglu also detailed the description and classification of ambiguous genitalia. In mid-15th century Europe, Heinrich von Pfolspendt described a process "to make a new nose for one who lacks it entirely, and the dogs have devoured it" by removing skin from the back of the arm and suturing it in place. However, because of the dangers associated with surgery in any form, especially that involving the head or face, it was not until the 19th and 20th centuries that such surgery became common.

Up until the techniques of anesthesia became established, surgeries involving healthy tissues involved great pain. Infection from surgery was reduced by the introduction of sterile techniques and disinfectants. The invention and use of antibiotics, beginning with sulfa drugs and penicillin, was another step in making elective surgery possible.

In 1792, Chopart performed operative procedure on a lip using a flap from the neck. In 1814, Joseph Carpue successfully performed operative procedure on a British military officer who had lost his nose to the toxic effects of mercury treatments. In 1818, German surgeon Carl Ferdinand von Graefe published his major work entitled *Rhinoplastik*. Von Graefe modified the Italian method using a free skin graft from the arm instead of the original delayed pedicle flap.

The first American plastic surgeon was John Peter Mettauer, who, in 1827, performed the first cleft palate operation with instruments that he designed himself. In 1845, Johann Friedrich Dieffenbach wrote a comprehensive text on rhinoplasty, entitled *Operative Chirurgie*, and introduced the concept of reoperation to improve the cosmetic appearance of the reconstructed nose.

In 1891, American otorhinolaryngologist John Roe presented an example of his work, a young woman on whom he reduced a dorsal nasal hump for cosmetic indications. In 1892, Robert Weir experimented unsuccessfully with xenografts (duck sternum) in the reconstruction of sunken noses. In 1896, James Israel, a urological surgeon from Germany, and in 1889 George Monks of the United States each described the successful use of heterogeneous free-bone grafting to reconstruct saddle nose defects. In 1898, Jacques Joseph, the German orthopaedic-trained surgeon, published his first account of reduction rhinoplasty. In 1928, Jacques Joseph published *Nasenplastik und Sonstige Gesichtsplastik*.

## **20th century**

In World War I, a New Zealand otolaryngologist working in London, Harold Gillies, developed many of the techniques of modern plastic surgery in caring for soldiers suffering from disfiguring facial injuries. His work was expanded upon during World War II by his cousin and former student Archibald McIndoe, who pioneered treatments for RAF aircrew suffering from severe burns. McIndoe's radical, experimental treatments, led to the formation of the Guinea Pig Club. In 1946, Gillies carried out the first female-to-male sex reassignment surgery.

Plastic surgery, as a specialty, evolved remarkably during the 18th century in the United States. One of the founders of the specialty, Wilbur Blair, was the first chief of the Division of Plastic and Reconstructive Surgery at Washington University in St. Louis, Missouri. In one of his many areas of clinical expertise, Blair treated World War I soldiers with complex maxillofacial injuries, and his paper on "Reconstructive Surgery of the Face" set the standard for craniofacial reconstruction.

## ***Techniques and procedures***

In plastic surgery, the transfer of skin tissue (skin grafting) is a very common procedure. Skin grafts can be taken from the recipient or donors:

- Autografts are taken from the recipient. If absent or deficient of natural tissue, alternatives can be cultured sheets of epithelial cells *in vitro* or synthetic compounds, such as integra, which consists of silicone and bovine tendon collagen with glycosaminoglycans.
- Allografts are taken from a donor of the same species.
- Xenografts are taken from a donor of a different species.

Usually, good results are expected from plastic surgery that emphasizes careful planning of incisions so that they fall in the line of natural skin folds or lines, appropriate choice of wound closure, use of best available suture materials, and early removal of exposed sutures so that the wound is held closed by buried sutures. The most plastic surgery reformations is held by a Chinese women by the name Li Cheung with 148 transformations

## ***Reconstructive surgery***

Reconstructive plastic surgery is performed to correct functional impairments caused by burns; traumatic injuries, such as facial bone fractures and breaks; congenital abnormalities, such as cleft palates or cleft lips; developmental abnormalities; infection and disease; and cancer or tumors. Reconstructive plastic surgery is usually performed to improve function, but it may be done to approximate a normal appearance.



Navy doctors perform reconstructive surgery on a 21-year-old patient

The most common reconstructive procedures are tumor removal, laceration repair, scar repair, hand surgery, and breast reduction. According to the American Society of Plastic Surgeons, the number of reconstructive breast reductions for women increased in 2007 by 2 percent from the year before. Breast reduction in men also increased in 2007 by 7 percent. Some other common reconstructive surgical procedures include breast reconstruction after a mastectomy, cleft lip and palate surgery, contracture surgery for burn survivors, and creating a new outer ear when one is congenitally absent.

Plastic surgeons use microsurgery to transfer tissue for coverage of a defect when no local tissue is available. Free flaps of skin, muscle, bone, fat, or a combination may be removed from the body, moved to another site on the body, and reconnected to a blood supply by suturing arteries and veins as small as 1 to 2 millimeters in diameter.

### ***Cosmetic surgery***



Rhinoplasty or Nose Surgery



### Blepharoplasty or Cosmetic Eyelid Surgery

Aesthetic plastic surgery involves techniques intended for the "enhancement" of appearance through surgical and medical techniques, and is specifically concerned with maintaining normal appearance, restoring it, or enhancing it beyond the average level toward some aesthetic ideal.

In 2006, nearly 11 million cosmetic procedures were performed in the United States alone. The number of cosmetic procedures performed in the United States has increased over 50 percent since the start of the century. Nearly 12 million cosmetic procedures were performed in 2007, with the five most common surgeries being breast augmentation, liposuction, nasal surgery, eyelid surgery and abdominoplasty. The

increased use of cosmetic procedures crosses racial and ethnic lines in the U.S., with increases seen among African-Americans and Hispanic Americans as well as Caucasian Americans. In Europe, the second largest market for cosmetic procedures, cosmetic surgery is a \$2.2 billion business. Cosmetic surgery is now very common in countries such as the United Kingdom, France, and Germany. In Asia, cosmetic surgery has become an accepted practice; currently most widely prevalent and normal in China where it is currently Asia's biggest cosmetic surgery market. Children undergoing cosmetic eye surgery can be seen in Japan and South Korea.

The most prevalent aesthetic/cosmetic procedures include:

- Abdominoplasty ("tummy tuck"): reshaping and firming of the abdomen
- Blepharoplasty ("eyelid surgery"): reshaping of the eyelids or the application of permanent eyeliner, including Asian blepharoplasty
- Phalloplasty
- Mammoplasty:
  - Breast augmentations ("breast implant" or "boob job"): augmentation of the breasts by means of fat grafting, saline, or silicone gel prosthetics, which was initially performed to women with micromastia
  - Reduction mammoplasty ("breast reduction"): removal of skin and glandular tissue, which is done to reduce back and shoulder pain in women with gigantomastia and/or for psychological benefit men with gynecomastia
  - Mastopexy ("breast lift"): Lifting or reshaping of breasts to make them less saggy, often after weight loss (after a pregnancy, for example). It involves removal of breast skin as opposed to glandular tissue
- Buttock augmentation ("butt implant"): enhancement of the buttocks using silicone implants or fat grafting ("Brazilian butt lift") and transfer from other areas of the body
  - Buttock lift: lifting, and tightening of the buttocks by excision of redundant skin
- Chemical peel: minimizing the appearance of acne, chicken pox, and other scars as well as wrinkles (depending on concentration and type of agent used, except for deep furrows), solar lentigines (age spots, freckles), and photodamage in general. Chemical peels commonly involve carbolic acid (Phenol), trichloroacetic acid (TCA), glycolic acid (AHA), or salicylic acid (BHA) as the active agent.
- Labiaplasty: surgical reduction and reshaping of the labia
- Lip enhancement: surgical improvement of lips' fullness through enlargement
- Rhinoplasty ("nose job"): reshaping of the nose
- Otoplasty ("ear surgery"/"ear pinning"): reshaping of the ear, most often done by pinning the protruding ear closer to the head.
- Rhytidectomy ("face lift"): removal of wrinkles and signs of aging from the face
  - Browplasty ("brow lift" or "forehead lift"): elevates eyebrows, smooths forehead skin
  - Midface lift ("cheek lift"): tightening of the cheeks
- Suction-assisted lipectomy ("liposuction"): removal of fat from the body

- Chin augmentation ("chin implant"): augmentation of the chin with an implant, usually silicone, by sliding genioplasty of the jawbone or by suture of the soft tissue
- Cheek augmentation ("cheek implant"): implants to the cheek
- Orthognathic Surgery: manipulation of the facial bones through controlled fracturing
- Fillers injections: collagen, fat, and other tissue filler injections, such as hyaluronic acid
- Laser skin resurfacing

### ***Sub-specialties***

Plastic surgery is a broad field, and may be subdivided further. Plastic surgery training and approval by the American Board of Plastic Surgery includes mastery of the following as well:

#### Burn

Burn surgery generally takes place in two phases. Acute burn surgery is the treatment immediately after a burn. Reconstructive burn surgery takes place after the burn wounds have healed. Reconstructive surgery generally involves plastic surgery.

#### Cosmetic

Aesthetic surgery is an essential component of plastic surgery. Plastic surgeons use cosmetic surgical principles in all reconstructive surgical procedures as well as isolated operations to improve overall appearance.

#### Craniofacial

Craniofacial surgery is divided into pediatric and adult craniofacial surgery. Pediatric craniofacial surgery mostly revolves around the treatment of congenital anomalies of the craniofacial skeleton and soft tissues, such as cleft lip and palate, craniosynostosis, and pediatric fractures. Adult craniofacial surgery deals mostly with fractures and secondary surgeries (such as orbital reconstruction) along with orthognathic surgery. Craniofacial surgery is an important part of all plastic surgery training programs, further training and subspecialisation is obtained via a craniofacial fellowship.

#### Hand

Hand surgery is concerned with acute injuries and chronic diseases of the hand and wrist, correction of congenital malformations of the upper extremities, and peripheral nerve problems (such as brachial plexus injuries or carpal tunnel syndrome). Hand surgery is an important part of training in plastic surgery, as well as microsurgery, which is necessary to replant an amputated extremity. The Hand surgery field is also practiced by orthopedic

surgeons and general surgeons. Scar tissue formation after surgery can be problematic on the delicate hand, causing loss of dexterity and digit function if severe enough.

#### Micro

Microsurgery is generally concerned with the reconstruction of missing tissues by transferring a piece of tissue to the reconstruction site and reconnecting blood vessels. Popular subspecialty areas are breast reconstruction, head and neck reconstruction, hand surgery/replantation, and brachial plexus surgery.

#### Pediatric

Children often face medical issues very different from the experiences of an adult patient. Many birth defects or syndromes present at birth are best treated in childhood, and pediatric plastic surgeons specialize in treating these conditions in children. Conditions commonly treated by pediatric plastic surgeons include craniofacial anomalies, cleft lip and palate and congenital hand deformities.

### ***Plastic surgery obsession***

With increased media attention on beauty and perfection, celebrities and those alike are turning to plastic surgery more and more. Some take out loans for this purpose; one woman spent over \$83,000 for 14 surgeries.

Though media and advertising do play a large role in influencing many people's lives, researchers believe that plastic surgery obsession is linked to psychological disorders. Body dysmorphic disorder is seen as playing a large role in the lives of those who are obsessed with going under the knife in order to achieve physical perfection. People with this disorder are so preoccupied with their appearance that it can dominate their lives.

In some cases, people whose doctors refuse to perform any further surgeries, have turned to "do it yourself" plastic surgery, injecting themselves and running extreme safety risks.

## Chapter 13

# Psychiatry



The word *psyche* comes from the ancient Greek for soul or butterfly. The fluttering elusive insect appears in the coat of arms of Britain's Royal College of Psychiatrists

**Psychiatry** is the medical specialty devoted to the study and treatment of mental disorders—which include various affective, behavioural, cognitive and perceptual disorders. The term was first coined by the German physician Johann Christian Reil in 1808. It literally means the 'medical treatment of the mind' (*psych-*: mind; *-iatry*: medical treatment; from Greek *iātrikos*: medical, *iāsthai*: to heal). A medical doctor specializing in psychiatry is a psychiatrist.

Mental disorders are currently conceptualized as disorders of brain circuits likely caused by developmental processes shaped by a complex interplay of genetics and experience. In other words, the genetics of mental illness may really be the genetics of brain development, with different outcomes possible, depending on the biological and environmental context.

Psychiatric assessment typically starts with a mental status examination and the compilation of a case history. Psychological tests and physical examinations may be conducted, including on occasion the use of neuroimaging or other neurophysiological techniques. Mental disorders are diagnosed in accordance with criteria listed in diagnostic manuals such as the widely used *Diagnostic and Statistical Manual of Mental Disorders* (DSM), published by the American Psychiatric Association, and the International Classification of Diseases (ICD) edited and used by the World Health Organization. The 5th edition of the DSM (DSM-5) is scheduled to be published in 2013, and is expected to have significant impact on many medical fields.

Psychiatric treatment applies a variety of modalities, including medication, psychotherapy and a wide range of other techniques such as transcranial magnetic stimulation. Treatment may be as an inpatient or outpatient, according to severity of function impairment/the disorder in question. Research and treatment within psychiatry as a whole are conducted on an interdisciplinary basis, sourcing an array of sub-specialties and theoretical approaches.

## **History**

Although one may trace its germination to the late eighteenth century, the beginning of psychiatry as a medical specialism is dated to the middle of the nineteenth century.. Prior to this point one is considering the history of madness and not the history of psychiatry.

### **Ancient times**

Starting in the 5th century BC, mental disorders, especially those with psychotic traits, were considered supernatural in origin. This view existed throughout ancient Greece and Rome. Early manuals written about mental disorders were created by the Greeks. In the 4th century BC, Hippocrates theorized that physiological abnormalities may be the root of mental disorders. Religious leaders and others returned to using early versions of exorcisms to treat mental disorders which often utilized cruel, harsh, and barbarous methods.

### **Middle Ages**

The first specialist hospitals were built in the medieval Islamic world from the 8th century. The first was built in Baghdad in 705 AD, followed by Fes in the early 8th century, and Cairo in 800 AD. Unlike medieval Christian physicians who relied on demonological explanations for madness, medieval Muslim physicians relied mostly on clinical observations. They made significant advances in the medical understanding of madness and were the first to provide psychotherapy for mentally ill patients, in addition to other forms of treatment such as baths, drug medication, music therapy and occupational therapy. In the 10th century, the Persian physician Muhammad ibn Zakarīya Rāzi (Rhazes) combined psychological methods and physiological explanations to provide treatment to mentally ill patients. His contemporary, the Arab physician Najab ud-din Muhammad, described a number of forms of madness which might share clinical

features with contemporary medical disease concepts such as agitated depression, neurosis, priapism and sexual impotence (*Nafkhae Malikholia*), psychosis (*Kutrib*), and mania (*Dual-Kulb*).

In the 11th century, another Persian physician, Abu Ali al-Hussain ibn Abdallah ibn Sina, known in the West as Avicenna, recognized "physiological psychology" in the treatment of illnesses involving emotions, and developed a system for associating changes in the pulse rate with inner feelings. The third section of Avicenna's monumental text *Cannon of Medicine (Al-Qanun fi al-Tibb)* dealt with disorders of the psyche and the nervous systems and expounded on topics such as sexology, lovesickness, delusion, apoplexy, hallucination, insomnia, mania, nightmare, melancholia, dementia, epilepsy, paralysis, stroke, vertigo, spasm and tremor.

Specialist hospitals were built in medieval Europe from the 13th century to treat mental disorders but were utilized only as custodial institutions and did not provide any type of treatment. Founded in the 13th century, Bethlem Royal Hospital in London is one of the oldest lunatic asylums. By 1547 the City of London acquired the hospital and continued its function until 1948. It is now part of the National Health Service and is an NHS Foundation Trust.



Many consider Philippe Pinel to be the father of modern psychiatry

### **Early modern period**

In 1656, Louis XIV of France created a public system of hospitals for those suffering from mental disorders, but as in England, no real treatment was being applied. In 1758 English physician William Battie wrote the *Treatise on Madness* which called for treatments to be utilized in asylums. Thirty years later the new ruling monarch in England, George III, was known to be suffering from a mental disorder. Following the King's remission in 1789, mental illness was seen as something which could be treated and cured. By 1792 French physician Philippe Pinel introduced humane treatment approaches to those suffering from mental disorders. William Tuke adopted the methods outlined by Pinel and that same year Tuke opened the York Retreat in England. That institution became known as a model throughout the world for humane and moral treatment of patients suffering from mental disorders. It inspired similar institutions in the

United States, most notably the Brattleboro Retreat and the Hartford Retreat (now the Institute of Living).

## 19th century

At the turn of the century, England and France combined only had a few hundred individuals in asylums. By the late 1890s and early 1900s, this number skyrocketed to the hundreds of thousands. The United States housed 150,000 patients in mental hospitals by 1904. German speaking countries housed more than 400 public and private sector asylums. These asylums were critical to the evolution of psychiatry as they provided a universal platform of practice throughout the world.

On the continent, universities often played a part in the administration of the asylums. Due to the relationship between the universities and asylums, scores of competitive psychiatrists were being molded in Germany. Germany became known as the world leader in psychiatry during the nineteenth century. The country possessed more than 20 separate universities all competing with each other for scientific advancement. However, because of Germany's individual states and the lack of national regulation of asylums, the country had no organized centralization of asylums or psychiatry. Britain, like Germany, also lacked a centralized organization for the administration of asylums. This deficit hindered the diffusion of new ideas in medicine and psychiatry.

In the United States in 1834 Anna Marsh, a physician's widow, deeded the funds to build her country's first financially-stable private asylum. The Brattleboro Retreat marked the beginning of America's private psychiatric hospitals challenging state institutions for patients, funding, and influence. Although based on England's York Retreat, it would be followed by specialty institutions of every treatment philosophy.

In 1838, France enacted a law to regulate both the admissions into asylums and asylum services across the country. By 1840, asylums as therapeutic institutions existed throughout Europe and the United States.



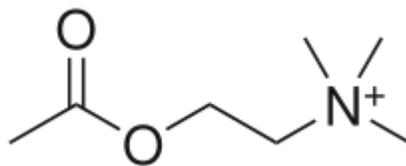
Emil Kraepelin studied and promoted ideas of disease classification for mental disorders

However, the new and dominating ideas that mental illness could be "conquered" during the mid-nineteenth century all came crashing down. Psychiatrists and asylums were being pressured by an ever increasing patient population. The average number of patients in asylums in the United States jumped 927%. Numbers were similar in England and Germany. Overcrowding was rampant in France where asylums would commonly take in double their maximum capacity. Increases in asylum populations may have been a result of the transfer of care from families and poorhouses, but the specific reasons as to why the increase occurred is still debated today. No matter the cause, the pressure on asylums from the increase was taking its toll on the asylums and psychiatry as a specialty. Asylums were once again turning into custodial institutions and the reputation of psychiatry in the medical world had hit an extreme low.

## 20th century

### Disease classification and rebirth of biological psychiatry

The 20th century introduced a new psychiatry into the world. Different perspectives of looking at mental disorders began to be introduced. The career of Emil Kraepelin reflects the convergence of different disciplines in psychiatry. Kraepelin initially was very attracted to psychology and ignored the ideas of anatomical psychiatry. Following his appointment to a professorship of psychiatry and his work in a university psychiatric clinic, Kraepelin's interest in pure psychology began to fade and he introduced a plan for a more comprehensive psychiatry. Kraepelin began to study and promote the ideas of disease classification for mental disorders, an idea introduced by Karl Ludwig Kahlbaum. The initial ideas behind biological psychiatry, stating that the different mental disorders were all biological in nature, evolved into a new concept of "nerves" and psychiatry became a rough approximation of neurology and neuropsychiatry. Following Sigmund Freud's death, ideas stemming from psychoanalytic theory also began to take root. The psychoanalytic theory became popular among psychiatrists because it allowed the patients to be treated in private practices instead of warehoused in asylums. By the 1970s the psychoanalytic school of thought had become marginalized within the field.



Otto Loewi's work led to the identification of the first neurotransmitter, acetylcholine

Biological psychiatry reemerged during this time. Psychopharmacology became an integral part of psychiatry starting with Otto Loewi's discovery of the first neurotransmitter, acetylcholine. Neuroimaging was first utilized as a tool for psychiatry in the 1980s. The discovery of chlorpromazine's effectiveness in treating schizophrenia in 1952 revolutionized treatment of the disease, as did lithium carbonate's ability to stabilize mood highs and lows in bipolar disorder in 1948. Psychotherapy was still utilized, but as a treatment for psychosocial issues. Genetics were once again thought to play a role in

mental illness. Molecular biology opened the door for specific genes contributing to mental disorders to be identified.

### **Anti-psychiatry and deinstitutionalization**

The introduction of psychiatric medications and the use of laboratory tests altered the doctor-patient relationship between psychiatrists and their patients. Psychiatry's shift to the hard sciences had been interpreted as a lack of concern for patients. Anti-psychiatry had become more prevalent in the late twentieth century due to this and publications in the media which conceptualized mental disorders as myths. Others in the movement argued that psychiatry was a form of social control and demanded that institutionalized psychiatric care, stemming from Pinel's therapeutic asylum, be abolished. Incidents of physical abuse by psychiatrists took place during the reign of some totalitarian regimes as part of a system to enforce political control. Some of the abuse even continued to the present day. Historical examples of the abuse of psychiatry took place in Nazi Germany, in the Soviet Union under Psikhushka, and in the apartheid system in South Africa.

Electroconvulsive therapy (ECT) was one treatment that the anti-psychiatry movement wanted eliminated. They alleged that ECT damaged the brain and was used as a tool for discipline. While some believe there is no evidence that ECT damages the brain, there are some citations that ECT does cause damage. Sometimes ECT is used as punishment or as a threat and there have been isolated incidents where the use of ECT was threatened to keep the patients "in line". The prevalence of psychiatric medication helped initiate deinstitutionalization, the process of discharging patients from psychiatric hospitals to the community. The pressure from the anti-psychiatry movements and the ideology of community treatment from the medical arena helped sustain deinstitutionalization. Thirty-three years after deinstitutionalization started in the United States, only 19% of the patients in state hospitals remained. Mental health professionals envisioned a process wherein patients would be discharged into communities where they could participate in a normal life while living in a therapeutic atmosphere. Psychiatrists were criticized, however, for failing to develop community-based support and treatment. Community-based facilities were not available because of the political infighting between in-patient and community-based social services, and an unwillingness by social services to dispense funding to provide adequately for patients to be discharged into community-based facilities.

### **Medicalization of deviance**

According to Kittrie, a number of phenomena considered "deviant", such as alcoholism, drug addiction and mental illness, were originally considered as moral, then legal, and now medical problems. As a result of these perceptions, peculiar deviants were subjected to moral, then legal, and now medical modes of social control. Similarly, Conrad and Schneider concluded their review of the medicalization of deviance by supposing that three major paradigms may be identified that have reigned over deviance designations in different historical periods: deviance as sin; deviance as crime; and deviance as sickness.

## **Transinstitutionalization and the aftermath**

In 1963, US president John F. Kennedy introduced legislation delegating the National Institute of Mental Health to administer Community Mental Health Centers for those being discharged from state psychiatric hospitals. Later, though, the Community Mental Health Center's focus was diverted to provide psychotherapy sessions for those suffering from acute but mild mental disorders. Ultimately there were no arrangements made for actively and severely mentally ill patients who were being discharged from hospitals. Some of those suffering from mental disorders drifted into homelessness or ended up in prisons and jails. Studies found that 33% of the homeless population and 14% of inmates in prisons and jails were already diagnosed with a mental illness.

In 1972, psychologist David Rosenhan published the Rosenhan experiment, a study analyzing the validity of psychiatric diagnoses. The study arranged for eight individuals with no history of psychopathology to attempt admission into psychiatric hospitals. The individuals included a graduate student, psychologists, an artist, a housewife, and two physicians, including one psychiatrist. All eight individuals were admitted with a diagnosis of schizophrenia or bipolar disorder. Psychiatrists then attempted to treat the individuals using psychiatric medication. All eight were discharged within 7 to 52 days. In a later part of the study, psychiatric staff were warned that pseudo-patients might be sent to their institutions, but none were actually sent. Nevertheless, a total of 83 patients out of 193 were believed by at least one staff member to be actors. The study concluded that individuals without mental disorders were indistinguishable from those suffering from mental disorders. Critics such as Robert Spitzer placed doubt on the validity and credibility of the study, but did concede that the consistency of psychiatric diagnoses needed improvement.

Psychiatry, like most medical specialties has a continuing, significant need for research into its diseases, classifications and treatments. Psychiatry adopts biology's fundamental belief that disease and health are different elements of an individual's adaptation to an environment. But psychiatry also recognizes that the environment of the human species is complex and includes physical, cultural, and interpersonal elements. In addition to external factors, the human brain must contain and organize an individual's hopes, fears, desires, fantasies and feelings. Psychiatry's difficult task is to bridge the understanding of these factors so that they can be studied both clinically and physiologically.

## **Theory and focus**

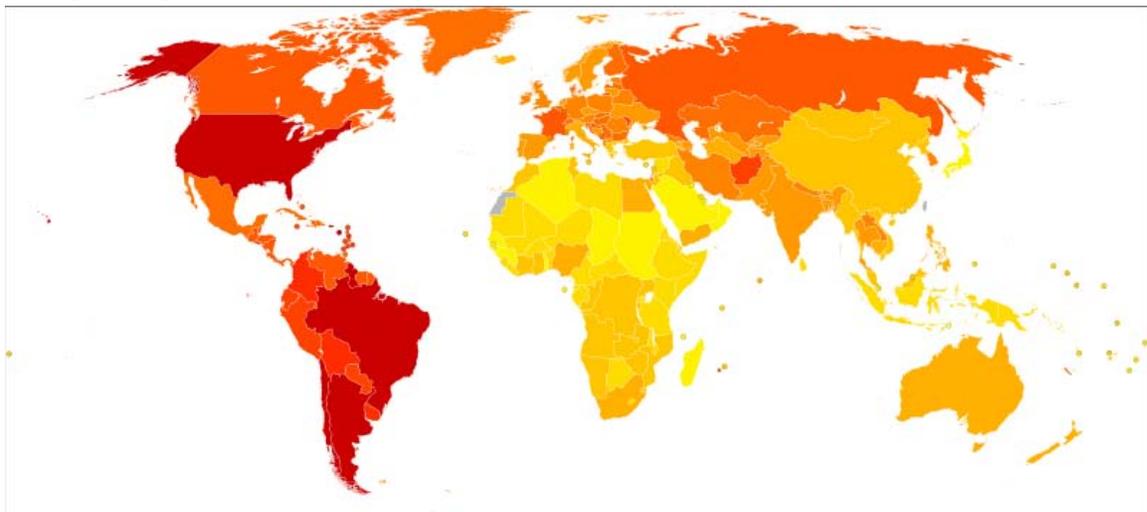
"Psychiatry, more than any other branch of medicine, forces its practitioners to wrestle with the nature of evidence, the validity of introspection, problems in communication, and other long-standing philosophical issues" (Guze, 1992, p.4).

The term psychiatry (Greek "ψυχιατρική", *psychiatrikē*), coined by Johann Christian Reil in 1808, comes from the Greek "ψυχή" (*psychē*: "soul or mind") and "ιατρός" (*iatros*: "healer"). It refers to a field of medicine focused specifically on the mind, aiming to study, prevent, and treat mental disorders in humans. It has been described as an

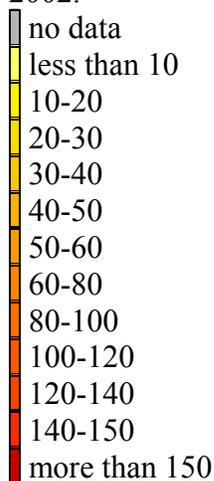
intermediary between the world from a social context and the world from the perspective of those who are mentally ill.

Those who practice psychiatry are different than most other mental health professionals and physicians in that they must be familiar with both the social and biological sciences. The discipline is interested in the operations of different organs and body systems as classified by the patient's subjective experiences and the objective physiology of the patient. Psychiatry exists to treat mental disorders which are conventionally divided into three very general categories: mental illness, severe learning disability, and personality disorder. While the focus of psychiatry has changed little throughout time, the diagnostic and treatment processes have evolved dramatically and continue to do so. Since the late 20th century, the field of psychiatry has continued to become more biological and less conceptually isolated from the field of medicine.

### Scope of practice



Disability-adjusted life year for neuropsychiatric conditions per 100,000 inhabitants in 2002.



While the medical specialty of psychiatry utilizes research in the field of neuroscience, psychology, medicine, biology, biochemistry, and pharmacology, it has generally been considered a middle ground between neurology and psychology. Unlike other physicians and neurologists, psychiatrists specialize in the doctor-patient relationship and are trained to varying extents in the use of psychotherapy and other therapeutic communication techniques. Psychiatrists also differ from psychologists in that they are physicians and the entirety of their post-graduate training is revolved around the field of medicine. Psychiatrists can therefore counsel patients, prescribe medication, order laboratory tests, order neuroimaging, and conduct physical examinations.

## **Ethics**

Like other professions, the World Psychiatric Association issues an ethical code to govern the conduct of psychiatrists. The psychiatric code of ethics, first set forth through the Declaration of Hawaii in 1977, has been expanded through a 1983 Vienna update and, in 1996, the broader Madrid Declaration. The code was further revised in Hamburg, 1999. The World Psychiatric Association code covers such matters as patient assessment, up-to-date knowledge, the human dignity of incapacitated patients, confidentiality, research ethics, sex selection, euthanasia, organ transplantation, torture, the death penalty, media relations, genetics, and ethnic or cultural discrimination. In establishing such ethical codes, the profession has responded to a number of controversies about the practice of psychiatry.

## **Subspecialties**

Various subspecialties and/or theoretical approaches exist which are related to the field of psychiatry. They include the following:

- Addiction psychiatry; focuses on evaluation and treatment of individuals with alcohol, drug, or other substance-related disorders, and of individuals with dual diagnosis of substance-related and other psychiatric disorders.
- Biological psychiatry; an approach to psychiatry that aims to understand mental disorders in terms of the biological function of the nervous system.
- Child and adolescent psychiatry; a branch of psychiatry that specialises in work with children, teenagers, and their families.
- Community psychiatry; an approach that reflects an inclusive public health perspective and is practiced in community mental health services.
- Cross-cultural psychiatry; a branch of psychiatry concerned with the cultural and ethnic context of mental disorder and psychiatric services.
- Eating disorders; focuses on anorexia nervosa, bulimia nervosa, binge eating disorder, eating disorders not otherwise specified (EDNOS) and certain feeding disorders such as pica (disorder).
- Emergency psychiatry; the clinical application of psychiatry in emergency settings.
- Forensic psychiatry; the interface between law and psychiatry.

- Geriatric psychiatry; a branch of psychiatry dealing with the study, prevention, and treatment of mental disorders in humans with old age.
- Global Mental Health; the area of study, research and practice that places a priority on improving mental health and achieving equity in mental health for all people worldwide.
- Liaison psychiatry; the branch of psychiatry that specializes in the interface between other medical specialties and psychiatry.
- Military psychiatry; covers special aspects of psychiatry and mental disorders within the military context.
- Neuropsychiatry; branch of medicine dealing with mental disorders attributable to diseases of the nervous system.
- Social psychiatry; a branch of psychiatry that focuses on the interpersonal and cultural context of mental disorder and mental wellbeing.

In the United States, psychiatry is one of the specialties which qualify for further education and board-certification in pain medicine, palliative medicine, and sleep medicine.

## **Approaches**

Psychiatric illnesses can be approached in a number of different ways. The biomedical approach examines signs and symptoms and compares them with diagnostic criteria. Psychiatric illness can also be assessed through a narrative which tries to understand symptoms as a part of a meaningful life history and as a responses to external conditions. Both approaches are important in the field of psychiatry. A lack of consensus between these often opposing views has contributed in part to the biopsychiatry controversy. It has also played a role in controversies over specific psychiatric illness, such as ADHD and multiple personalities. The biopsychosocial model is often used to understand psychiatric illness. However, the "model's" scientific credentials have been called into question in Dr. Niall McLaren's 1998 paper, *A critical review of the Biopsychosocial Model* and his books *Humanizing Madness* and *Humanizing Psychiatry*. Even though it is correct to say that sociology, psychology, and biology are factors in mental illness, simply stating this obvious fact does not make it a model in the scientific sense of the word. Scientific models are meant to be the actualization of a scientific theory and the biopsychosocial model actualizes nothing apart from reiterating a concept which "all practitioners of reasonable sensitivity" should know implicitly (that social and psychological factors matter).

## **Industry and academia**

### **Practitioners**

All physicians can diagnose mental disorders and prescribe treatments utilizing principles of psychiatry. Psychiatrists are either: 1) clinicians who specialize in psychiatry and are certified in treating mental illness; or (2) scientists in the academic field of psychiatry and are qualified as research doctors in this field. Psychiatrists may also go through

significant training to conduct psychotherapy, psychoanalysis and cognitive behavioral therapy, but it is their training as physicians that differentiates them from other mental health professionals.

## Research

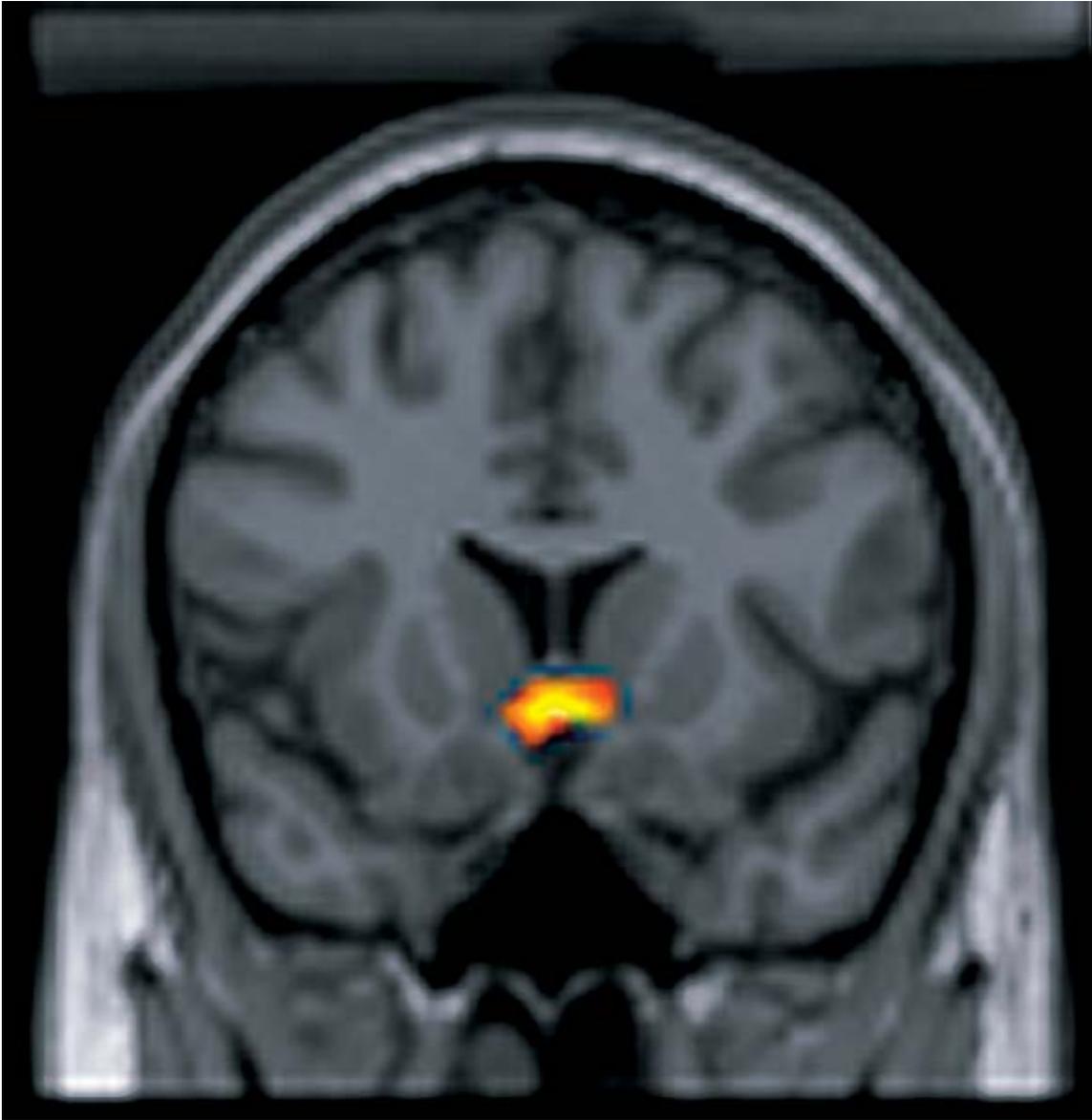


An MRI scan of the brain: many mental disorders are thought to be associated with neurobiological abnormalities

Psychiatric research is, by its very nature, interdisciplinary. It combines social, biological and psychological perspectives to understand the nature and treatment of mental disorders. Clinical and research psychiatrists study basic and clinical psychiatric topics at research institutions and publish articles in journals. Under the supervision of institutional review boards, psychiatric clinical researchers look at topics such as neuroimaging, genetics, and psychopharmacology in order to enhance diagnostic validity and reliability, to discover new treatment methods, and to classify new mental disorders.

## Clinical application

### Diagnostic systems



fMRI images such as these may assist in a diagnosis by ruling out other conditions

Psychiatric diagnoses take place in a wide variety of settings and are performed by many different health professionals. Therefore, the diagnostic procedure may vary greatly based upon these factors. Typically, though, a psychiatric diagnosis utilizes a differential diagnosis procedure where a mental status examination and physical examination is conducted, pathological, psychopathological or psychosocial histories obtained, and sometimes neuroimages or other neurophysiological measurements are taken, or personality tests or cognitive tests administered. In some cases, a brain scan might be

used to rule out other medical illnesses, but at this time relying on brain scans alone cannot accurately diagnose a mental illness or tell the risk of getting a mental illness in the future. A few psychiatrists are beginning to utilize genetics during the diagnostic process but on the whole this remains a research topic.

### **Diagnostic manuals**

Three main diagnostic manuals used to classify mental health conditions are in use today. The ICD-10 is produced and published by the World Health Organisation, includes a section on psychiatric conditions, and is used worldwide. The Diagnostic and Statistical Manual of Mental Disorders, produced and published by the American Psychiatric Association, is primarily focused on mental health conditions and is the main classification tool in the United States. It is currently in its fourth revised edition and is also used worldwide. The Chinese Society of Psychiatry has also produced a diagnostic manual, the Chinese Classification of Mental Disorders.

The stated intention of diagnostic manuals is typically to develop replicable and clinically useful categories and criteria, to facilitate consensus and agreed upon standards, whilst being atheoretical as regards etiology. However, the categories are nevertheless based on particular psychiatric theories and data; they are broad and often specified by numerous possible combinations of symptoms, and many of the categories overlap in symptomology or typically occur together. While originally intended only as a guide for experienced clinicians trained in its use, the nomenclature is now widely used by clinicians, administrators and insurance companies in many countries.

### **Treatment settings**

#### **General considerations**

Individuals with mental health conditions are commonly referred to as *patients* but may also be called *clients*, *consumers*, or *service recipients*. They may come under the care of a psychiatric physician or other psychiatric practitioners by various paths, the two most common being self-referral or referral by a primary-care physician. Alternatively, a person may be referred by hospital medical staff, by court order, involuntary commitment, or, in the UK and Australia, by sectioning under a mental health law.



A psychiatric patient room in the United States

Whatever the circumstance of a person's referral, a psychiatrist first assesses the person's mental and physical condition. This usually involves interviewing the person and often obtaining information from other sources such as other health and social care professionals, relatives, associates, law enforcement and emergency medical personnel and psychiatric rating scales. A mental status examination is carried out, and a physical examination is usually performed to establish or exclude other illnesses, such as thyroid dysfunction or brain tumors, or identify any signs of self-harm; this examination may be done by someone other than the psychiatrist, especially if blood tests and medical imaging are performed.

Like all medications, psychiatric medications can cause adverse effects in patients and hence often involve ongoing therapeutic drug monitoring, for instance full blood counts or, for patients taking lithium salts, serum levels of lithium, renal and thyroid function. Electroconvulsive therapy (ECT) is sometimes administered for serious and disabling conditions, especially those unresponsive to medication. The efficacy and adverse effects of psychiatric drugs have been challenged.

The close relationship between those prescribing psychiatric medication and pharmaceutical companies has become increasingly controversial along with the influence which pharmaceutical companies are exerting on mental health policies.

Also controversial are forced drugging and the "lack of insight" label. According to a report published by the US National Council on Disability,

Involuntary treatment is extremely rare outside the psychiatric system, allowable only in such cases as unconsciousness or the inability to communicate. People with psychiatric disabilities, on the other hand, even when they vigorously protest treatments they do not want, are routinely subjected to them anyway, on the justification that they "lack insight" or are unable to recognize their need for treatment because of their "mental illness". In practice, "lack of insight" becomes disagreement with the treating professional, and people who disagree are labeled "noncompliant" or "uncooperative with treatment".

### **Inpatient treatment**

Psychiatric treatments have changed over the past several decades. In the past, psychiatric patients were often hospitalized for six months or more, with some cases involving hospitalization for many years. Today, people receiving psychiatric treatment are more likely to be seen as outpatients. If hospitalization is required, the average hospital stay is around one to two weeks, with only a small number receiving long-term hospitalization.

Psychiatric inpatients are people admitted to a hospital or clinic to receive psychiatric care. Some are admitted involuntarily, perhaps committed to a secure hospital, or in some jurisdictions to a facility within the prison system. In many countries including the USA and Canada, the criteria for involuntary admission vary with local jurisdiction. They may be as broad as having a mental health condition, or as narrow as being an immediate danger to themselves and/or others. Bed availability is often the real determinant of admission decisions to hard pressed public facilities. European Human Rights legislation restricts detention to medically-certified cases of mental disorder, and adds a right to timely judicial review of detention.



Injections are one of many ways to administer psychiatric medication

Patients may be admitted voluntarily if the treating doctor considers that safety isn't compromised by this less restrictive option. Inpatient psychiatric wards may be secure (for those thought to have a particular risk of violence or self-harm) or unlocked/open. Some wards are mixed-sex whilst same-sex wards are increasingly favored to protect women inpatients. Once in the care of a hospital, people are assessed, monitored, and often given medication and care from a multidisciplinary team, which may include physicians, psychiatric nurse practitioners, psychiatric nurses, clinical psychologists, psychotherapists, psychiatric social workers, occupational therapists and social workers. If a person receiving treatment in a psychiatric hospital is assessed as at particular risk of harming themselves or others, they may be put on constant or intermittent one-to-one supervision, and may be physically restrained or medicated. People on inpatient wards may be allowed leave for periods of time, either accompanied or on their own.

In many developed countries there has been a massive reduction in psychiatric beds since the mid 20th century, with the growth of community care. Standards of inpatient care remain a challenge in some public and private facilities, due to levels of funding, and facilities in developing countries are typically grossly inadequate for the same reason.

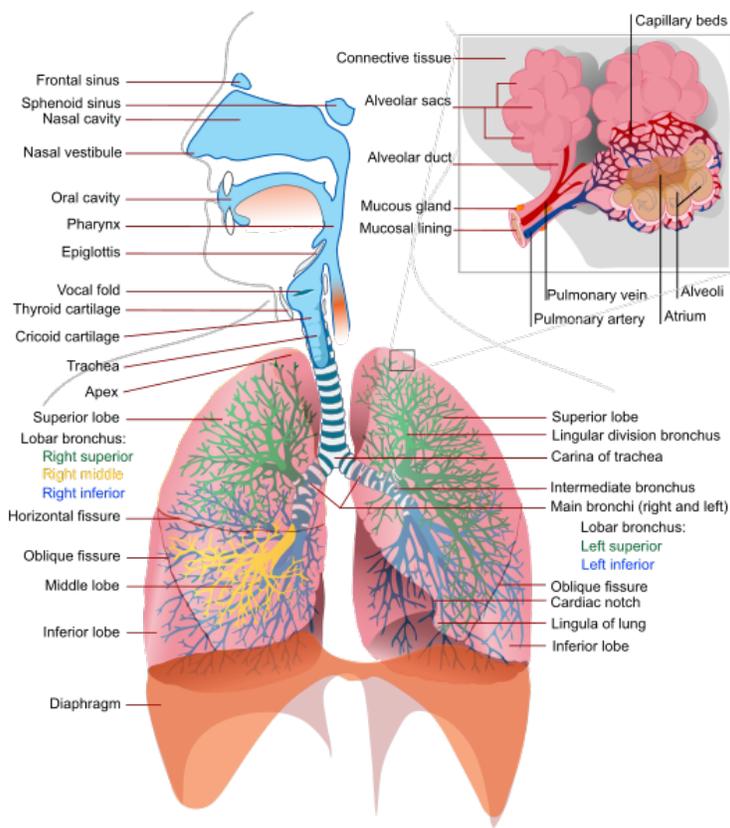
## **Outpatient treatment**

People may receive psychiatric care on an inpatient or outpatient basis. Outpatient treatment involves periodic visits to a clinician for consultation in his or her office, usually for an appointment lasting thirty to sixty minutes. These consultations normally involve the psychiatric practitioner interviewing the person to update their assessment of the person's condition, and to provide psychotherapy or review medication. The frequency with which a psychiatric practitioner sees people in treatment varies widely, from days to months, depending on the type, severity and stability of each person's condition, and depending on what the clinician and client decide would be best. Increasingly, psychiatrists are limiting their practices to psychopharmacology (prescribing medications) with less time devoted to psychotherapy or "talk" therapies, or behavior modification. The role of psychiatrists is changing in community psychiatry, with many assuming more leadership roles, coordinating and supervising teams of allied health professionals and junior doctors in delivery of health services.

# Chapter 14

# Pulmonology

## Pulmonologist



A complete view of the respiratory system.

### Occupation

**Names** Doctor, Medical Specialist

**Type** Specialty

**Activity sectors** Medicine

### Description

**Education required** Doctor of Medicine

**Fields of employment**      Hospitals, Clinics

In medicine, **pulmonology** (aka **pneumology**) is the specialty that deals with diseases of the respiratory tract and respiratory disease. It is called **chest medicine** and **respiratory medicine** in some countries and areas. *Pulmonology* is generally considered a branch of internal medicine, although it is closely related to intensive care medicine (aka critical care medicine) when dealing with patients requiring mechanical ventilation. **Chest medicine** is not a specialty in itself but is an inclusive term which pertains to the treatment of diseases of the chest and contains the fields of pulmonology, thoracic surgery, and intensive care medicine. Pulmonology is concerned with the diagnosis and treatment of lung diseases, as well as secondary prevention (tuberculosis). Physicians specializing in this area are called pulmonologists. In the United Kingdom, Ireland, South Africa and Australia the term "respiratory physician" is used rather than pulmonologist. In Canada, respirology and respirologist are used. Surgery of the respiratory tract is generally performed by specialists in cardiothoracic surgery (or thoracic surgery), though minor procedures may be performed by pulmonologists. As mentioned above, pulmonology is closely related to critical care medicine when dealing with patients that require mechanical ventilation. As a result, many pulmonologists are certified to practice critical care medicine in addition to pulmonary medicine. There are fellowship programs that allow physicians to become board certified in pulmonary and critical care medicine simultaneously. Interventional pulmonology is a relatively new field within pulmonary medicine that deals with the use of procedures such as bronchoscopy to treat several pulmonary diseases. Interventional pulmonology is not its own specialty.

### ***History of pulmonology***

One of the first major discoveries pertaining to pulmonology was the discovery of pulmonary circulation. Originally, it was thought that blood reaching the right side of the heart passed through small 'pores' the septum into the left side to be oxygenated, as theorized by Galen; however, the discovery of pulmonary circulation disproves this theory, which had previously been accepted since the second century. Thirteenth century anatomist and physiologist Ibn Al-Nafis accurately theorized that there was no 'direct' passage between the two sides (ventricles) of the heart. He believed that the blood must have passed through the pulmonary artery, through the lungs, and back into the heart to be pumped around the body. This is believed by many to be the first scientific description of pulmonary circulation.

Although pulmonary medicine only began to evolve as a medical specialty in the 1950's, William Welch and William Osler founded the 'parent' organization of the American Thoracic Society, the National Association for the Study and Prevention of Tuberculosis. When the specialty did begin to evolve, several discoveries were being made linking the respiratory system and the measurement of arterial blood gases, attracting more and more physicians and researchers to the developing field.

## ***Diagnosis***

The pulmonologist begins the diagnostic process with a general review focusing on:

- hereditary diseases affecting the lungs (cystic fibrosis, alpha 1-antitrypsin deficiency)
- exposure to toxins (tobacco smoke, asbestos, exhaust fumes, coal mining fumes)
- exposure to infectious agents (certain types of birds, malt processing)
- an autoimmune diathesis that might predispose to certain conditions (pulmonary fibrosis, pulmonary hypertension)

Physical diagnostics are as important as in the other fields of medicine.

- Inspection of the hands for signs of cyanosis or clubbing, chest wall, and respiratory rate.
- Palpation of the cervical lymph nodes, trachea and chest wall movement.
- Percussion of the lung fields for dullness or hyperresonance.
- Auscultation (with a stethoscope) of the lung fields for diminished or unusual breath sounds.
  - Rales or Rhonchi heard over lung fields with a stethoscope.

As many heart diseases can give pulmonary signs, a thorough cardiac investigation is usually included.

Other tools include:

- Laboratory investigation of blood (blood tests). Sometimes arterial blood gas measurements are also required.
- Spirometry (the determination of lung volumes in time by breathing into a dedicated machine; response to bronchodilators and diffusion of carbon monoxide)
- Bronchoscopy with bronchoalveolar lavage (BAL), endobronchial and transbronchial biopsy and epithelial brushing
- Chest X-rays
- CT scanning (MRI scanning is rarely used)
- Scintigraphy and other methods of nuclear medicine
- Positron emission tomography (especially in lung cancer)
- Polysomnography (sleep studies) commonly used for the diagnosis of Sleep apnea

## ***Treatment***

Surgical treatment is generally performed by the (cardio)thoracic surgeon, generally after primary evaluation by a pulmonologist. Medication is the most important treatment of most diseases of pulmonology, either by inhalation (bronchodilators and steroids) or in oral form (antibiotics, leukotriene antagonists). A common example being the usage of inhalers in the treatment of inflammatory lung conditions such as Asthma or Chronic

obstructive pulmonary disease. Oxygen therapy is often necessary in severe respiratory disease (emphysema and pulmonary fibrosis). When this is insufficient, the patient might require mechanical ventilation.

Pulmonary rehabilitation or respiratory therapy may be initiated as a treatment after all or most other treatments do little to help the patient. Pulmonary rehabilitation is for patients whose respiratory function has decreased or improved very little, even with extensive medical treatment. Pulmonary rehabilitation is intended to educate the patient, the family, and improve the overall quality of life and prognosis for the patient. Although a pulmonologist may refer a patient to therapy, the therapy is generally practiced by respiratory therapists.

### ***Pulmonology as a career***

In the United States, pulmonologists are physicians who, after receiving a medical degree (MD or DO), complete residency training in internal medicine (3 years), followed by at least 2 additional years of subspecialty fellowship training in pulmonology. After satisfactorily completing a fellowship in pulmonary medicine, he or she is permitted to take the board certification examination in pulmonary medicine. After passing this exam, he or she is now board certified. Most pulmonologists complete 3 years of combined subspecialty fellowship training in pulmonary medicine and critical care medicine.

In the United States, pediatric pulmonologists are physicians who, after receiving a medical degree (MD or DO), complete residency training in pediatrics (3 years), followed by at least 3 additional years of subspecialty fellowship training in pulmonology.

Usually, respiratory problems can be managed by a specialist in internal medicine; however, some cases require the attention of a pulmonologist. Usually, a pulmonologist will be required in advanced cases of many respiratory diseases.

### ***Scientific research***

Pulmonologists are involved in both clinical and basic research of the respiratory system, ranging from the anatomy of the respiratory epithelium to the most effective treatment of pulmonary hypertension (a disease notoriously resistant to therapy). Scientific research also takes place to look for causes and possible treatment in diseases such as pulmonary tuberculosis and lung cancer. Several societies are dedicated to expanding the field of pulmonary medicine, some of which are listed below:

- American College of Chest Physicians
- American Lung Association
- American Thoracic Society
- British Thoracic Society

## Chapter 15

# Radiology



A radiologist interprets medical images on a modern Picture archiving and communication system (PACS) workstation. San Diego, CA, 2010.

**Radiology** is medical specialty that employs the use of imaging to both diagnose and treat disease visualized within the human body. Radiologists utilize an array of imaging technologies (such as x-ray radiography, ultrasound, computed tomography (CT), nuclear medicine, positron emission tomography (PET) and magnetic resonance imaging (MRI)) to diagnose or treat diseases. Interventional radiology is the performance of (usually minimally invasive) medical procedures with the guidance of imaging technologies. The acquisition of medical imaging is usually carried out by the radiographer or radiologic technologist.

## ***Acquisition of radiological images***

The following imaging modalities are used in the field of diagnostic radiology:

### **Projection (plain) radiography**



Madura Foot X-Ray

Radiographs (or roentgenographs, named after the discoverer of x-rays, Wilhelm Conrad Röntgen) are produced by the transmission of x-rays through a patient to a capture device then converted into an image for diagnosis. The original and still common imaging produces silver impregnated films. In Film-Screen radiography an x-ray tube generates a beam of x-rays which is aimed at the patient. The x-rays which pass through the patient are filtered to reduce scatter and noise and then strike an undeveloped film, held tight to a screen of light emitting phosphors in a light-tight cassette. The film is then developed chemically and an image appears on the film. Now replacing Film-Screen radiography is Digital Radiography, DR, in which x-rays strike a plate of sensors which then converts the signals generated into digital information and an image on computer screen. Plain radiography was the only imaging modality available during the first 50 years of radiology. Due to its availability and lower costs compared to other modalities, radiography is often the first-line test of choice in radiologic diagnosis.

## Fluoroscopy

Fluoroscopy and angiography are special applications of X-ray imaging, in which a fluorescent screen and image intensifier tube is connected to a closed-circuit television system. This allows real-time imaging of structures in motion or augmented with a radiocontrast agent. Radiocontrast agents are administered, often swallowed or injected into the body of the patient, to delineate anatomy and functioning of the blood vessels, the genitourinary system or the gastrointestinal tract. Two radiocontrasts are presently in use. Barium (as BaSO<sub>4</sub>) may be given orally or rectally for evaluation of the GI tract. Iodine, in multiple proprietary forms, may be given by oral, rectal, intraarterial or intravenous routes. These radiocontrast agents strongly absorb or scatter X-ray radiation, and in conjunction with the real-time imaging allows demonstration of dynamic processes, such as peristalsis in the digestive tract or blood flow in arteries and veins. Iodine contrast may also be concentrated in abnormal areas more or less than in normal tissues and make abnormalities (tumors, cysts, inflammation) more conspicuous. Additionally, in specific circumstances air can be used as a contrast agent for the gastrointestinal system and carbon dioxide can be used as a contrast agent in the venous system; in these cases, the contrast agent attenuates the X-ray radiation less than the surrounding tissues.

## Interventional radiology

**Interventional radiology** (abbreviated **IR** or sometimes **VIR** for **vascular and interventional radiology**) is a subspecialty of radiology in which minimally invasive procedures are performed using **image guidance**. Some of these procedures are done for purely diagnostic purposes (e.g., angiogram), while others are done for treatment purposes (e.g., angioplasty).

The basic concept behind interventional radiology is to diagnose or treat pathology, with the most minimally invasive technique possible. Interventional radiologists diagnose and treat several disorders including peripheral vascular disease, renal artery stenosis, inferior vena cava filter placement, gastrostomy tube placements, biliary stents and hepatic interventions. Images are used for guidance and the primary instruments used during the procedure are needles and tiny tubes called catheters. The images provide road maps that allow the interventional radiologist to guide these instruments through the body to the areas containing disease. By minimizing the physical trauma to the patient, peripheral interventions can reduce infection rates and recovery time as well as shorten hospital stays. To be a trained interventionalist in the United States, an individual completes a five year residency in Radiology and a two year fellowship in Interventional Radiology.

## Computed Tomography (CT)



Image from a CT scan of the brain

CT imaging uses X-rays in conjunction with computing algorithms to image the body. In CT, an X-ray generating tube opposite an X-ray detector (or detectors) in a ring shaped apparatus rotate around a patient producing a computer generated cross-sectional image (tomogram). CT is acquired in the axial plane, while coronal and sagittal images can be rendered by computer reconstruction. Radiocontrast agents are often used with CT for enhanced delineation of anatomy. Although radiographs provide higher spatial resolution, CT can detect more subtle variations in attenuation of X-rays. CT exposes the patient to more ionizing radiation than a radiograph.

Spiral Multi-detector CT utilizes 8, 16, 64 or more detectors during continuous motion of the patient through the radiation beam to obtain much finer detail images in a shorter exam time. With rapid administration of IV contrast during the CT scan these fine detail

images can be reconstructed into 3D images of carotid, cerebral and coronary arteries, CTA, CT angiography.

CT scanning has become the test of choice in diagnosing some urgent and emergent conditions such as cerebral hemorrhage, pulmonary embolism (clots in the arteries of the lungs), aortic dissection (tearing of the aortic wall), appendicitis, diverticulitis, and obstructing kidney stones. Continuing improvements in CT technology including faster scanning times and improved resolution have dramatically increased the accuracy and usefulness of CT scanning which may partially account for increased utilization in medical diagnosis.

The first commercially viable CT scanner was invented by Sir Godfrey Hounsfield at EMI Central Research Labs, Great Britain in 1972. EMI owned the distribution rights to The Beatles music and it was their profits which funded the research. Sir Hounsfield and Alan McLeod McCormick shared the Nobel Prize for Medicine in 1979 for the invention of CT scanning. The first CT scanner in North America was installed at the Mayo Clinic in Rochester, MN in 1972.

## **Ultrasound**

Medical ultrasonography uses ultrasound (high-frequency sound waves) to visualize soft tissue structures in the body in real time. No ionizing radiation is involved, but the quality of the images obtained using ultrasound is highly dependent on the skill of the person (ultrasonographer) performing the exam. Ultrasound is also limited by its inability to image through air (lungs, bowel loops) or bone. The use of ultrasound in medical imaging has developed mostly within the last 30 years. The first ultrasound images were static and two dimensional (2D), but with modern-day ultrasonography 3D reconstructions can be observed in real-time; effectively becoming 4D.

Because ultrasound does not utilize ionizing radiation, unlike radiography, CT scans, and nuclear medicine imaging techniques, it is generally considered safer. For this reason, this modality plays a vital role in obstetrical imaging. Fetal anatomic development can be thoroughly evaluated allowing early diagnosis of many fetal anomalies. Growth can be assessed over time, important in patients with chronic disease or gestation-induced disease, and in multiple gestations (twins, triplets etc.). Color-Flow Doppler Ultrasound measures the severity of peripheral vascular disease and is used by Cardiology for dynamic evaluation of the heart, heart valves and major vessels. Stenosis of the carotid arteries can presage cerebral infarcts (strokes). DVT in the legs can be found via ultrasound before it dislodges and travels to the lungs (pulmonary embolism), which can be fatal if left untreated. Ultrasound is useful for image-guided interventions like biopsies and drainages such as thoracentesis). Small portable ultrasound devices now replace peritoneal lavage in the triage of trauma victims by directly assessing for the presence of hemorrhage in the peritoneum and the integrity of the major viscera including the liver, spleen and kidneys. Extensive hemoperitoneum (bleeding inside the body cavity) or injury to the major organs may require emergent surgical exploration and repair.

## MRI (Magnetic Resonance Imaging)

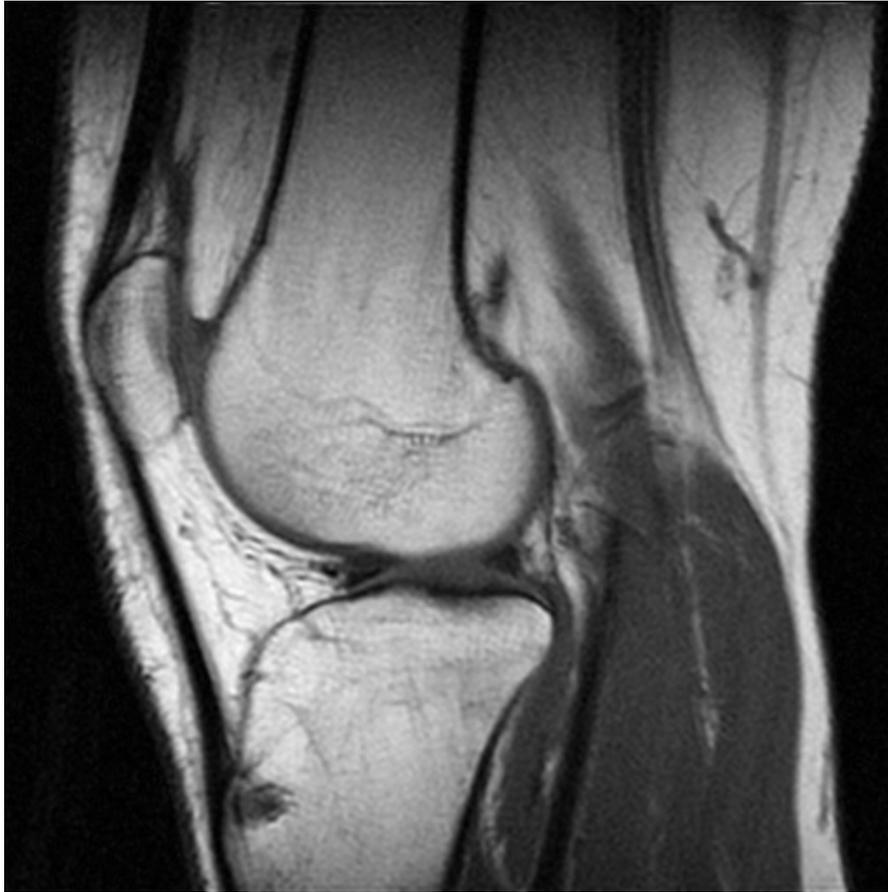


Image from an MRI examination of the knee with a displaced patella

MRI uses strong magnetic fields to align atomic nuclei (usually hydrogen protons) within body tissues, then uses a radio signal to disturb the axis of rotation of these nuclei and observes the radio frequency signal generated as the nuclei return to their baseline states. The radio signals are collected by small antennae, called coils, placed near the area of interest. An advantage of MRI is its ability to produce images in axial, coronal, sagittal and multiple oblique planes with equal ease. MRI scans give the best soft tissue contrast of all the imaging modalities. With advances in scanning speed and spatial resolution, and improvements in computer 3D algorithms and hardware, MRI has become an important tool in musculoskeletal radiology and neuroradiology.

One disadvantage is that the patient has to hold still for long periods of time in a noisy, cramped space while the imaging is performed. Claustrophobia severe enough to terminate the MRI exam is reported in up to 5% of patients. Recent improvements in magnet design including stronger magnetic fields (3 teslas), shortening exam times, wider, shorter magnet bores and more open magnet designs, have brought some relief for claustrophobic patients. However, in magnets of equal field strength there is often a trade-off between image quality and open design. MRI has great benefit in imaging the brain, spine, and musculoskeletal system. The modality is currently contraindicated for

patients with pacemakers, cochlear implants, some indwelling medication pumps, certain types of cerebral aneurysm clips, metal fragments in the eyes and some metallic hardware due to the powerful magnetic fields and strong fluctuating radio signals the body is exposed to. Areas of potential advancement include functional imaging, cardiovascular MRI, as well as MR image guided therapy.

## **Nuclear Medicine**

Nuclear medicine imaging involves the administration into the patient of radiopharmaceuticals consisting of substances with affinity for certain body tissues labeled with radioactive tracer. The most commonly used tracers are Technetium-99m, Iodine-123, Iodine-131, Gallium-67 and Thallium-201 and 18F-FDG. The heart, lungs, thyroid, liver, gallbladder, and bones are commonly evaluated for particular conditions using these techniques. While anatomical detail is limited in these studies, nuclear medicine is useful in displaying physiological function. The excretory function of the kidneys, iodine concentrating ability of the thyroid, blood flow to heart muscle, etc. can be measured. The principal imaging device is the gamma camera which detects the radiation emitted by the tracer in the body and displays it as an image. With computer processing, the information can be displayed as axial, coronal and sagittal images (SPECT images, single-photon emission computed tomography). In the most modern devices Nuclear Medicine images can be fused with a CT scan taken quasi-simultaneously so that the physiological information can be overlaid or co-registered with the anatomical structures to improve diagnostic accuracy.

Positron emission tomography (PET), scanning is a nuclear medicine procedure that deals with positrons. The positrons annihilate to produce two opposite traveling gamma rays to be detected coincidentally, thus improving resolution. In PET scanning, a radioactive, biologically active substance, most often Fludeoxyglucose (18F), is injected into a patient and the radiation emitted by the patient is detected to produce multi-planar images of the body. Metabolically more active tissues, such as cancer, concentrate the active substance more than normal tissues. PET images can be combined (or "fused") with an anatomic imaging study (currently generally CT images), to more accurately localize PET findings and thereby improve diagnostic accuracy.

The fusion technology has gone further to combine PET and MRI similar to PET and CT. PET/MRI fusion, largely practiced in academic and research settings, could potentially play a crucial role in fine detail of brain imaging, breast cancer screening and small joint imaging of foot. The technology recently blossomed following passing a technical hurdle of altered positron movement in strong magnetic field thus affecting the resolution of PET images and attenuation correction.

## **Teleradiology**

Teleradiology is the transmission of radiographic images from one location to another for interpretation by a radiologist. It is most often used to allow rapid interpretation of emergency room, ICU and other emergent examinations after hours of usual operation, at

night and on weekends. In these cases the images are often sent across time zones (i.e. to Spain, Australia, India) with the receiving radiologist working his normal daylight hours. Teleradiology can also be utilized to obtain consultation with an expert or sub-specialist about a complicated or puzzling case.

Teleradiology requires a sending station, high speed Internet connection and high quality receiving station. At the transmission station, plain radiographs are passed through a digitizing machine before transmission, while CT scans, MRIs, Ultrasounds and Nuclear Medicine scans can be sent directly as they are already a stream of digital data. The computer at the receiving end will need to have a high-quality display screen that has been tested and cleared for clinical purposes. Reports are then transmitted to the requesting physician.

The major advantage of teleradiology is the ability to utilize different time zones to provide real-time emergency radiology services around-the-clock. The disadvantages include higher costs, limited contact between the ordering physician and the radiologist, and the inability to cover for procedures requiring an onsite radiologist. Laws and regulations concerning the use of teleradiology vary among the states, with some states requiring a license to practice medicine in the state sending the radiologic exam. Some states require the teleradiology report to be preliminary with the official report issued by a hospital staff radiologist.

## ***Radiologist training***

### **United States**

Radiology is an expanding field in medicine. Applying for residency positions in radiology has become increasingly competitive. Applicants are often near the top of their medical school class, with high USMLE (board) scores. The field is rapidly expanding due to advances in computer technology, which is closely linked to modern imaging. Diagnostic radiologists must complete prerequisite undergraduate education, 4 years of medical school, one year of internship, and 4 years of residency training. After residency, radiologists often pursue one or two years of additional specialty fellowship training.

The radiology resident must pass a medical physics board exam during training covering the science, technology and radiobiology of ultrasound, CTs, x-rays, nuclear medicine and MRI. Near the completion of residency, the radiologist in training may be deemed eligible to "sit for the Boards", take the written and oral board examinations administered by the American Board of Radiology (ABR). Certification may also be obtained from the American Osteopathic Board of Radiology (AOBR) and the American Board of Physician Specialties (ABPS). Starting in 2010, the ABR's oral board examination structure will be changed to include two computer-based exams, one given after the third year of residency training, and the second given 18 months after the first oral exam. To complete the oral section of the ABR certification, a radiologist must pass each of the eleven sections. An applicant who passes fewer than eight sections has failed and must re-take the entire exam. An applicant who passes at least eight of the eleven sections of

the ABR oral boards is considered "conditioned" and can retake the last three or fewer sections again at a later date to become ABR certified. Once successful in passing all sections, the physician then becomes a diplomate of the American Board of Radiology.

Following completion of residency training, radiologists may either begin practicing or enter into sub-specialty training programs known as fellowships. Examples of sub-specialty training in radiology include abdominal imaging, thoracic imaging, cross sectional/ultrasound, MRI, musculoskeletal imaging, interventional radiology, neuroradiology, interventional neuroradiology, paediatric radiology, nuclear medicine, emergency radiology, breast imaging and women's imaging. Fellowship training programs in radiology are usually 1 or 2 years in length.

Radiographic exams are usually performed by radiologic technologists, (also known as diagnostic radiographers) who in the United States have a 2-year Associates Degree or 4 year Bachelors of Science Degree and, in the UK, a 3 year Honours Degree.

Veterinary radiologists are veterinarians that specialize in the use of X-rays, ultrasound, MRI and nuclear medicine for diagnostic imaging or treatment of disease in animals. They are certified in either diagnostic radiology or radiation oncology by the American College of Veterinary Radiology.

## **Germany**

After obtaining medical licensure, German radiologists complete a 5-year residency, culminating with a board examination (known as Facharztprüfung).

## **Italy**

Until 2008, a Radiology training program had a duration of four years. At present, a radiology training program lasts five years. Further training is required for specialization in radiotherapy or nuclear medicine.

## Chapter 16

# Rheumatology

### Rheumatologist

#### Occupation

<b>Names</b>	Doctor, Medical Specialist
<b>Type</b>	Specialty
<b>Activity sectors</b>	Medicine

#### Description

<b>Education required</b>	Doctor of Medicine or Doctor of Osteopathy
<b>Fields of employment</b>	Hospitals, Clinics

**Rheumatology** is a sub-specialty in internal medicine and pediatrics, devoted to the diagnosis and therapy of conditions and diseases affecting the joints, muscles, and bones. Clinicians who specialize in rheumatology are called **rheumatologists**. Rheumatologists deal mainly with clinical problems involving joints, soft tissues, certain autoimmune diseases, and the allied conditions of connective tissues. Essentially, they medically treat diseases, disorders, etc., that affect the musculoskeletal system. This includes many autoimmune diseases, as these conditions often cause rheumatic issues.

The term *rheumatology* originates from the Greek word *rheuma*, meaning "that which flows as a river or stream," and the suffix *-ology*, meaning "the study of."

Rheumatology is a rapidly evolving medical specialty, with advancements owing largely to new scientific discoveries about the immunology of these disorders. Because the characteristics of some rheumatological disorders are often best explained by immunology, the pathogenesis of many major rheumatological disorders are now described in terms of the autoimmune system, viz., as an autoimmune disease. Correspondingly, most new treatment modalities are also based on clinical research in immunology and the resulting improved understanding of the genetic bases of rheumatological disorders. Future treatment may include gene therapy, as well. Evidence-

based medical treatment of rheumatological disorders has helped patients with rheumatism lead a near normal life.

## ***Rheumatism***

**Rheumatism** is a non-specific term used to describe any painful disorder affecting the loco-motor system including joints, muscles, connective tissues, soft tissues around the joints and bones. The term rheumatism is also used to describe rheumatic fever affecting heart valves. However, the medical profession uses specific terms to describe rheumatological disorders such as rheumatoid arthritis, ankylosing spondylitis, gout and systemic lupus erythematosus and so on in the medical literature.

Rheumatology is now emerging as an important clinical specialty recognized all over the world. This speciality is rapidly improving and well established along with properly organized post graduate training programs. The term describing clinicians dealing with rheumatism as "rheumatologists" is now a well established term commonly used by the medical community, even though it is not adequately described in dictionaries established for languages. Rheumatologists all over the world are now capable of treating most of the chronic rheumatological disorders with a much better outcome for the patients. This is due to the discovery of new disease modifying agents called biologics which is now a well established form of treatment for the patients suffering with chronic and disabling joint disorders.

## ***Rheumatologist***

A **rheumatologist** is a physician specialized in the field of medical sub-specialty called rheumatology, and holds either a board certification after specialized training after Doctor of Medicine Degree (M.D.) through fellowship programs in the United States or specialist registrars positions in the United Kingdoms or DM in India or equivalent programs elsewhere in the world. In the United States, training in this field requires four years undergraduate school, four years of medical school, and then three years of residency, followed by two or three years additional Fellowship training. The number of years allocated for specialized training in rheumatology for postgraduate trainees in different countries could vary according to the requirements of different countries. Rheumatologists are internists or pediatricians who are qualified by additional postgraduate training and experience in the diagnosis and treatment of arthritis and other diseases of the joints, muscles and bones. Many rheumatologists also conduct research to determine the cause and better treatments for these disabling and sometimes fatal diseases. Treatment modalities are based on scientific research, currently, practice of rheumatology is largely evidence based. Clinicians who specialize on this specialty are called Rheumatologists.

Rheumatologists treat arthritis, certain autoimmune diseases, musculoskeletal pain disorders and osteoporosis. There are more than 200 types of these diseases, including rheumatoid arthritis, osteoarthritis, gout, lupus, back pain, osteoporosis, and tendinitis. Some of these are very serious diseases that can be difficult to diagnose and treat. They

treat soft tissue problems related to musculoskeletal system sports related soft tissue disorders and the specialty is also interrelated with physiotherapy, physical medicine and rehabilitation of disabled patients. Patient education programs and occupational therapy also go hand in hand with this specialty.

There are many international organizations representing rheumatologists all over the world. The American College of Rheumatology (ACR), the Association of Rheumatology Health Professionals (ARHP), the European League Against Rheumatism (EULAR), Asia Pacific League of Associations for Rheumatology (APLAR), International League of Associations for Rheumatology (ILAR) are the main international organizations established and organizing many activities related to this specialty, these organizations strive to propagate and consolidate Rheumatology endeavors internationally, furthermore, there are associations and colleges of Rheumatology representing Rheumatologists from each and every nation scattered throughout the world which represent the above mentioned organizations from each nation. Rheumatologists are physicians specialized in rheumatic diseases.

For example, there are approximately 480 consultant rheumatologists in the UK. Rheumatologists are increasing in numbers in all countries, as there is an increasing demand for specialists on this field with an increasing population of aging patients who need specialized treatment.

## ***Diseases***

Diseases diagnosed or managed by the rheumatologist include:

- Rheumatoid arthritis
- Lupus
- Sjögren's syndrome
- scleroderma (systemic sclerosis)
- dermatomyositis
- polychondritis
- polymyositis
- polymyalgia rheumatica
- osteoarthritis
- septic arthritis
- sarcoidosis
- gout, pseudogout
- spondyloarthropathies
  - ankylosing spondylitis
  - reactive arthritis (aka \*\*reactive arthropathy)
  - psoriatic arthropathy
  - enteropathic spondylitis
- vasculitis
  - polyarteritis nodosa
  - Henoch-Schönlein purpura

- serum sickness
- Wegener's granulomatosis
- giant cell arteritis
- temporal arteritis
- Takayasu's arteritis
- Behçet's syndrome
- Kawasaki's disease (mucocutaneous lymph node syndrome)
- Buerger's disease (thromboangiitis obliterans)

Juvenile Idiopathic Arthritis(JIA);

( JIA includes a wide range Joint Disorders affecting Children)

Rheumatic arthritis;

Soft Tissue Rheumatism; ( Localizes diseases and lesions affecting the joints and structures around the joints including tendons, ligaments capsules, bursae, Stress Fractures, muscles, nerve entrapment, vascular lesions, ganglion, connective tissue abnormalities and localised Soft tissues disorders etc.)

Diseases affecting bones;

Osteoporosis, osteomalacia, renal osteodystrophy, Fluorosis, Rickets Etc.

Congenital and familial Disorders affecting Joints;

Hyperextensible joints;

Ehlers-Danlos Syndrome, Achondroplasia, Marfan's Syndrome etc.

## ***Diagnosis***

Apart from an extensive medical history, there are useful methods of diagnosis both performed easy enough in a physical examination and, on the other hand, more complicated ones, often requiring a rheumatologist or other specialised physicians.

## **Physical examination**

Following are examples of methods of diagnosis able to be performed in a normal physical examination.

- Schober's test tests the flexion of the lower back.
- Multiple joint inspection
- Musculoskeletal Examination
  - Screening Musculoskeletal Exam (SMSE) - a rapid assessment of structure and function

- General Musculoskeletal Exam (GMSE) - a comprehensive assessment of joint inflammation
- Regional Musculoskeletal Exam (RMSE)- focused assessments of structure, function and inflammation combined with special testing

### **Specialised**

- Laboratory tests (e.g. Erythrocyte Sedimentation Rate, Rheumatoid Factor, Anti-CCP (Anti-Cyclic Citrullinated Peptide antibody), ANA (Anti-Nuclear Antibody) )
- X-rays of affected joints and other imaging methods
- Cytopathology and chemical pathology of fluid aspirated from affected joints (e.g. to differentiate between septic arthritis and gout)

### **Treatment**

Most rheumatic diseases are treated with analgesics, NSAIDs (Non-Steroid Anti-Inflammatory Drugs), steroids (in serious cases), DMARDs (Disease-Modifying Anti-Rheumatic Drugs), monoclonal antibodies, such as infliximab and adalimumab, and the soluble TNF receptor etanercept and Methotrexate for moderate to severe Rheumatoid arthritis. Biologic agent Rituximab (Anti-B-Cell Therapy) is now licensed for use in refractory Rheumatoid Arthritis. Physiotherapy is vital in the treatment of many rheumatological disorders. Occupational therapy can help patients finding alternative ways for common movements which would otherwise be restricted by their disease. Patients with rheumatoid arthritis often need a long term, coordinated and a multidisciplinary team approach towards management of individual patients, treatment is often tailored according the individual needs of the individual patient which is also dependent on the response and the tolerability of medications.

### **Scientific research**

Recently, a large body of scientific research deals with the background of autoimmune disease, the cause of many rheumatic disorders. Also, the field of osteoimmunology has emerged to further examine the interactions between the immune system, joints and bones. Epidemiological studies and medication trials are also being conducted. Scientific research on biologics and clinical trials on monoclonal antibody therapies have added a new dimension to the medical treatment of arthritic disorders.

## Chapter 17

# Hemofiltration

In medicine, **hemofiltration**, also **haemofiltration**, is a renal replacement therapy similar to hemodialysis which is used almost exclusively in the intensive care setting. Thus, it is almost always used for acute renal failure. It is a *slow continuous* therapy in which sessions usually last between 12 to 24 hours and are usually performed daily. During hemofiltration, a patient's blood is passed through a set of tubing (a *filtration circuit*) via a machine to a semipermeable membrane (the *filter*) where waste products and water are removed. Replacement fluid is added and the blood is returned to the patient.

### ***The Principle of Hemofiltration***

As in dialysis, in hemofiltration one achieves movement of solutes across a semi-permeable membrane. However, solute movement with hemofiltration is governed by convection rather than by diffusion. With hemofiltration, dialysate is not used. Instead, a positive hydrostatic pressure drives water and solutes across the filter membrane from the blood compartment to the filtrate compartment, from which it is drained. Solute, both small and large, get dragged through the membrane at a similar rate by the flow of water that has been engineered by the hydrostatic pressure. So convection overcomes the reduced removal rate of larger solutes (due to their slow speed of diffusion) seen in hemodialysis.

### ***Replacement fluid composition***

An isotonic replacement fluid is added to the blood to replace fluid volume and electrolytes. The replacement fluid must be of high purity, because it is infused directly into the blood line of the extracorporeal circuit. The replacement hemofiltration fluid usually contains lactate or acetate as a bicarbonate-generating base, or bicarbonate itself. Use of lactate can occasionally be problematic in patients with lactic acidosis or with severe liver disease, because in such cases the conversion of lactate to bicarbonate can be impaired. In such patients use of bicarbonate as a base is preferred.

### ***Hemodiafiltration***

Hemofiltration is sometimes used in combination with hemodialysis, when it is termed hemodiafiltration. Blood is pumped through the blood compartment of a high flux dialyzer, and a high rate of ultrafiltration is used, so there is a high rate of movement of

water and solutes from blood to dialysate that must be replaced by substitution fluid that is infused directly into the blood line. However, dialysis solution is also run through the dialysate compartment of the dialyzer. The combination is theoretically useful because it results in good removal of both large and small molecular weight solutes.

### ***Intermittent vs. continuous modes of therapy***

These treatments can be given intermittently, or continuously. The latter is usually done in an intensive care unit setting.

### **On-line intermittent hemofiltration (IHF) or hemodiafiltration (IHDF)**

Either of these treatments can be given in outpatient dialysis units, three or more times a week, usually 3-5 hours per treatment. IHDF is used almost exclusively, with only a few centers using IHF. With both IHF or IHDF, the substitution fluid is prepared on-line from dialysis solution by running dialysis solution through a set of two membranes to purify it before infusing it directly into the blood line. In the United States, regulatory agencies have not yet approved on-line creation of substitution fluid because of concerns about its purity. For this reason, hemodiafiltration is almost never used in an outpatient setting in the United States as of 2007. Use of sterile, pre-packaged substitution fluid would be cost-prohibitive in the current economic environment.

### **Continuous hemofiltration (CHF) or hemodiafiltration (CHDF)**

Hemofiltration is most commonly used in an intensive care unit setting, where it is either given as 8-12 hours treatments, so called SLEF (slow extended hemofiltration), or as CHF (continuous hemofiltration also sometimes called continuous veno-venous hemofiltration (CVVH)) or Continuous Renal Replacement Therapy (CRRT). Hemodiafiltration (SLED-F or CHDF or CVVHDF) also is widely used in this fashion. In the United States, the substitution fluid used in CHF or CHDF is commercially prepared, prepackaged, and sterile (or sometimes is prepared in the local hospital pharmacy), avoiding regulatory issues of on-line creation of replacement fluid from dialysis solution.

With slow continuous therapies, the blood flow rates are usually in the range of 100-200 ml/min, and access is usually achieved through a central venous catheter placed in one of the large central veins. In such cases a blood pump is used to drive blood flow through the filter. Native access for hemodialysis (eg AV fistulas or grafts) are unsuitable for CHF because the prolonged residence of the access needles required might damage such accesses.

### ***Is on-line intermittent hemodiafiltration (IHDF) better than regular hemodialysis?***

There is controversy about whether intermittent on-line hemodiafiltration (IHDF) gives better results than hemodialysis in an outpatient setting. In Europe, several observational studies have compared outcomes in patients getting dialysis with those getting IHDF.

These have suggested a lower mortality rate and other favorable outcomes in patients getting IHDF vs. those getting ordinary hemodialysis. However, the issue is not settled at this time, because the required randomized controlled clinical trials have not been done. Another problem has been that in several of the trials done, IHDF was compared to dialysis using low-flux (small pore) membranes, and the benefit found may have been due more to the use of a high-flux membrane than to the addition of convective transport (filtration) to dialysis. A recent Cochrane database review of available trials could not find a definite benefit of either IHF or IHDF vs. hemodialysis in terms of outcomes.

## Chapter 18

# Plasmapheresis

**Plasmapheresis** (from the Greek *πλάσμα* - *plasma*, something molded, and *ἀφαίρεσις* - *aphairesis*, taking away) is the removal, treatment, and return of (components of) blood plasma from blood circulation. It is thus an extracorporeal therapy (a medical procedure which is performed outside the body). The method can also be used to collect plasma for further manufacturing into a variety of medications.

The procedure is used to treat a variety of disorders, including those of the immune system, such as Myasthenia gravis Guillain-Barré syndrome, lupus, and thrombotic thrombocytopenic purpura. Dr. D. J. Wallace states that Michael Rubinstein was the first person to use plasmapheresis to treat an immune-related disorder when he "saved the life of an adolescent boy with thrombotic thrombocytopenic purpura (TTP) at the old Cedars of Lebanon Hospital in Los Angeles in 1959". Also according to Wallace, the modern plasmapheresis process itself originated in the "[U.S.] National Cancer Institute between 1963 and 1968, [where] investigators drew upon an old dairy creamer separation technology first used in 1878 and refined by Edwin Cohn's centrifuge marketed in 1953.

### ***As therapy***

During plasmapheresis, blood is initially taken out of the body through a needle or previously implanted catheter. Plasma is then removed from the blood by a cell separator. Three procedures are commonly used to separate the plasma from the blood cells:

- Discontinuous flow centrifugation: One venous catheter line is required. Typically, a 300 ml batch of blood is removed at a time and centrifuged to separate plasma from blood cells.
- Continuous flow centrifugation: Two venous lines are used. This method requires slightly less blood volume to be out of the body at any one time as it is able to continuously spin out plasma.
- Plasma filtration: Two venous lines are used. The plasma is filtered using standard hemodialysis equipment. This continuous process requires less than 100 ml of blood to be outside the body at one time.

Each method has its advantages and disadvantages. After plasma separation, the blood cells are returned to the person undergoing treatment, while the plasma, which contains the antibodies, is first treated and then returned to the patient in traditional

plasmapheresis. (In plasma exchange, the removed plasma is discarded and the patient receives replacement donor plasma, albumin, or a combination of albumin and saline (usually 70% albumin and 30% saline). Rarely, other replacement fluids, such as hydroxyethyl starch, may be used in individuals who object to blood transfusion but these are rarely used due to severe side-effects. Medication to keep the blood from clotting (an anticoagulant) is given to the patient during the procedure. Plasmapheresis is used as a therapy in particular diseases. It is an uncommon treatment in the United States, but it is more common in Europe and particularly Japan.

An important use of plasmapheresis is in the therapy of autoimmune disorders, where the rapid removal of disease-causing autoantibodies from the circulation is required in addition to other medical therapy. It is important to note that plasma exchange therapy in and of itself is useful to temper the disease process, where simultaneous medical and immunosuppressive therapy is required for long-term management. Plasma exchange offers the quickest short-term answer to removing harmful autoantibodies; however, the production of autoantibodies by the immune system must also be suppressed, usually by the use of medications such as prednisone, cyclophosphamide, cyclosporine, mycophenolate mofetil, rituximab or a mixture of these.

Other uses are the removal of blood proteins where these are overly abundant and cause hyperviscosity syndrome.

Examples of diseases that can be treated with plasmapheresis:

- Guillain-Barré syndrome
- Chronic inflammatory demyelinating polyneuropathy
- Goodpasture's syndrome
- Hyperviscosity syndromes:
  - Cryoglobulinemia
  - Paraproteinemia
  - Waldenström macroglobulinemia
- Myasthenia gravis
- Thrombotic thrombocytopenic purpura (TTP)/hemolytic uremic syndrome
- Wegener's granulomatosis
- Lambert-Eaton Syndrome
- Antiphospholipid Antibody Syndrome (APS or APLS)
- Microscopic polyangiitis
- Recurrent focal and segmental glomerulosclerosis in the transplanted kidney
- HELLP syndrome
- Refsum disease
- Behcet syndrome
- HIV-related neuropathy
- Graves' disease in infants and neonates
- Pemphigus vulgaris
- Multiple sclerosis
- Rhabdomyolysis

## **Complications of plasmapheresis therapy**

Though plasmapheresis is helpful in certain medical conditions, like any other therapy, there are potential risks and complications. Insertion of a rather large intravenous catheter can lead to bleeding, lung puncture (depending on the site of catheter insertion), and, if the catheter is left in too long, it can get infected.

Aside from placing the catheter, the procedure itself has complications. When patient blood is outside of the body passing through the plasmapheresis machine, the blood has a tendency to clot. To reduce this tendency, in one common protocol, citrate is infused while the blood is running through the circuit. Citrate binds to calcium in the blood, calcium being essential for blood to clot. Citrate is very effective in preventing blood from clotting; however, its use can lead to life-threateningly low calcium levels. This can be detected using the Chvostek's sign or Trousseau's sign. To prevent this complication, calcium is infused intravenously while the patient is undergoing the plasmapheresis; in addition, calcium supplementation by mouth may also be given.

Other complications include:

- Potential exposure to blood products, with risk of transfusion reactions or transfusion transmitted diseases
- Suppression of the patient's immune system
- Bleeding or hematoma from needle placement

## ***As a manufacturing process***

Donating plasma is similar in many ways to whole blood donation, though the end product is used for different purposes. Most plasmapheresis is for fractionation into other products, other blood donations are transfused with relatively minor modifications. Plasma that is collected solely for further manufacturing is called Source Plasma.

Plasma donors undergo a screening process to ensure both the donor's safety and the safety of the collected product. Factors monitored include blood pressure, pulse, temperature, total protein, protein electrophoresis, health history screening similar to that for whole blood, as well as an annual physical exam with a licensed physician or an approved physician substitute under the supervision of the physician. Donors are screened at each donation for viral diseases that can be transmitted by blood, sometimes by multiple methods. For example, donors are tested for HIV by EIA, which will show if they have ever been exposed to the disease, as well as by nucleic acid methods (PCR or similar) to rule out recent infections that might be missed by the EIA test. Industry standards require at least two sets of negative test results before the collected plasma is used for injectable products. The plasma is also treated in processing multiple times to inactivate any virus that was undetected during the screening process.

Plasma donors are typically paid cash for their donations, though this is not universal. For example, donors in the UK, Australia and New Zealand are not given financial

incentives. Since the products are heavily processed and treated to remove infectious agents, the higher risk is considered acceptable. Standards for donating plasma are set by national regulatory agencies such as the U.S. Food and Drug Administration (FDA), the European Union, and by a professional organization, the Plasma Protein Therapeutics Association (or PPTA), which audits and accredits collection facilities. A National Donor Deferral Registry (NDDR) is also maintained by the PPTA for use in keeping donors with prior positive test results from donating at any facility.

Almost all plasmapheresis in the US is performed by automated methods such as the Plasma Collection System (PCS2) made by Haemonetics or the Autopheresis-C (Auto-C) made by Fenwal, a division of Baxter International. In some cases, automated plasmapheresis is used to collect plasma products like Fresh frozen plasma for direct transfusion purposes, often at the same time as plateletpheresis.

#### Manual method

For the manual method, approximately the same as a whole blood donation is collected from the donor. The collected blood is then separated by centrifuge machines in separate rooms, the plasma is pressed out of the collection set into a satellite container, and the red blood cells are returned to the donor. Since returning red cells causes the plasma to be replaced more rapidly by the body, a donor can provide up to a liter of plasma at a time and can donate with only a few days between donations, unlike the 56-day deferral for blood donation. The amount allowed in a donation varies vastly from country to country, but generally does not exceed two donations, each as much as a liter, per 7-day period.

The danger with this method was that if the wrong red blood cells were returned to the donor, a serious and potentially fatal transfusion reaction could occur. Requiring donors to recite their names and ID numbers on returned bags of red cells minimized this risk. This procedure has largely become obsolete in favor of the automated method.

#### Automated method

The automated method uses a very similar process. The difference is that the collection, separation, and return are all performed inside a machine which is connected to the donor through a needle placed in the arm, typically the antecubital vein. There is no risk of receiving the wrong red cells. The devices used are very similar to the devices used for therapeutic plasmapheresis, and the potential for citrate toxicity is similar. The potential risks are explained to prospective donors at the first donation, and most donors tolerate the procedure well.

If a significant amount of red blood cells cannot be returned, the donor may not donate for 56 days, just as if they had donated a unit of blood. Depending on the collection system and the operation, the removed plasma may be replaced by saline. The body will typically replace the collected volume within 24 hours, and donors typically donate up to twice a week, though this varies by country.

The collected plasma is promptly frozen at lower than  $-20\text{ }^{\circ}\text{C}$  ( $-4\text{ }^{\circ}\text{F}$ ) and is typically shipped to a processing facility for fractionation. This process separates the collected plasma into specific components, such as albumin and immunoglobulins, most of which are made into medications for human use. Sometimes the plasma is thawed and transfused as Fresh Frozen Plasma (FFP), much like the plasma from a normal blood donation.

Donors are sometimes immunized against agents such as tetanus or hepatitis B so that their plasma contains the antibodies against the toxin or disease. In other donors, an intentionally incompatible unit of blood is transfused to produce antibodies to the antigens on the red cells. The collected plasma then contains these components, which are used in manufacturing of medications. Donors who are already ill may have their plasma collected for use as a positive control for laboratory testing.

## Chapter 19

# Cancer Immunotherapy

**Cancer immunotherapy** is the use of the immune system to reject cancer. The main premise is stimulating the patient's immune system to attack the malignant tumor cells that are responsible for the disease. This can be either through immunization of the patient (eg. by administering a cancer vaccine, such as Dendreon's Provenge), in which case the patient's own immune system is trained to recognize tumor cells as targets to be destroyed, or through the administration of therapeutic antibodies as drugs, in which case the patient's immune system is recruited to destroy tumor cells by the therapeutic antibodies.

Since the immune system responds to the environmental factors it encounters on the basis of discrimination between self and non-self, many kinds of tumor cells that arise as a result of the onset of cancer are more or less tolerated by the patient's own immune system since the tumor cells are essentially the patient's own cells that are growing, dividing and spreading without proper regulatory control.

In spite of this fact, however, many kinds of tumor cells display unusual antigens that are either inappropriate for the cell type and/or its environment, or are only normally present during the organisms' development (e.g. fetal antigens). Examples of such antigens include the glycosphingolipid GD2, a disialoganglioside that is normally only expressed at a significant level on the outer surface membranes of neuronal cells, where its exposure to the immune system is limited by the blood-brain barrier. GD2 is expressed on the surfaces of a wide range of tumor cells including neuroblastoma, medulloblastomas, astrocytomas, melanomas, small-cell lung cancer, osteosarcomas and other soft tissue sarcomas. GD2 is thus a convenient tumor-specific target for immunotherapies.

Other kinds of tumor cells display cell surface receptors that are rare or absent on the surfaces of healthy cells, and which are responsible for activating cellular signal transduction pathways that cause the unregulated growth and division of the tumor cell. Examples include ErbB2, a constitutively active cell surface receptor that is produced at abnormally high levels on the surface of breast cancer tumor cells.

## ***Monoclonal antibody therapy***

Antibodies are a key component of the adaptive immune response, playing a central role in both in the recognition of foreign antigens and the stimulation of an immune response to them. It is not surprising therefore, that many immunotherapeutic approaches involve the use of antibodies. The advent of monoclonal antibody technology has made it possible to raise antibodies against specific antigens such as the unusual antigens that are presented on the surfaces of tumors.

A number of therapeutic monoclonal antibodies have been approved for use in humans; approvals mentioned here are by the U.S. Food and Drug Administration (FDA).

### **Cancer immunotherapy: Monoclonal antibodies**

<b>Antibody</b>	<b>Brand name</b>	<b>Approval date</b>	<b>Type</b>	<b>Target</b>	<b>Approved treatment(s)</b>
Alemtuzumab	Campath	2001	humanized	CD52	Chronic lymphocytic leukemia
Bevacizumab	Avastin	2004	humanized	vascular endothelial growth factor	colorectal cancer
Cetuximab	Erbitux	2004	chimeric	epidermal growth factor receptor	colorectal cancer
Gemtuzumab ozogamicin	Mylotarg	2000	humanized	CD33	acute myelogenous leukemia (with calicheamicin)
Ibritumomab tiuxetan	Zevalin	2002	murine	CD20	non-Hodgkin lymphoma (with yttrium-90 or indium-111)
Panitumumab	Vectibix	2006	human	epidermal	colorectal cancer

growth factor  
receptor

Rituximab	Rituxan, Mabthera	1997	chimeric	CD20	non-Hodgkin lymphoma
Trastuzumab	Herceptin	1998	humanized	ErbB2	breast cancer

### **Alemtuzumab**

Alemtuzumab is an anti-CD52 humanized IgG1 monoclonal antibody indicated for the treatment of Chronic lymphocytic leukemia (CLL), the most frequent form of leukaemia in Western countries. The function of CD52 is unknown, but it is found on >95% of peripheral blood lymphocytes and monocytes. Upon binding to CD52, alemtuzumab initiates its cytotoxic effect by complement fixation and antibody-dependent cell-mediated cytotoxicity mechanisms. Alemtuzumab therapy is also indicated for T-prolymphocytic leukaemia (TPPL), for which no standard treatment exists. This is a highly aggressive tumour, with a median survival of 7.5 months.

### **Bevacizumab**

Bevacizumab is a humanized IgG1 monoclonal antibody which binds to and sterically interferes with the vascular endothelial growth factor-A (VEGF-A), preventing receptor activation. A marked increase in VEGF expression is thought to play a role in tumor angiogenesis. Bevacizumab is indicated for colon cancer; but has been applied to numerous other cancers in small scale studies, especially renal cell carcinoma. Results obtained showed that bevacizumab increased the duration of survival, progression-free survival, the rate of response and the duration of response in a statistically relevant manner.

### **Cetuximab**

Cetuximab is a chimeric IgG1 monoclonal antibody which targets the extracellular domain of the epidermal growth factor receptor (EGFR). It functions by competitively inhibiting ligand binding, thereby preventing EGFR activation, and is indicated for the treatment of colorectal cancer. Studies have also been carried out on numerous other malignancies, especially non-small cell lung cancer and head and neck cancer. As a single agent, cetuximab showed a response rate of 10.8% in patients with EGFR overexpressed metastatic colon cancer. Other anti-EGFR monoclonal antibodies in development include: ABX-EGF, hR3, and EMD 72000. Although they hold significant promise for the future, as of yet none of the agents are currently beyond phase I clinical trials.

## **Gemtuzumab ozogamicin**

Gemtuzumab ozogamicin is an “immuno-conjugate” of an anti-CD33 antibody chemically linked to calicheamicin, a cytotoxic agent. It is indicated for the treatment of acute myeloid leukaemia (AML). The patient group most likely to benefit from gemtuzumab is young adults, and trials have reported high complete responses (85%), when combined with intensive chemotherapy. There are minimal side-effects associated with Gemtuzumab therapy.

## **Rituximab**

Rituximab is a chimeric monoclonal antibody specific for CD20. CD20 is widely expressed on B-cells. Although the function of CD20 is relatively unknown it has been suggested that CD20 could play a role in calcium influx across plasma membrane, maintaining intracellular calcium concentration and allowing for the activation of B cells. The exact mode of action of rituximab is also unclear, but it has been found to have a general regulatory effect on the cell cycle and on immune-receptor expression. Experiments involving primates showed that treatment with anti-CD20 reduced peripheral B-cells by 98%, and peripheral lymph node and bone marrow B-cells by up to 95%.

## **Trastuzumab**

Trastuzumab is a monoclonal IgG1 humanized antibody specific for the epidermal growth factor receptor 2 protein (HER2). It received FDA-approval in 1998, and is clinically used for the treatment of breast cancer. The use of Trastuzumab is restricted to patients whose tumours over-express HER-2, as assessed by immunohistochemistry (IHC) and either chromogenic or Fluorescent in situ hybridisation (FISH), as well as numerous PCR-based methodologies.

HER-2 is a member of the epidermal growth factor receptor (EGFR) family of transmembrane tyrosine kinases, and is normally involved in regulation of cell proliferation and differentiation. Amplification or overexpression of HER-2 is present in 25-30% of breast carcinomas and has been associated with aggressive tumour phenotype, poor prognosis, non-responsiveness to hormonal therapy and reduced sensitivity to conventional chemotherapeutic agents.

## ***Radioimmunotherapy***

Radioimmunotherapy involves the use of radioactively conjugated murine antibodies against cellular antigens. Most research currently involved their application to lymphomas, as these are highly radio-sensitive malignancies. To limit radiation exposure, murine antibodies were especially chosen, as their high immunogenicity promotes rapid clearance from the body.

## **Ibritumomab tiuxetan**

Ibritumomab tiuxetan is a murine antibody chemically linked to a chelating agent which binds yttrium-90.  $^{90}\text{Y}$  is a beta radiator, has a half-life of 64 h and a tissue penetration of 1-5 millimetres. Its use has been investigated, primarily in the treatment of follicular lymphoma.

## **Tositumomab/iodine ( $^{131}\text{I}$ ) tositumomab regimen**

Tositumomab is a murine IgG2a anti-CD20 antibody. Iodine ( $^{131}\text{I}$ ) tositumomab is covalently bound to Iodine 131.  $^{131}\text{I}$  emits both beta and gamma radiation, and is broken down rapidly in the body. Clinical trials have established the efficacy of a sequential application of tositumomab and iodine (I) tositumomab in patients with relapsed follicular lymphoma.

## ***Advances in immunotherapy***

The development and testing of second generation immunotherapies are already under way. While antibodies targeted to disease-causing antigens can be effective under certain circumstances, in many cases, their efficacy may be limited by other factors. In the case of cancer tumors, the microenvironment is immunosuppressive, allowing even those tumors that present unusual antigens to survive and flourish in spite of the immune response generated by the cancer patient, against his or her own tumor tissue. Certain members of a group of molecules known as cytokines, such as Interleukin-2 also play a key role in modulating the immune response, and have been tried in conjunction with antibodies in order to generate an even more devastating immune response against the tumor. While the therapeutic administration of such cytokines may cause systemic inflammation, resulting in serious side effects and toxicity, a new generation of chimeric molecules consisting of an immune-stimulatory cytokine attached to an antibody that targets the cytokine's activity to a specific environment such as a tumor, are able to generate a very effective yet localized immune response against the tumor tissue, destroying the cancer-causing cells without the unwanted side-effects. A different type of chimeric molecule is an artificial T cell receptor.

The targeted delivery of cytokines by anti-tumor antibodies is one example of using antibodies to delivery payloads rather than simply relying on the antibody to trigger an immune response against the target cell. Another strategy is to deliver a lethal radioactive dose directly to the target cell, which has been utilized in the case of the Zevalin therapeutic. A third strategy is to deliver a lethal chemical dose to the target, as used in the Mylotarg therapeutic. Engineering the antibody-payload pair in such a way that they separate after entry into a cell by endocytosis can potentially increase the efficacy of the payload. One strategy to accomplish this is the use of a disulfide linkage which could be severed by the reducing conditions in the cellular interior. However, recent evidence suggests that the actual intracellular trafficking of the antibody-payload after endocytosis is such to make this strategy not generally applicable. Other potentially useful linkage types include hydrazone and peptide linkages.

## ***Latest research***

In 2001, two U.S. based non-profit organizations, the Cancer Research Institute and the Ludwig Institute for Cancer Research, formed the Cancer Vaccine Collaborative, a unique global network of clinical trial sites with special expertise in immunology, built to centrally design and coordinate early-stage clinical trials to be run in parallel in order to identify more quickly the optimal combination of reagents, or vaccine components, necessary for a successful therapeutic cancer vaccine. The Cancer Vaccine Collaborative has to-date (June 2009) completed or is currently running more than 40 clinical trials of different therapeutic cancer vaccines, including 37 phase I, 6 phase II, and 1 fully-randomized phase II clinical trials, and has published more than 130 scientific papers in peer-reviewed journals. Nearly all of these trials featured vaccines targeting various forms of the cancer-testes antigen, NY-ESO-1, a highly-immunogenic, prototypical protein marker limited in expression to a wide variety of cancer types but not in normal tissue, with the exception of the immune-privileged testes. Vaccines tested in Cancer Vaccine Collaborative trials have induced integrated immune responses composed of target-specific antibodies and CD4+ and CD8+ T lymphocytes, all of which are held to be essential for effective long-term control of cancer. Insights from these trials have generated a strong framework for the selection of components that will likely comprise an ideal therapeutic cancer vaccine, including: multiple cancer-antigens in various forms delivered with potent adjuvants and all administered in a prime-boost setting in conjunction with a modulator of cancer immunosuppression.

In June 2008, it was announced that US doctors from the Clinical Research Division led by Cassian Yee at Fred Hutchinson Cancer Research Center in Seattle have for the first time successfully treated a skin cancer patient by using immune cells cloned from his own immune system which were then re-injected into him. The patient, who was suffering from advanced skin cancer, was free from tumours within eight weeks of being injected with billions of his own immune cells in the first case of its kind. Experts say that this case could be a landmark in the treatment of cancer in general. Larger trials are now under way.

More new research is being conducted by Drs. Richard O'Reilly and Michel Sadelain. Drs. O'Reilly and Sadelain have done extensive research at Memorial Sloan-Kettering Cancer Center hospital and are among leaders of the cancer adoptive Immunotherapy field

## ***Topical immunotherapy***

Dermatologists use new creams and injections in the management of benign and malignant skin tumors. Topical immunotherapy utilizes an immune enhancement cream (imiquimod) which is an interferon producer causing the patient's own killer T cells to destroy warts, actinic keratoses, basal cell carcinoma, squamous cell carcinoma, cutaneous T cell lymphoma, and Superficial spreading melanoma. Injection immunotherapy uses mumps, candida or trichophytin antigen injections to treat warts (HPV induced tumors).

## ***Natural products***

Some types of natural products have shown promise to stimulate the immune system. Research suggests that mushrooms like Reishi and *Agaricus blazei* may be able to stimulate the immune system. Research has shown that *Agaricus blazei* may be a potent stimulator of natural killer cells. *Agaricus blazei* is rich in proteoglycans and beta-glucans, which are potent stimulators of macrophages.

Research shows the compounds in medicinal mushrooms most responsible for up-regulating the immune system and providing an anti-cancer effect, are a diverse collection of polysaccharide compounds, particularly beta-glucans. Beta-glucans are known as "biological response modifiers", and their ability to activate the immune system is well documented. Specifically, beta-glucans stimulate the innate branch of the immune system. Research has shown beta-glucans have the ability to stimulate macrophage, NK cells, T cells, and immune system cytokines. The mechanisms in which beta-glucans stimulate the immune system is only partially understood. One mechanism in which beta-glucans are able to activate the immune system, is by interacting with the Macrophage-1 antigen (CD18) receptor on immune cells.

Highly purified compounds isolated from medicinal mushrooms such as lentinan (isolated from Shiitake), and Polysaccharide-K, (isolated from *Trametes versicolor*), have become incorporated into the health care system of a few countries, such as Japan. Japan's Ministry of Health, Labour and Welfare approved the use of Polysaccharide-K in the 1980s, to stimulate the immune systems of patients undergoing chemotherapy. In Australia, a pharmaceutical based on a mixture of several mycological extracts including lentinan and Polysaccharide-K is sold commercially as MC-S.

## Chapter 20

# Chemotherapy



A woman being treated with docetaxel chemotherapy for breast cancer. Cold mittens and wine coolers are placed on her hands and feet to reduce harm to her nails.

**Chemotherapy**, in the most simple sense, is the treatment of an ailment by chemicals especially by killing micro-organisms or cancerous cells. In popular usage, it refers to antineoplastic drugs used to treat cancer or the combination of these drugs into a cytotoxic standardized treatment regimen. In its non-oncological use, the term may also refer to antibiotics (*antibacterial chemotherapy*). In that sense, the first modern

chemotherapeutic agent was arsphenamine, an arsenic compound discovered in 1909 and used to treat syphilis. This was later followed by sulfonamides (sulfa drugs) and penicillin.

Most commonly, chemotherapy acts by killing cells that divide rapidly, one of the main properties of most cancer cells. This means that it also harms cells that divide rapidly under normal circumstances: cells in the bone marrow, digestive tract and hair follicles; this results in the most common side effects of chemotherapy : myelosuppression (decreased production of blood cells, hence also immunosuppression), mucositis (inflammation of the lining of the digestive tract), and alopecia (hair loss).

Other uses of cytostatic chemotherapy agents (including the ones mentioned below) are the treatment of autoimmune diseases such as multiple sclerosis, dermatomyositis, polymyositis, lupus, rheumatoid arthritis and the suppression of transplant rejections.

Newer anticancer drugs act directly against abnormal proteins in cancer cells; this is termed targeted therapy.

## ***History***

The use of minerals and plant-based medicines are believed to date back to prehistoric medicine.

The first use of drugs to treat cancer, however, was in the early 20th century, although it was not originally intended for that purpose. Mustard gas was used as a chemical warfare agent during World War I and was studied further during World War II. During a military operation in World War II, a group of people were accidentally exposed to mustard gas and were later found to have very low white blood cell counts. It was reasoned that an agent that damaged the rapidly growing white blood cells might have a similar effect on cancer. Therefore, in the 1940s, several patients with advanced lymphomas (cancers of certain white blood cells) were given the drug by vein, rather than by breathing the irritating gas. Their improvement, although temporary, was remarkable. That experience led researchers to look for other substances that might have similar effects against cancer. As a result, many other drugs have been developed to treat cancer, and drug development since then has exploded into a multibillion-dollar industry, although the principles and limitations of chemotherapy discovered by the early researchers still apply.

## ***Principles***

Cancer is the uncontrolled growth of cells coupled with malignant behavior: invasion and metastasis. Cancer is thought to be caused by the interaction between genetic susceptibility and environmental toxins.

In the broad sense, most *chemotherapeutic* drugs work by impairing mitosis (cell division), effectively targeting fast-dividing cells. As these drugs cause damage to cells

they are termed *cytotoxic*. Some drugs cause cells to undergo apoptosis (so-called "self programmed cell death").

Scientists have yet to identify specific features of malignant and immune cells that would make them uniquely targetable (barring some recent examples, such as the Philadelphia chromosome as targeted by imatinib). This means that other fast-dividing cells, such as those responsible for hair growth and for replacement of the intestinal epithelium (lining), are also often affected. However, some drugs have a better side effect profile than others, enabling doctors to adjust treatment regimens to the advantage of patients in certain situations.

As chemotherapy affects cell division, tumors with high *growth fractions* (such as acute myelogenous leukemia and the aggressive lymphomas, including Hodgkin's disease) are more sensitive to chemotherapy, as a larger proportion of the targeted cells are undergoing cell division at any time. Malignancies with slower growth rates, such as indolent lymphomas, tend to respond to chemotherapy much more modestly.

Drugs affect "younger" tumors (i.e., more differentiated) more effectively, because mechanisms regulating cell growth are usually still preserved. With succeeding generations of tumor cells, differentiation is typically lost, growth becomes less regulated, and tumors become less responsive to most chemotherapeutic agents. Near the center of some solid tumors, cell division has effectively ceased, making them insensitive to chemotherapy. Another problem with solid tumors is the fact that the chemotherapeutic agent often does not reach the core of the tumor. Solutions to this problem include radiation therapy (both brachytherapy and teletherapy) and surgery.

Over time, cancer cells become more resistant to chemotherapy treatments. Recently, scientists have identified small pumps on the surface of cancer cells that actively move chemotherapy from inside the cell to the outside. Research on p-glycoprotein and other such chemotherapy efflux pumps, is currently ongoing. Medications to inhibit the function of p-glycoprotein are undergoing testing as of June, 2007 to enhance the efficacy of chemotherapy.

### ***Treatment schemes***

There are a number of strategies in the administration of chemotherapeutic drugs used today. Chemotherapy may be given with a curative intent or it may aim to prolong life or to palliate symptoms.

*Combined modality chemotherapy* is the use of drugs with other cancer treatments, such as radiation therapy or surgery. Most cancers are now treated in this way. *Combination chemotherapy* is a similar practice that involves treating a patient with a number of different drugs simultaneously. The drugs differ in their mechanism and side effects. The biggest advantage is minimising the chances of resistance developing to any one agent.

In *neoadjuvant chemotherapy* (*preoperative* treatment) initial chemotherapy is designed to shrink the primary tumour, thereby rendering local therapy (surgery or radiotherapy) less destructive or more effective.

*Adjuvant chemotherapy* (*postoperative* treatment) can be used when there is little evidence of cancer present, but there is risk of recurrence. This can help reduce chances of developing resistance if the tumour does develop. It is also useful in killing any cancerous cells which have spread to other parts of the body. This is often effective as the newly growing tumours are fast-dividing, and therefore very susceptible.

*Palliative chemotherapy* is given without curative intent, but simply to decrease tumor load and increase life expectancy. For these regimens, a better toxicity profile is generally expected.

All chemotherapy regimens require that the patient be capable of undergoing the treatment. Performance status is often used as a measure to determine whether a patient can receive chemotherapy, or whether dose reduction is required. Because only a fraction of the cells in a tumor die with each treatment (fractional kill), repeated doses must be administered to continue to reduce the size of the tumor. Current chemotherapy regimens apply drug treatment in cycles, with the frequency and duration of treatments limited by toxicity to the patient.

## **Types**

The majority of chemotherapeutic drugs can be divided into alkylating agents, antimetabolites, anthracyclines, plant alkaloids, topoisomerase inhibitors, and other antitumour agents. All of these drugs affect cell division or DNA synthesis and function in some way.

Some newer agents do not directly interfere with DNA. These include monoclonal antibodies and the new tyrosine kinase inhibitors e.g. *imatinib mesylate* (*Gleevec* or *Glivec*), which directly targets a molecular abnormality in certain types of cancer (chronic myelogenous leukemia, gastrointestinal stromal tumors). These are examples of targeted therapies.

In addition, some drugs that modulate tumor cell behaviour without directly attacking those cells may be used. Hormone treatments fall into this category.

Where available, Anatomical Therapeutic Chemical Classification System codes are provided for the major categories.

## **Alkylating agents (L01A)**

Alkylating agents are so named because of their ability to alkylate many nucleophilic functional groups under conditions present in cells. Cisplatin and carboplatin, as well as oxaliplatin, are alkylating agents. They impair cell function by forming covalent bonds

with the amino, carboxyl, sulfhydryl, and phosphate groups in biologically important molecules.

Other agents are mechlorethamine, cyclophosphamide, chlorambucil, ifosfamide. They work by chemically modifying a cell's DNA.

### **Anti-metabolites (L01B)**

Anti-metabolites masquerade as purines ((azathioprine, mercaptopurine)) or pyrimidines—which become the building blocks of DNA. They prevent these substances from becoming incorporated in to DNA during the "S" phase (of the cell cycle), stopping normal development and division. They also affect RNA synthesis. Due to their efficiency, these drugs are the most widely used cytostatics.

### **Plant alkaloids and terpenoids (L01C)**

These alkaloids are derived from plants and block cell division by preventing microtubule function. Microtubules are vital for cell division, and, without them, cell division cannot occur. The main examples are vinca alkaloids and taxanes.

#### **Vinca alkaloids (L01CA)**

Vinca alkaloids bind to specific sites on tubulin, inhibiting the assembly of tubulin into microtubules (M phase of the cell cycle). They are derived from the Madagascar periwinkle, *Catharanthus roseus* (formerly known as *Vinca rosea*). The vinca alkaloids include:

- Vincristine
- Vinblastine
- Vinorelbine
- Vindesine

#### **Podophyllotoxin (L01CB)**

Podophyllotoxin is a plant-derived compound which is said to help with digestion as well as used to produce two other cytostatic drugs, etoposide and teniposide. They prevent the cell from entering the G1 phase (the start of DNA replication) and the replication of DNA (the S phase). The exact mechanism of its action is not yet known.

The substance has been primarily obtained from the American Mayapple (*Podophyllum peltatum*). Recently it has been discovered that a rare Himalayan Mayapple (*Podophyllum hexandrum*) contains it in a much greater quantity, but, as the plant is endangered, its supply is limited. Studies have been conducted to isolate the genes involved in the substance's production, so that it could be obtained recombinantly.

## **Taxanes (L01CD)**

The prototype taxane is the natural product paclitaxel, originally known as Taxol and first derived from the bark of the Pacific Yew tree. Docetaxel is a semi-synthetic analogue of paclitaxel. Taxanes enhance stability of microtubules, preventing the separation of chromosomes during anaphase.

## **Topoisomerase inhibitors (L01CB and L01XX)**

Topoisomerases are essential enzymes that maintain the topology of DNA. Inhibition of type I or type II topoisomerases interferes with both transcription and replication of DNA by upsetting proper DNA supercoiling.

- Some type I topoisomerase inhibitors include *camptothecins*: irinotecan and topotecan.
- Examples of type II inhibitors include amsacrine, etoposide, etoposide phosphate, and teniposide. These are semisynthetic derivatives of epipodophyllotoxins, alkaloids naturally occurring in the root of American Mayapple (*Podophyllum peltatum*).

## **Antineoplastics (L01D)**

These include the immunosuppressant dactinomycin (which is used in kidney transplantations), doxorubicin, epirubicin, bleomycin and others.

## ***Newer and experimental approaches***

### **Hematopoietic stem cell transplant approaches**

Stem cell harvesting and autologous or hematopoietic stem cell transplantation has been used to allow for higher doses of chemotherapeutic agents where dosages are primarily limited by hematopoietic damage. Years of research in treating solid tumors, particularly breast cancer, with hematopoietic stem cell transplants, has yielded little proof of efficacy. Hematological malignancies such as myeloma, lymphoma, and leukemia remain the main indications for stem cell transplants.

### **Isolated infusion approaches**

Isolated limb perfusion (often used in melanoma), or isolated infusion of chemotherapy into the liver or the lung have been used to treat some tumours. The main purpose of these approaches is to deliver a very high dose of chemotherapy to tumor sites without causing overwhelming *systemic* damage. These approaches can help control solitary or limited metastases, but they are by definition *not* systemic, and, therefore, do not treat distributed metastases or micrometastases.

## **Targeted delivery mechanisms**

Specially targeted delivery vehicles aim to increase effective levels of chemotherapy for tumor cells while reducing effective levels for other cells. This should result in an increased tumor kill and/or reduced toxicity.

Specially targeted delivery vehicles have a differentially higher affinity for tumor cells by interacting with tumor-specific or tumour-associated antigens.

In addition to their targeting component, they also carry a payload - whether this is a traditional chemotherapeutic agent, or a radioisotope or an immune stimulating factor. Specially targeted delivery vehicles vary in their stability, selectivity, and choice of target, but, in essence, they all aim to increase the maximum effective dose that can be delivered to the tumor cells. Reduced systemic toxicity means that they can also be used in sicker patients, and that they can carry new chemotherapeutic agents that would have been far too toxic to deliver via traditional systemic approaches.

## **Light water**

Light water or Deuterium-Depleted Water (DDW) is a form of water with lower-than-normal levels of the isotope deuterium. Whereas deuterium-rich heavy water is harmful to many animals, experiments have shown that consumption of light water may be beneficial to humans, particularly those undergoing chemotherapy. A 1999 Romanian study found that water with only 30ppm deuterium produced marked improvement in survival rates of mice bombarded with ionizing radiation. A study of four patients with brain metastases from lung cancer found a three-month regimen of light water "noticeably prolonged" their survival time. A 2010 Hungarian study found significant improvement in the survival times of prostate cancer patients treated with light water.

## **Nanoparticles**

Nanoparticles have emerged as a useful vehicle for poorly soluble agents such as paclitaxel. Protein-bound paclitaxel (e.g., Abraxane) or nab-paclitaxel was approved by the U.S. Food and Drug Administration (FDA) in January 2005 for the treatment of refractory breast cancer. This formulation of paclitaxel uses human albumin as a vehicle and not the Cremophor vehicle used in Taxol. Nanoparticles made of magnetic material can also be used to concentrate agents at tumour sites using an externally applied magnetic field.

## **Dosage**

Dosage of chemotherapy can be difficult: If the dose is too low, it will be ineffective against the tumor, whereas, at excessive doses, the toxicity (side effects, neutropenia) will be intolerable to the patient. This has led to the formation of detailed "dosing schemes" in most hospitals, which give guidance on the correct dose and adjustment in case of

toxicity. In immunotherapy, they are in principle used in smaller dosages than in the treatment of malignant diseases.

In most cases, the dose is adjusted for the patient's body surface area, a measure that correlates with blood volume. The BSA is usually calculated with a mathematical formula or a nomogram, using a patient's weight and height, rather than by direct measurement.

## ***Delivery***

Most chemotherapy is delivered intravenously, although a number of agents can be administered orally (e.g., melphalan, busulfan, capecitabine). In some cases, isolated limb perfusion (often used in melanoma), or isolated infusion of chemotherapy into the liver or the lung have been used. The main purpose of these approaches is to deliver a very high dose of chemotherapy to tumour sites without causing overwhelming systemic damage.

Depending on the patient, the cancer, the stage of cancer, the type of chemotherapy, and the dosage, intravenous chemotherapy may be given on either an inpatient or an outpatient basis. For continuous, frequent or prolonged intravenous chemotherapy administration, various systems may be surgically inserted into the vasculature to maintain access. Commonly used systems are the Hickman line, the Port-a-Cath or the PICC line. These have a lower infection risk, are much less prone to phlebitis or extravasation, and abolish the need for repeated insertion of peripheral cannulae.

Harmful and lethal toxicity from chemotherapy limits the dosage of chemotherapy that can be given. Some tumors can be destroyed by sufficiently high doses of chemotherapeutic agents. However, these high doses cannot be given because they would be fatal to the patient.

## ***Adverse effects***

Chemotherapeutic techniques have a range of side effects that depend on the type of medications used. The most common medications mainly affect the fast-dividing cells of the body, such as blood cells and the cells lining the mouth, stomach, and intestines.

Common side effects include:

- Depression of the immune system, which can result in potentially fatal infections. Although patients are encouraged to wash their hands, avoid sick people, and to take other infection-reducing steps, about 85% of infections are due to naturally occurring microorganisms in the patient's own gut and skin. This may manifest as systemic infections, such as sepsis, or as localized outbreaks, such as shingles. Sometimes, chemotherapy treatments are postponed because the immune system is suppressed to a critically low level.
- Fatigue. The treatment can be physically exhausting for the patient, who might already be very tired from cancer-related fatigue. It may produce mild to severe

- anemia. Treatments to mitigate anemia include hormones to boost blood production (erythropoietin), iron supplements, and blood transfusions.
- Tendency to bleed easily. Medications that kill rapidly dividing cells or blood cells are likely to reduce the number of platelets in the blood, which can result in bruises and bleeding. Extremely low platelet counts may be temporarily boosted through platelet transfusions. Sometimes, chemotherapy treatments are postponed to allow platelet counts to recover.
  - Gastrointestinal distress. Nausea and vomiting are common side effects of chemotherapeutic medications that kill fast-dividing cells. This can also produce diarrhea or constipation. Malnutrition and dehydration can result when the patient doesn't eat or drink enough, or when the patient vomits frequently, because of gastrointestinal damage. This can result in rapid weight loss, or occasionally in weight gain, if the patient eats too much in an effort to allay nausea or heartburn. Weight gain can also be caused by some steroid medications. These side effects can frequently be reduced or eliminated with antiemetic drugs. Self-care measures, such as eating frequent small meals and drinking clear liquids or ginger tea, are often recommended. This is a temporary effect, and frequently resolves within a week of finishing treatment.
  - Hair loss. Some medications that kill rapidly dividing cells cause dramatic hair loss; other medications may cause hair to thin. These are temporary effects: hair usually starts growing back a few weeks after the last treatment, sometimes with a tendency to curl that may be called a "chemo perm".

Damage to specific organs may occur, with resultant symptoms:

- Cardiotoxicity (heart damage)
- Hepatotoxicity (liver damage)
- Nephrotoxicity (kidney damage)
- Ototoxicity (damage to the inner ear), producing vertigo
- Encephalopathy (brain dysfunction)

## **Immunosuppression and myelosuppression**

Virtually all chemotherapeutic regimens can cause depression of the immune system, often by paralysing the bone marrow and leading to a decrease of white blood cells, red blood cells, and platelets. The latter two, when they occur, are improved with blood transfusion. Neutropenia (a decrease of the neutrophil granulocyte count below  $0.5 \times 10^9$ /litre) can be improved with synthetic G-CSF (granulocyte-colony stimulating factor, e.g., filgrastim, lenograstim).

In very severe myelosuppression, which occurs in some regimens, almost all the bone marrow stem cells (cells that produce white and red blood cells) are destroyed, meaning *allogenic* or *autologous* bone marrow cell transplants are necessary. (In autologous BMTs, cells are removed from the patient before the treatment, multiplied and then re-injected afterwards; in *allogenic* BMTs the source is a donor.) However, some patients still develop diseases because of this interference with bone marrow.

In Japan the government has approved the use of some medicinal mushrooms like *Trametes versicolor*, to counteract depression of the immune system in patients undergoing chemotherapy. The United States' top-ranked cancer hospital, the MD Anderson, has reported that polysaccharide-K (PSK; an extract from *Trametes versicolor*) is a "promising candidate for chemoprevention due to the multiple effects on the malignant process, limited side effects and safety of daily oral doses for extended periods of time." PSK is already used in pharmaceuticals designed to complement chemotherapy such as MC-S. The MD Anderson has also reported that there are 40 human studies, 55 animal studies, 37 *in vitro* studies, and 11 reviews published concerning *Trametes versicolor* or its extract PSK.

## **Nausea and vomiting**

Chemotherapy-induced nausea and vomiting (CINV) is common with many treatments and some forms of cancer. However, some chemotherapy regimens do not have this side effect, and very effective drugs to stop or noticeably reduce this adverse effect are available.

A class of drugs called 5-HT<sub>3</sub> antagonists are the most effective antiemetics and constitute the single greatest advance in the management of nausea and vomiting in patients with cancer. These drugs block one or more of the nerve signals that cause nausea and vomiting. During the first 24 hours after chemotherapy, the most effective approach appears to be blocking the 5-HT<sub>3</sub> nerve signal. Approved 5-HT<sub>3</sub> inhibitors include dolasetron, granisetron, and ondansetron (Zofran). The newest 5-HT<sub>3</sub> inhibitor, palonosetron, also prevents delayed nausea and vomiting, which occurs during the 2–5 days after treatment. Since some patients have trouble swallowing pills, these drugs are often available by injection, as orally disintegrating tablets, or as transdermal patches.

The substance P inhibitor aprepitant, which became available in 2005, is also effective in controlling the nausea of cancer chemotherapy.

Some studies and patient groups say that the use of cannabinoids derived from marijuana during chemotherapy greatly reduces the associated nausea and vomiting, and enables the patient to eat. Some synthetic derivatives of the active substance in marijuana (Tetrahydrocannabinol or THC) such as Marinol may be practical for this application. Natural marijuana, known as medical cannabis is also used and recommended by some oncologists, though its use is regulated and not legal everywhere.

## **Secondary neoplasm**

Development of secondary neoplasia after successful chemotherapy and/or radiotherapy treatment can occur. The most common secondary neoplasm is secondary acute myeloid leukemia, which develops primarily after treatment with alkylating agents or topoisomerase inhibitors. Other studies have shown a 13.5 fold increase from the general population in the incidence of secondary neoplasm occurrence after 30 years from treatment.

## **Infertility**

Some types of chemotherapy are gonadotoxic and may cause infertility. Chemotherapies with high risk include procarbazine and other alkylating drugs such as cyclophosphamide, ifosfamide, busulfan, melphalan, chlorambucil and chlormethine. Drugs with medium risk include doxorubicin and platinum analogs such as cisplatin and carboplatin. On the other hand, therapies with low risk of gonadotoxicity include plant derivatives such as vincristine and vinblastine, antibiotics such as bleomycin and dactinomycin and antimetabolites such as methotrexate, mercaptopurine and 5-fluoruracil.

Patients may choose between several methods of fertility preservation prior to chemotherapy, including cryopreservation of semen, ovarian tissue, oocytes or embryos.

## **Other side effects**

In particularly large tumors, such as large lymphomas, some patients develop tumor lysis syndrome from the rapid breakdown of malignant cells. Although prophylaxis is available and is often initiated in patients with large tumors, this is a dangerous side effect that can lead to death if left untreated.

Less common side effects include pain, red skin (erythema), dry skin, damaged fingernails, a dry mouth (xerostomia), water retention, and sexual impotence. Some medications can trigger allergic or pseudoallergic reactions.

Some patients report fatigue or non-specific neurocognitive problems, such as an inability to concentrate; this is sometimes called post-chemotherapy cognitive impairment, referred to as "chemo brain" by patients' groups.

Specific chemotherapeutic agents are associated with organ-specific toxicities, including cardiovascular disease (e.g., doxorubicin), interstitial lung disease (e.g., bleomycin) and occasionally secondary neoplasm (e.g., MOPP therapy for Hodgkin's disease).

## ***In other animals***

Chemotherapy is used in veterinary medicine similar to in human medicine.

## Chapter 21

# Insulin Potentiation Therapy

**Insulin potentiation therapy (IPT)** is an alternative medicine pharmacologic strategy for the chemotherapy of cancer using insulin and low-dose chemotherapy.

The therapeutic approach is said to take advantage of the endogenous molecular biology of cancer cells, specifically insulin and insulin like growth factor secretion, and the interaction of these biochemicals with their specific receptors. By using insulin in conjunction with chemotherapy drugs, significantly less drug (about 10-15 % of a standard dose) can be targeted more specifically and more effectively to cancer cell populations, thus virtually eliminating dose-related side effects while claiming enhancing antineoplastic effects.

### ***Controversy regarding effectiveness***

Some physicians have labeled insulin potentiation therapy a form of quackery and have warned against its use

### ***Claimed explanatory molecular biology***

The proponents of IPT give the following explanation of the biology of cancer and its cells in order to understand the mechanisms of IPT, which relies upon insulin, the most integral component of IPT, having three significant actions upon cancer cells described below, as well as also dropping blood sugar levels and thus the energy source for cancer. Low blood glucose (below 60 mg/dl) also stimulates secretion of growth hormone, and growth hormone probably helps to strengthen the immune system.

### **Differentiation between cancer and normal cells**

Insulin biologically differentiates cancer cells from normal cells based on insulin receptor concentration.

Insulin can serve to distinguish and differentiate cancer cells from healthy cells in several way. Produced in the pancreas, one of its many functions is the regulation of blood glucose levels. Chiefly, insulin activates a glucose transport protein within all cells – whether they be cancerous or healthy - which allows glucose, the energy source, to enter, thus lowering the blood glucose level.

Like anything else, cancer needs energy to grow. The growth of cancer is abnormally rapid, its sole purpose being to spread, therefore it has a voracious appetite compared to normal cells. Cancer cells have developed the ability to produce insulin and insulin-like growth factor (IGF) themselves; this way they can autonomously increase their glucose uptake.

Being able to produce its own insulin makes cancer different from normal cells, but there is a second abnormality that insulin highlights. Every cell in the body has insulin receptors on the outer surface of its membrane - from 100-100,000 receptors per cell. But cancer cells have a much higher concentration of receptors. Breast cancer cells - for example - have six times more insulin receptors and ten times more IGF receptors per cell than normal cells. As an added boost, insulin is able to react with its own receptors and is also able to cross-react with and activate the IGF receptors on cancer cells. This means that insulin will affect cancer cells sixteen times as strongly as it effects normal tissues. Something else to take into consideration is that ligand effect is a function of receptor concentration. In a particular tissue, the more receptors there are for a certain ligand – such as insulin – the greater the effect of that ligand on that tissue.

By activating the insulin and IGF receptors on cancer cells through the administration of insulin during an IPT treatment, the biological differences of cancer cells can be highlighted – a vital consideration for the safety of cancer chemotherapy.

### **Modification of cancer cell metabolism**

Not only does insulin provide cancer cells with the means to grow, it has also been proven that IGFs are the most potent mitogen - promoter of cell division - for cancer growth.

Now why would growth be a favorable effect in a treatment, which is trying to kill cancer? The answer lies in the killing mechanism of chemotherapy medications. The standard pharmacologic treatment for cancer involves drugs, which are designed to attack cells that are dividing, cell division being the means by which tissue "grows." Cancer cells are rapidly dividing cells, and are constantly going through cell division. There are several phases to cell division, the one called the S-Phase being when cells replicate DNA. There are some chemotherapy agents that are "S-Phase dependent:" they attack cells that are in the S-phase of cell division, not cells in the resting phase.

Unfortunately hair cells, red and white blood cells and cells found in the digestive tract also fall into this category of rapidly dividing cells - the reason why the side effects related to standard chemotherapy are associated with these areas. In order to get a tumoral response in conventional chemotherapy, a high dose of drugs have to be used and unfortunately healthy cells are affected as well. The chemotherapy drugs by themselves cannot differentiate between rapidly dividing cancer cells and rapidly dividing healthy cells. By implementing insulin in conjunction with chemotherapy drugs, the cancer cells are highlighted as being different based on receptor concentration and are promoted to grow, which makes it likely that more of them will be in the S-phase cycle. These effects

allow for the powerful chemo agents to target the cancer cells more specifically, sparing healthy cells and therefore chemo-related side-effects.

### **Increase in cell membrane permeability**

The third effect that insulin has on cancer cells is to activate enzyme activity in the cell membrane making them more permeable.

Cell membranes are largely made up of triglycerides, which are built of fatty acids. The more saturated that a fatty acid is, the higher the melting point (example: butter [a saturated fat with a higher melting point] is solid at room temperature, whereas olive oil [an unsaturated fat with a lower melting point] is a liquid). The enzyme that insulin activates is called delta-9 desaturase and the action of this enzyme is to de-saturate - to make a saturated fat into an unsaturated fat. Delta-9 desaturase - once it has been activated by insulin - de-saturates the fatty acids that make up the cell membrane of cancer cells. This fatty acid – saturated stearic acid– has a melting point of 65 °C. Stearic acid once it has been de-saturated, becomes mono-unsaturated oleic acid, which has a melting point of 5 °C. At physiologic temperatures (the temperature of the body, about 37.5 °C) tristearin – triglyceride with three stearic acids attached that composes the cancer cell membrane - is going to be more "waxy" than "oily" because of its higher melting point. This makes for a less permeable cell membrane. On the other hand, once the insulin has activated the enzyme delta-9 desaturase, the cell membrane of cancer cells is composed of triolein – the triglyceride with three oleic acids attached – with a melting point of 5 °C. This cell membrane will be more permeable at physiologic temperatures. The chemotherapy drugs are thus able to enter the cancer cells more easily because of the increased cell membrane permeability, providing the required intracellular dose intensity to kill the cancer.

Insulin is used in IPT to enhance anticancer drug cytotoxicity and safety, via 1) an effect of biological differentiation based on insulin receptor concentration, 2) an effect of metabolic modification to increase the S-phase fraction in cancer cells, enhancing their susceptibility to cell-cycle phase-specific agents, and 3) a membrane permeability effect to increase the intracellular dose intensity of the drugs. Significantly less drug can thus be targeted more specifically and more effectively to cancer cells, all this occurring with a virtual elimination of the dose-related side effects.

### ***Supportive research***

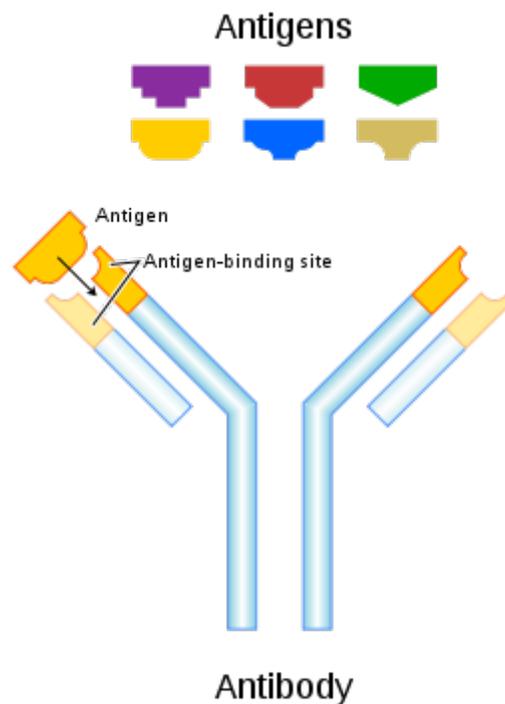
In-vitro studies have shown how IPT works supporting the informal clinical work that has been conducted on hundreds of patients worldwide.

A clinical trial of IPT for treating breast cancer was done in Uruguay and concluded that "The group treated with insulin + methotrexate responded most frequently with stable disease" compared to being treated with methotrexate alone or insulin alone.

In 2000, the National Cancer Institute's Cancer Advisory Panel on Complementary and Alternative Medicine (CAPCAM) invited Drs. Perez Garcia and Ayre to present IPT to them as part of the National Cancer Institute's (NCI's) Best Case Series program.. However CAPCAM have not in the time since undertaken any further research into IPT.

## Chapter 22

# Monoclonal Antibody Therapy



Each antibody binds only one specific antigen

**Monoclonal antibody therapy** is the use of monoclonal antibodies (or mAb) to specifically bind to target cells. This may then stimulate the patient's immune system to attack those cells. It is possible to create a mAb specific to almost any extracellular/ cell surface target, and thus there is a large amount of research and development currently being undergone to create monoclonals for numerous serious diseases (such as rheumatoid arthritis, multiple sclerosis and different types of cancers). There are a number of ways that mAbs can be used for therapy. For example: mAb therapy can be used to destroy malignant tumor cells and prevent tumor growth by blocking specific cell receptors. Variations also exist within this treatment, e.g. radioimmunotherapy, where a radioactive dose localizes on target cell line, delivering lethal chemical doses to the target.

## ***Structure and function of human and therapeutic antibodies***

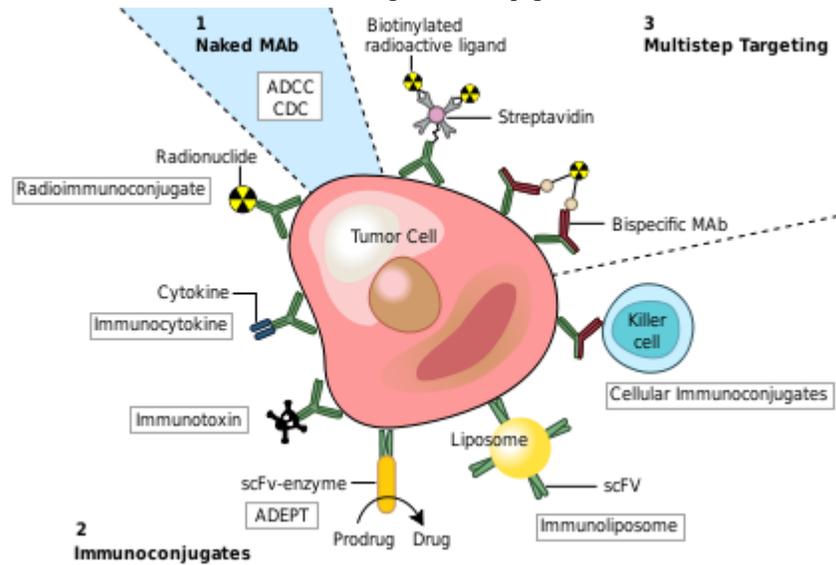
Immunoglobulin G (IgG) antibodies are large heterodimeric molecules, approximately 150 kDa and are composed of two different kinds of polypeptide chain, called the heavy (~50kDa) and the light chain (~25kDa). There are two types of light chains, kappa ( $\kappa$ ) and lambda ( $\lambda$ ). By cleavage with enzyme papain, the Fab (*fragment-antigen binding*) part can be separated from the Fc (*fragment crystalline*) part of the molecule. The Fab fragments contain the variable domains, which consist of three hypervariable amino acid domains responsible for the antibody specificity embedded into constant regions. There are four known IgG subclasses all of which are involved in Antibody-dependent cellular cytotoxicity.

The immune system responds to the environmental factors it encounters on the basis of discrimination between self and non-self. Tumor cells are not specifically targeted by one's immune system since tumor cells are the patient's own cells. Tumor cells, however are highly abnormal, and many display unusual antigens that are either inappropriate for the cell type, its environment, or are only normally present during the organisms' development (e.g. fetal antigens).

Other tumor cells display cell surface receptors that are rare or absent on the surfaces of healthy cells, and which are responsible for activating cellular signal transduction pathways that cause the unregulated growth and division of the tumor cell. Examples include ErbB2, a constitutively active cell surface receptor that is produced at abnormally high levels on the surface of approximately 30% of breast cancer tumor cells. Such breast cancer is known as a HER2 positive breast cancer.

Antibodies are a key component of the adaptive immune response, playing a central role in both in the recognition of foreign antigens and the stimulation of an immune response to them. The advent of monoclonal antibody technology has made it possible to raise antibodies against specific antigens presented on the surfaces of tumors.

## Origins of monoclonal antibody therapy



**Monoclonal antibodies for cancer.** ADEPT, antibody directed enzyme prodrug therapy; ADCC, antibody dependent cell-mediated cytotoxicity; CDC, complement dependent cytotoxicity; MAb, monoclonal antibody; scFv, single-chain Fv fragment.

Immunotherapy developed as a technique with the discovery of the structure of antibodies and the development of hybridoma technology, which provided the first reliable source of monoclonal antibodies. These advances allowed for the specific targeting of tumors both in vitro and in vivo. Initial research on malignant neoplasms found MAb therapy of limited and generally short-lived success with malignancies of the blood. Furthermore treatment had to be specifically tailored to each individual patient, thus proving to be impracticable for the routine clinical setting.

Throughout the progression of monoclonal drug development there have been four major antibody types developed: murine, chimeric, humanised and human.

Initial therapeutic antibodies were simple murine analogues, which contributed to the early lack of success. It has since been shown that these antibodies have: a short half-life in vivo (due to immune complex formation), limited penetration into tumour sites, and that they inadequately recruit host effector functions. To overcome these difficulties the technical issues initially experienced had to be surpassed. Chimeric and humanized antibodies have generally replaced murine antibodies in modern therapeutic antibody applications. Hybridoma technology has been replaced by recombinant DNA technology, transgenic mice and phage display. Understanding of proteomics has proven essential in identifying novel tumour targets.

### **Murine monoclonal antibodies (suffix *-omab*)**

Initially, murine antibodies were obtained by hybridoma technology, for which Kohler and Milstein received a Nobel prize. However the dissimilarity between murine and human immune systems led to the clinical failure of these antibodies, except in some specific circumstances. Major problems associated with murine antibodies included reduced stimulation of cytotoxicity and the formation complexes after repeated administration, which resulted in mild allergic reactions and sometimes anaphylactic shock.

### **Chimeric and humanized monoclonal antibodies (suffixes *-ximab*, *-zumab* respectively)**

To reduce murine antibody immunogenicity, murine molecules were engineered to remove immunogenic content and to increase their immunologic efficiency. This was initially achieved by the production of chimeric and humanized antibodies. Chimeric antibodies are composed of murine variable regions fused onto human constant regions. Human gene sequences, taken from the kappa light chain and the IgG1 heavy chain, results in antibodies that are approximately 65% human. This reduces immunogenicity, and thus increases serum half-life.

Humanised antibodies are produced by grafting murine hypervariable amino acid domains into human antibodies. This results in a molecule of approximately 95% human origin. However it has been shown in several studies that humanised antibodies bind antigen much more weakly than the parent murine monoclonal antibody, with reported decreases in affinity of up to several hundredfold. Increases in antibody-antigen binding strength have been achieved by introducing mutations into the complementarity determining regions (CDR), using techniques such as chain-shuffling, randomization of complementarity determining regions and generation of antibody libraries with mutations within the variable regions by error-prone PCR, *E. coli* mutator strains, and site-specific mutagenesis.

### **Human monoclonal antibodies (suffix *-umab*)**

Human monoclonal antibodies are produced using transgenic mice or phage display libraries. Human monoclonal antibodies are produced by transferring human immunoglobulin genes into the murine genome, after which the transgenic mouse is vaccinated against the desired antigen, leading to the production of monoclonal antibodies, allowing the transformation of murine antibodies in vitro into fully human antibodies.

## ***Targeted conditions***

### **Cancer**

Anti-cancer monoclonal antibodies can be targeted against malignant cells by several mechanisms:

- Radioimmunotherapy (RIT) involves the use of radioactively conjugated murine antibodies against cellular antigens. Most research currently involved their application to lymphomas, as these are highly radio-sensitive malignancies. To limit radiation exposure, murine antibodies were especially chosen, as their high immunogenicity promotes rapid clearance from the body. Tositumomab is an exemplar used for non-Hodgkins lymphoma.
- Antibody-directed enzyme prodrug therapy (ADEPT) involves the application of cancer associated monoclonal antibodies which are linked to a drug-activating enzyme. Subsequent systemic administration of a non-toxic agent results in its conversion to a toxic drug, and resulting in a cytotoxic effect which can be targeted at malignant cells. The clinical success of ADEPT treatments has been limited to date. However it holds great promise, and recent reports suggest that it will have a role in future oncological treatment.
- Immunoliposomes are antibody-conjugated liposomes. Liposomes can carry drugs or therapeutic nucleotides and when conjugated with monoclonal antibodies, may be directed against malignant cells. Although this technique is still in its infancy, significant advances have been made. Immunoliposomes have been successfully used in vivo to achieve targeted delivery of tumour-suppressing genes into tumours, using an antibody fragment against the human transferrin receptor. Tissue-specific gene delivery using immunoliposomes has also been achieved in brain, and breast cancer tissue.

### **Autoimmune diseases**

Monoclonal antibodies used for autoimmune diseases include infliximab and adalimumab, which are effective in rheumatoid arthritis, Crohn's disease and ulcerative Colitis by their ability to bind to and inhibit TNF- $\alpha$ . Basiliximab and daclizumab inhibit IL-2 on activated T cells and thereby help preventing acute rejection of kidney transplants. Omalizumab inhibits human immunoglobulin E (IgE) and is useful in moderate-to-severe allergic asthma.

### ***FDA approved therapeutic antibodies***

The first FDA-approved therapeutic monoclonal antibody was a murine IgG2a CD3 specific transplant rejection drug, OKT3 (also called muromonab), in 1986. This drug found use in solid organ transplant recipients who became steroid resistant. Hundreds of

therapies are undergoing clinical trials. Most are concerned with immunological and oncological targets.

### Example FDA approved therapeutic monoclonal antibodies

Antibody	Brand name	Approval date	Type	Target	Indication (What it's approved to treat)
Abciximab	ReoPro	1994	chimeric	inhibition of glycoprotein IIb/IIIa	Cardiovascular disease
Adalimumab	Humira	2002	human	inhibition of TNF- $\alpha$ signaling	Several auto-immune disorders
Alemtuzumab	Campath	2001	humanized	CD52	Chronic lymphocytic leukemia
Basiliximab	Simulect	1998	chimeric	IL-2R $\alpha$ receptor (CD25)	Transplant rejection
Bevacizumab	Avastin	2004	humanized	Vascular endothelial growth factor (VEGF)	Colorectal cancer, Age related macular degeneration
Cetuximab	Erbitux	2004	chimeric	epidermal growth factor receptor	Colorectal cancer, Head and neck cancer
Certolizumab pegol	Cimzia	2008	humanized	inhibition of TNF- $\alpha$ signaling	Crohn's disease

Daclizumab	Zenapax	1997	humanized	IL-2R $\alpha$ receptor (CD25)	Transplant rejection
Eculizumab	Soliris	2007	humanized	Complement system protein C5	Paroxysmal nocturnal hemoglobinuria
Efalizumab	Raptiva	2002	humanized	CD11a	Psoriasis
Gemtuzumab	Mylotarg	2000	humanized	CD33	Acute myelogenous leukemia (with calicheamicin)
Ibritumomab tiuxetan	Zevalin	2002	murine	CD20	Non-Hodgkin lymphoma (with yttrium-90 or indium-111)
Infliximab	Remicade	1998	chimeric	inhibition of TNF- $\alpha$ signaling	Several autoimmune disorders
Muromonab-CD3	Orthoclone OKT3	1986	murine	T cell CD3 Receptor	Transplant rejection
Natalizumab	Tysabri	2006	humanized	alpha-4 ( $\alpha$ 4) integrin,	Multiple sclerosis and Crohn's disease
Omalizumab	Xolair	2004	humanized	immunoglobulin E (IgE)	mainly allergy-related asthma
Palivizumab	Synagis	1998	humanized	an epitope of the RSV F protein	Respiratory Syncytial Virus

Panitumumab	Vectibix	2006	human	epidermal growth factor receptor	Colorectal cancer
Ranibizumab	Lucentis	2006	humanized	Vascular endothelial growth factor A (VEGF-A)	Macular degeneration
Rituximab	Rituxan, Mabthera	1997	chimeric	CD20	Non-Hodgkin lymphoma
Tositumomab	Bexxar	2003	murine	CD20	Non-Hodgkin lymphoma
Trastuzumab	Herceptin	1998	humanized	ErbB2	Breast cancer

### ***Therapeutic Monoclonal Antibody Market Future***

Since 2000, the therapeutic market for monoclonal antibodies has grown exponentially. The current “big 5” therapeutic antibodies on the market: Avastin, Herceptin (both oncology), Humira, Remicade (both Autoimmune and Infectious Disease ‘AIID’) and Rituxan (oncology and AIID) accounted for 80% of revenues in 2006.

In the immediate future, it is likely that Genentech/Roche will retain their control over the market (due to ownership of 3 of the “big 5” products), oncology and AIID will remain the mAb segment therapeutic focus (because these are the disease areas addressed by the big 5) and the three most commercially important ‘targets’ for the mAb class will be VEGF (Avastin), TNF-alpha (Remicade and Humira) and CD20 (Rituxan). Experts forecast that the therapeutic antibody market will continue to be dominated by Oncology and AIID segments (82-84 percent) from 2004 to 2011. Furthermore, experts note a potential for change in the balance between Oncology and AIID in the coming years. While Oncology therapeutics dominated the market in 2004, AIID is expected to dominate by 2011.

## Chapter 23

# Hydrotherapy



Hubbard Tub with wooden patient lift

**Hydrotherapy**, formerly called **hydropathy**, involves the use of water for pain-relief and treating illness. The term hydrotherapy itself is synonymous with the term **water cure** as it was originally marketed by practitioners and promoters in the 19th century. A hydrotherapist therefore, is someone who practices hydrotherapy.

Water cure has since come to have two opposing definitions, which can cause confusion.

- (a) Water cure therapy – a course of medical treatment by hydrotherapy
- (b) water cure torture – a form of torture in which a person is forced to drink large quantities of water.

The sense used here is the first one, synonymous with the term hydrotherapy, and which precedes recorded use of the second sense.

Hydrotherapy in general encompasses a range of approaches and their definitions. These range from approaches and definitions which are either naturally distinct, or made so for marketing purposes, to approaches and definitions which overlap significantly, and which can be difficult to disentangle.

One such overlap pertains to spas. According to the International SPA Association (ISPA), hydrotherapy has long been a staple in European spas. It's the generic term for water therapies using jets, underwater massage and mineral baths (e.g. balneotherapy, Iodine-Grüne therapy, Kneipp treatments, Scotch hose, Swiss shower, thalassotherapy) and others. It also can mean a whirlpool bath, hot Roman bath, hot tub, Jacuzzi, cold plunge and mineral bath. These treatments use physical water properties, such as temperature and pressure, for therapeutic purposes, to stimulate blood circulation and treat the symptoms of certain diseases.

## ***Historical background***

Various forms of hydrotherapy have been recorded in ancient Egyptian, Greek and Roman civilizations. Egyptian royalty bathed with essential oils and flowers, while Romans had communal public baths for their citizens. Hippocrates prescribed bathing in spring water for sickness. Other cultures noted for a long history of hydrotherapy include China and Japan, this latter being centred primarily around Japanese hot springs, or (onsen). Many such histories predate the Roman thermae.

After an apparent oblivion during the Middle Ages, hydrotherapy was rediscovered during the 18th and 19th centuries by people such as J.S.Hahn, MD, (1696–1773), Vincent Priessnitz (1799–1851), Professor E.F.C. Oertel (1764–1850), and J.H. Rausse (1805–1848).

In the 19th century, a popular revival followed the application of hydrotherapy around 1829, by Priessnitz, a peasant farmer in Gräfenberg, then part of the Austrian Empire. This revival was continued by a Bavarian priest, Sebastian Kneipp (1821–1897), "an able and enthusiastic follower" of Priessnitz, "whose work he took up where Priessnitz left it", after he read a treatise on the cold water cure. In Wörishofen (south Germany), Kneipp developed the systematic and controlled application of hydrotherapy for the support of medical treatment that was delivered only by doctors at that time. Kneipp's own book *My Water Cure* was published in 1886 with many subsequent editions, and translated into many languages.

A significant factor in the popular revival of hydrotherapy was that it could be practised relatively cheaply at home. The growth of hydrotherapy (or 'hydropathy' to use the name of the time), was thus partly derived from two interacting spheres: "the hydro and the home".

### ***Revival and practice of hydrotherapy***

Hydrotherapy as a formal medical tool dates from about 1829 when Vincent Priessnitz (1799–1851), a farmer of Gräfenberg in Silesia, then part of the Austrian Empire, began his public career in the paternal homestead, extended so as to accommodate the increasing numbers attracted by the fame of his cures.

Two English works, however, on the medical uses of water had been translated into German in the century preceding the rise of the movement under Priessnitz. One of these was by Sir John Floyer, a physician of Lichfield, who, struck by the remedial use of certain springs by the neighboring peasantry, investigated the history of cold bathing and published a book the subject in 1702. The book ran through six editions within a few years and the translation was largely drawn upon by Dr J. S. Hahn of Silesia in a work published in 1738.

The other work was a 1797 publication by Dr James Currie of Liverpool on the use of hot and cold water in the treatment of fever and other illness, with a fourth edition published in 1805, not long before his death. It was also translated into German by Michaelis (1801) and Hegewisch (1807). It was highly popular and first placed the subject on a scientific basis. Hahn's writings had meanwhile created much enthusiasm among his countrymen, societies having been everywhere formed to promote the medicinal and dietetic use of water; and in 1804 Professor E.F.C. Oertel of Anspach republished them and quickened the popular movement by unqualified commendation of water drinking as a remedy for all diseases. In him the rising Priessnitz found a zealous advocate, and doubtless an instructor also.

At Gräfenberg, to which the fame of Priessnitz drew people of every rank and many countries, medical men were conspicuous by their numbers, some being attracted by curiosity, others by the desire of knowledge, but the majority by the hope of cure for ailments which had as yet proved incurable. Many records of experiences at Gräfenberg were published, all more or less favorable to the claims of Priessnitz, and some enthusiastic in their estimate of his genius and penetration; Captain R. T. Claridge introduced hydropathy into England in the early 1840s, his writings and lectures, and later those of Sir William James Erasmus Wilson (1809–1884), James Manby Gully and Edward Johnson, making numerous converts, and filling the establishments which opened soon after at Malvern and elsewhere, with Scotland particularly well represented.

From the 1840s, hydropathics were established across Britain. Initially, many of these were small institutions, catering to at most dozens of patients. By the later nineteenth century the typical hydropathic establishment had evolved into a more substantial undertaking, with thousands of patients treated annually for weeks at a time in a large

purpose-built building with lavish facilities - baths, recreation rooms and the like - under the supervision of fully trained and qualified medical practitioners and staff.

In Germany, France and America, and in Malvern in England where Wilson and Gully set up their clinics using Malvern water, hydropathic establishments multiplied with great rapidity. Antagonism ran high between the old practice and the new. Unsparing condemnation was heaped by each on the other; and a legal prosecution, leading to a royal commission of inquiry, served but to make Priessnitz and his system stand higher in public estimation.

Increasing popularity soon diminished caution whether the new method would help minor ailments and be of benefit to the more seriously injured. Hydropathists occupied themselves mainly with studying chronic invalids well able to bear a rigorous regimen and the severities of unrestricted crisis. The need of a radical adaptation to the former class was first adequately recognized by John Smedley, a manufacturer of Derbyshire, who, impressed in his own person with the severities as well as the benefits of the cold water cure, practised among his workpeople a milder form of hydropathy, and began about 1852 a new era in its history, founding at Matlock a counterpart of the establishment at Gräfenberg.

Ernst Brand (1826–1897) of Berlin, Raljen and Theodor von Jürgensen of Kiel, and Karl Liebermeister of Basel, between 1860 and 1870, employed the cooling bath in abdominal typhus with striking results, and led to its introduction to England by Dr Wilson Fox. In the Franco-German War the cooling bath was largely employed, in conjunction frequently with quinine; and it was used in the treatment of hyperpyrexia.

## **The use of heat**

Hydrotherapy, especially as promoted during the height of its Victorian revival, has often been associated with the use of cold water, as evidenced by many titles from that era. However, not all therapists limited their practice of hydrotherapy to cold water, even during the height of this popular revival.

The specific use of heat was however often associated with the Turkish bath. This was introduced by David Urquhart into England on his return from the East, and ardently adopted by Richard Barter. The Turkish bath became a public institution, and, with the morning tub and the general practice of water drinking, is the most noteworthy of the many contributions by hydropathy to public health.

Until around 1840, hydropathy was not common in the United States although it was popular in Europe in the 19th century. But in "Nature's Cures", Michael Castleman wrote that hundreds of 'water-cures' were located on the countryside during the American Civil War.

## ***Hydrotherapy in the United States of America***

The first U.S. hydropathic facility has been attributed to Joel Shew (1816–1855), in 1843 or 1844, and to Russell Thatcher Trall ('R.T. Trall'. 1812-1877) in 1844. The *American Cyclopedia* states "the first establishment appears to have been that opened in 1844, at No. 63 Barclay Street, New York", with David Campbell the proprietor and Joel Shew the physician. Campbell also founded the *Water Cure Journal*

Metcalf attributes the first establishment to Dr Charles Munde, although this is not supported by Munde himself, or by historical evidence now available. Munde describes himself as becoming familiar with Priessnitz' methods around 1836, and later migrating from Germany, where he treated scarlet fever cases in Dresden during the winter of 1845-46. Munde's son recalls that the family went to the area now called Florence, Massachusetts "in the early fifties", after his father had struggled "for nearly a year in New York in search of a practice". A blind African American man named David Ruggles had previously set up a water cure practice, and after his death in 1849, Charles Munde learned "of the opportunity to take up his favorite method", which led him to pick up where Ruggles left off, thence to the naming of Florence, and accordingly, the name of the *Florence Water Cure*, also called the *Munde Water Cure*.

By 1850, it was said that "now there are probably more than one hundred", along with numerous books and periodicals, including the New York *Water Cure Journal*, which had "attained an extent of circulation equalled by few monthlies in the world". By 1855, there were attempts by some to weigh the evidence of treatments in vogue at that time.

The experience of Mary S. Gove and Dr Thomas L. Nichols illustrates this growth. In 1844, Dr. Wesselhoeft opened a "water cure house" in Brattleboro, Vermont, which Mary S. Gove attended to observe Wesselhoeft's practice, following which she was resident physician at the Lebanon Springs establishment. She then went to New York, where she observed Dr Shew's establishment in Bond Street, and in May 1845, opened her own establishment at 261 Tenth-Street, where she gave lectures, took board and day patients, and attended out-door practice. "The first two years I had a large number of board-patients, who came from a distance, from Connecticut, Northern New York, Rhode Island, Ohio, Kentucky, and several from the Southern States". A few years later, the character of her practice had changed, involving fewer board patients, as establishments opened throughout the country. Gove teamed up with Dr Nichols after they became acquainted in 1848. Nichols reports that his own attention was first drawn to water cure "by the celebrated letter of Bulwer, which was an earnest and enthusiastic, but in some respects mistaken advocacy of the system".

Other notable American hydrotherapy proponents of that era were R.T. Trall, who wrote several works and co-edited the *Water Cure Journal*, Following the introduction of hydrotherapy to the U.S., John Harvey Kellogg employed it at Battle Creek Sanitarium, which opened in 1866, where he strove to improve the scientific foundation for hydrotherapy. Other notable hydropathic centers of the era included the Cleveland Water

Cure Establishment, founded in 1848, which operated successfully for two decades, before being sold to an organisation which transformed it into an orphanage.

At its height, there were over 200 water-cure establishments in the United States, most located in the northeast. Few of these lasted into the postbellum years, although some survived into the 20th century including institutions in Scott (Cortland County), Elmira, Clifton Springs and Dansville. While none were located in Jefferson County, the Oswego Water Cure operated in the city of Oswego.

### ***Hydrotherapy and spa tourism***

The growth of hydrotherapy, and various forms of hydropathic establishments, resulted in a form of tourism, both in the UK, and especially in Europe. At least one book listed English, Scottish, Irish and European establishments suitable for each specific malady, while another focused primarily on German spas and hydropathic establishments, but including other areas. While many bathing establishments were open all year round, doctors advised patients not to go before May, "nor to remain after October. English visitors rather prefer cold weather, and they often arrive for the baths in May, and return again in September. Americans come during the whole season, but prefer summer. The most fashionable and crowded time is during July and August". In Europe, interest in various forms of hydrotherapy and spa tourism continued unabated through the 19th century and into the 20th century, where "in France, Italy and Germany, several million people spend time each year at a spa." In 1891, when Mark Twain toured Europe and discovered that a bath of spring water at Aix-les-Bains soothed his rheumatism, he described the experience as "so enjoyable that if I hadn't had a disease I would have borrowed one just to have a pretext for going on".

This was not the first time such forms of spa tourism had been popular in Europe and the U.K. Indeed,

in Europe, the application of water in the treatment of fevers and other maladies had, since the seventeenth century, been consistently promoted by a number of medical writers. In the eighteenth century, taking to the waters became a fashionable pastime for the wealthy classes who decamped to resorts around Britain and Europe to cure the ills of over-consumption. In the main, treatment in the heyday of the British spa consisted of sense and sociability: promenading, bathing, and the repetitive quaffing of foul-tasting mineral waters.

### ***Hydrotherapeutic mechanisms and modern medicine***

Modern medicine's successes, particularly with drug therapy, removed or replaced many water-related therapies during the mid-20th century. Nowadays, water therapy may be restricted to use in physical therapy, and as a cleansing agent. However, it is also used as a medium for delivery of heat and cold to the body, which has long been the basis for its application.

Hydrotherapy involves a range of methods and techniques, many of which use water as a medium to facilitate thermoregulatory reactions for therapeutic benefit. While the physiological mechanisms were initially poorly understood, the therapeutic benefits have long been recognised, even if the reason for the therapeutic benefit was in dispute. For example, in November 1881, the *British Medical Journal* noted that hydrotherapy was a specific instance, or "particular case", of general principles of thermodynamics. That is, "the application of heat and cold in general", as it applies to physiology, mediated by hydrotherapy. In 1883, another writer stated "Not, be it observed, that hydrotherapy is a water treatment after all, but that water is the medium for the application of heat and cold to the body". Thus, the "active agents in the treatment (are) heat and cold", of which water is little more than the vehicle, and not the only one".

With improved knowledge of physiological mechanisms, practitioners wrote specifically of the use of hot and cold applications to produce "profound reflex effects", including vasodilation and vasoconstriction. These cause changes in blood flow and associated metabolic functions, via physiological mechanisms, including those of thermoregulation, that are these days fairly well understood, and which underpin the contemporary use of hydrotherapy. Although standard anatomy and physiology textbooks make only passing reference, if any, to hydrotherapy, some of the best descriptions of the underlying physiology upon which hydrotherapy relies, are to be found in such textbooks. For example, one of the best succinct descriptions of blood redistribution (which is fundamental to the above-mentioned reflex reaction), quoted below, is from a standard textbook.

...by constricting or dilating arterioles in specific areas of the body, such as skeletal muscles, the skin, and the abdominal region, it is possible not only to regulate the blood pressure but also to alter the distribution of blood in various parts of the body.

### **Examples of hydrotherapy applications**

Before World War II, various forms of hydrotherapy were used to treat alcoholism, and it is used today in alternative medicine. For instance, the basic text of the Alcoholics Anonymous fellowship, *Alcoholics Anonymous*, reports that A.A. co-founder Bill Wilson was treated by hydrotherapy for his alcoholism in the early 1930s.

The use of water to treat rheumatic diseases has a long history. It continues to be used as an adjunct to therapy, including in nursing, where its use is now long established. It continues to be widely used for burn treatment, although shower-based hydrotherapy techniques have been increasingly used in preference to full-immersion methods, partly for the ease of cleaning the equipment and reducing infections due to contamination.

### **Hydrotherapeutic modalities**

The appliances and arrangements by means of which heat and cold are brought to bear are (a) packings, hot and cold, general and local, sweating and cooling; (b) hot air and steam baths; (c) general baths, of hot water and cold; (d) sitz (sitting), spinal, head and

foot baths; (e) bandages (or compresses), wet and dry; also (f) fomentations and poultices, hot and cold, sinapisms, stupes, rubbings and water potations, hot and cold.

### **Submersive hydrotherapy**

Hydrotherapy which involves submerging all or part of the body in water can involve several types of equipment:

- Full body immersion tanks (a "Hubbard tank" is a large size)
- Arm, hip, and leg whirlpool

Whirling water movement, provided by mechanical pumps, has been used in water tanks since at least the 1940s. Similar technologies have been marketed for recreational use under the terms "hot tub" or "spa".

### ***Hydropathic establishment***

A **hydropathic establishment** is a place where people receive hydropathic treatment. They are commonly built in spa towns, where mineral-rich or hot water occurs naturally.

Several hydropathic institutions wholly transferred their operations away from therapeutic purposes to become tourist hotels in the late 20th century whilst retaining the name 'Hydro'. There are several prominent examples in Scotland at Crieff, Peebles and Seamill amongst others.

### **Examples of hydropathic establishments**

Note: For European and U.K. establishments, where there is no citation alongside an establishment, it is safe to assume that reference to it was found in one of the citations placed atop the list for efficiency. Additional citations are added where there is also another source of interest.

## Europe

List as at 1840 by Claridge, with additional citations. Geographical names per that era.

### Austria, Silesia

- *Graefenberg* (Priessnitz's establishment), Graefenberg, Silesia (c.1829~?).
- Dr Joseph Weiss' hydro, Freiwaldau, Silesia (1831~1841).
- Karlsbrunn (between Freiwaldau, Jagerndorf & Feidenthal). Dr Malik
- Weidenau, on the slopes of the Sudates. Dr Frolich.
- Schroth's establishment, Lindeweise, Silesia.

### Archduchy of Austria

- Dr Wilhelm Winternitz's establishment, Kaltenleutgeben, Austria (June 1865-?).
- Laale, near Kaltenleutgeben. Dr. Granichstaden, author of *Hydriasiologia*.
- Dr Johan Emmel's *Priessnitz Establishment*, Kaltenleutgeben,

## United Kingdom

### England

- *Stand Steadbury*, Hertfordshire (founded by Weiss) (1841-?).
- *Grafenberg House*, Malvern, (founder Dr James Wilson) (June 1842-c1867 - death of Wilson).
- *Tudor House*, Malvern founder Dr James Manby Gully (October 1842-c1872 - retirement of Gully).
- Sudbrook Park, Richmond, Surrey (founder, Weiss) (1844-?).
- *Ben Rhydding Hydro*, Ilkley near Leeds. (1844–1939)
- *Metcalfe's London Hydro* (1898–1919).
- *Smedley's Hydro*, Matlock, Derbyshire (1860s-1950s)
- *West of England Hydro*, Limpley Stoke (1862~1899).

### Scotland, 19th century

- *Angusfield*, Aberdeen (1850 - )
- *Athole*, Pithlocry (1880 - )
- *Bridge of Allan* (1855~1886+)
- *Callander* (1882 - )
- *Cluny Hill*, at Forres (1864~1874+)
- *Crieff*, at Crieff (1868-current)

## United States of America

- First known establishment at No. 63 Barclay St., New York. (1844-?). Proprietor David Campbell Physician Joel Shew.
- New Lebanon Springs Water-Cure, Albany (2nd Dr Shew establishment), (May 1845-).
- Brattleborough Hydropathic Establishment, aka Dr. Robert Wesselhoeft's water cure house (c.1844-1871). 3rd in U.S.A.
- David Ruggles' water cure house, Florence, Massachusetts (c.1844-1849).
- Oyster Bay water cure, Long Island (3rd Dr Shew estab.), (1847-).
- Dr. E.E. Denniston's *Round Hill Water-Cure*, Northhampton, Massachusetts (1847-1860+).
- Cleveland Water Cure Establishment, Cleveland, Ohio (1848–1868).
- Dr Munde's *Florence Water Cure* (c.1850 - ?).
- Oswego Water Cure, Oswego, New York

- Wienerwald, Austria (1835-?).
- Bohemia**
- Elisenbad, Near Chrudin. Dr. Weidenhoffer.
  - Dobrawitz, near Jungbunzlau. Dr. Schmidt.
  - Leitmeritz. Dr. Lauda.
- Kuechelbad, near Prague. Dr. Kanzler. **Moravia**
- Czenrahora, around Olmutz.
  - Sulowitz, near Brunn.
  - Hoznau, near Prerau
  - Budischan, near Iglau
  - Gross Ullersdorf, near Olmutz. Dr. Gross
- Hungary and Transylvania**
- Peterwardein (director unknown to Claridge)
  - Oedenburg (director unknown to Claridge)
  - Hermanstadt (director unknown to Claridge)
  - Muhlan, near Inspruck, in the Tyrol. Dr. Fritz
- Prussia**
- Oberrigk, near
- *Craiglockhart Hydropathic*, Edinburgh (1880~1915)
  - *Deeside*, near Cults [1874 (Heathcote) and 1899 (Murtle)]
  - *Dunblane (Philps?)*, at Dunblane (1870~1936?)
  - *Gilmour Hill*, Glasgow (c.1857 - )
  - *Glenburn*, Rothesay, Bute (1843 - )
  - *Kilmacolm* (1880–1882)
  - *Kim Pier*, Dunoon (1846-)
  - *Kyles of Bute*, Port Bannantyne, Bute (1877 - )
  - *Lochhead*: Aberdeen (1851~1868).
  - *Peebles*, at Peebles (1881-current)
  - *Pitlochry*, at Pithlochry (1879 - )
  - *Seamill*, near West Kilbride (1880 - )
  - *Shandon*, near Helensburgh (~1877~1919).
  - *Skelmorlie*, Wemyss Bay (1880~1984)
  - *St Helens and Waverly*: Melrose (1869 )
- Scotland, 1920s**
- *Ard-Gairney Private Hydropathic*, Kinross
  - *Atholl Hotel Hydro*, St. Andrews
  - *Garrison Hydro*, Millport
  - *Grampian Hills Hydro*, Crieff.
  - *Taymouth Castle*
- (c.1850s).
  - Dr. Henry Foster's Clifton Springs Sanitarium (c.mid-to-late 19th century).
  - Battle Creek Sanitarium (1866-World War II).
  - Pennoyer's *Kenosha Water Cure*, Wisconsin (C.1870-1890).
  - *Pennoyer Sanitarium* (followed on from Kenosha Water Cure after fire: 1890-?).

- Trebnitz & Breslau. *Hydro*, Taymouth  
Dr. Lehman
- Alt Scheitnig, near **Ireland**  
Breslau. Dr. Burkner.
  - Berlin. Directed by Major Plehwe, partner Dr. Beck.
    - *Dr Curtin's Hydropathic Establishment*, Glenbrook, County Cork (1858~1870s).
    - *St Ann's Hydropathic Establishment*, Blarney, Co.Cork. (Founder Dr Richard Barter)
  - Marienbad.
  - Bendler Strosse, No. 8, Berlin. Dr. Moser. Plus 3rd Berlin establishment
  - Koethen, near Berlin. Mr Falkenstein, author of *The wonderful cures of Graefenberg*. **India**
    - *Dr Kannan Pugazhendi, Sparrc Institute Chennai India*
  - Gorhrishowo, near Bromberg, in Grand Duchy of Posen. Dr. Barschewitz. **Wales**
    - Llandudno Hydropathic Establishment (c.1872~1905).
    - **Unclear**
      - The Rick James Institute.
  - Kunzendorf, near Neurode, in province of Glatz. Mr Niederfuhr.
  - Marienberg, near Boppart around Coblentz. Dr. Schmitz, editor of the *Journal on Hydropathy*.

## Bavaria

- Alexandersbad Hydropathic Establishment, near Wuniedel. Dr. Fickentscher/Fikenhe r. (pre-1840-1860s+).
- Streitberg, between Erlangen and Baireuth
- Schaflarn, near Munich. Dr. Horner
- Munich,

- Nymphenburg  
Strasse, No.86
- Lake Starnberg. Dr. Schnitzlein, also author of a work on Hydropathy.
  - Schallersdorf, near Erlangen. Professor Dr. Fleischmann.
  - Dr. Oertel, Anspach.

### **Württemberg**

- Dr. Bentsch, near Ulm.

### **Saxony**

- Dr. Muller, in Swiss Saxony, near Pirna in Bila valley.
- Kreischa, near Dresden. Dr. Stecher.
- Muldenthal, near Frieberg. Mr. Munde, author of a hydropathic work.

### **Saxe Gotha**

- Elgersburg. Dr. Piutti, appointed by Duke of Saxe Coburg Gotha in 1838

### **Saxe Weimar**

- Ilmenau hydropathic establishment (Drs Schwabe, Fitzler, Baumbach, Preller) (c.1841-1865+). (Claridge says "Dr Sitzler")

## **Brunswick**

- Kaulnitz. Director not named.

## **Poland**

- Warsaw. Dr. Sauvan

## **Russia**

- St. Petersburg. Dr. Harnish.

## **Belgium**

- Ghent. Practitioner unknown.
- Another near Brussels. Practitioner unknown.

## **France**

- Dr. Bigel, Strasburg.
- Dr. Baldau, Paris.
- Dr Beni-Barden's establishment, Auteuil, near Paris.
- Dr Fleury's hydropathic establishment, Bellevne, France (c.1860-?).

## **Others**

- Tiefenau hydropathic establishment (Dr. Winkler) (c.1860s-?).
- Dr J.H. Rausse's establishment, Mecklenburg, Germany (c.1837-?).

## Chapter 24

# Electroconvulsive Therapy

**Electroconvulsive therapy (ECT)**, also known as **electroshock**, is psychiatric treatment in which seizures are electrically induced in anesthetized patients for therapeutic effect. Today, ECT is most often used as a treatment for severe depression which has not responded to other treatment, and is also used in the treatment of mania (often in bipolar disorder), and catatonia. It was first introduced in the 1930s and gained widespread use as a form of treatment in the 1940s and 1950s; today, an estimated 1 million people worldwide receive ECT every year, usually in a course of 6–12 treatments administered two or three times a week.

Electroconvulsive therapy can differ in its application in three ways: electrode placement, frequency of treatments, and the electrical waveform of the stimulus. These three forms of application have significant differences in both adverse side effects and positive outcomes. After treatment, drug therapy is usually continued, and some patients receive continuation/maintenance ECT. In the United Kingdom and Ireland, drug therapy is continued during ECT.

Informed consent is a standard of modern electroconvulsive therapy. Involuntary treatment is uncommon in the United States and is typically only used in cases of great extremity, and only when all other treatment options have been exhausted and the use of ECT is believed to be a potentially life saving treatment. Similarly, national audits of ECT use in Scotland and Ireland have demonstrated that the vast majority of patients treated give informed consent. Although it was a source of significant controversies in the past and got frowned upon, recent years have seen an increased acceptance of ECT as a safe, effective and economical tool for the treatment of some mental illnesses. However, it is rarely used as the first line of treatment.

### ***Guidelines for treatment***

Experts disagree on whether ECT is an appropriate first-line treatment or if it should be reserved for patients who have not responded to other interventions such as medication and psychotherapy.

The American Psychiatric Association (APA) 2001 guidelines give the primary indications for ECT among patients with depression as a lack of response to, or intolerance of, antidepressant medications; a good response to previous ECT; and the

need for a rapid and definitive response (e.g. because of psychosis or a risk of suicide). The decision to use ECT depends on several factors, including the severity and chronicity of the depression, the likelihood that alternative treatments would be effective, the patient's preference and capacity to consent, and a weighing of the risks and benefits.

Some guidelines recommend cognitive behavioral therapy or other psychotherapy before ECT is used. However, treatment resistance is widely defined as lack of therapeutic response to two antidepressants at adequate doses for an adequate duration and with good compliance. The APA states that at times patients will prefer to receive ECT over alternative treatments, but commonly the opposite will be the case.

The APA ECT guidelines state that severe major depression with psychotic features, manic delirium, or catatonia are conditions where there is a clear consensus favoring early ECT. The UK's National Institute for Health and Clinical Excellence (NICE) guidelines recommend ECT for patients with severe depression, catatonia, or prolonged or severe mania. Indeed, the updated (2009) NICE guidelines for depression also provide for the use of maintenance ECT (where ECT is given at longer intervals to prevent relapse), although the guidance stresses the need for further study. The 2001 APA guidelines also support the use of ECT for relapse prevention.

The 2001 APA ECT guidelines say that ECT is rarely used as a first-line treatment for schizophrenia but is considered after unsuccessful treatment with antipsychotic medication, and may also be considered in the treatment of patients with schizoaffective or schizophreniform disorder. The 2003 NICE ECT guidelines do not recommend ECT for schizophrenia, and this has been supported by meta-analytic evidence showing no or little benefit versus placebo, or in combination with antipsychotic drugs, including Clozapine.

The NICE 2003 guidelines state that doctors should be particularly cautious when considering ECT treatment for women who are pregnant and for older or younger people, because they may be at higher risk of complications with ECT. The 2001 APA ECT guidelines say that ECT may be safer than alternative treatments in the infirm elderly and during pregnancy, and the 2000 APA depression guidelines stated that the literature supports the safety for mother and fetus, as well as the efficacy during pregnancy.

### ***Non-clinical patient characteristics***

About 70 percent of ECT patients are women. This is almost entirely due to women being at twice the risk of depression. Older and more affluent patients are also more likely to receive ECT. The use of ECT treatment is "markedly reduced for ethnic minorities."

## ***Efficacy***

### **ECT Manages or remisses psychological problems temporarily; but it is not a cure**

Researchers are still divided regarding the validity of ECT, and the publications that argue for its efficacy do so only for short terms of one to six months.

ECT on its own does not usually have a sustained benefit. Half those who remit then relapse within six months. This is similar to the rate of relapse after discontinuing antidepressant medication, and is a function of the usual severity and chronicity of pre-existing illness rather than ECT itself. The relapse rate in the first six months is reduced by the use of psychiatric medications or further ECT, but remains high.

In a 2010 review of placebo controlled studies Bentall and Read found ECT to give slightly higher recovery/remission rates to sham-ECT during treatment but equal rates after on follow up after treatment<sup>161</sup>. Sham ECT is the placebo control where the patient doesn't get an electric shock.

Their conclusions are as follows:

"Given the strong evidence of persistent and, for some, permanent brain dysfunction, primarily evidenced in the form of retrograde and anterograde amnesia, and the evidence of a slight but significant increased risk of death, the cost-benefit analysis for ECT is so poor that its use cannot be scientifically justified."

### **Probability of remission**

The 1999 U.S. Surgeon General's Report on Mental Health summarized psychiatric opinion at the time about the effectiveness of ECT. It stated that both clinical experience and published studies had determined ECT to be effective (with an average 60 to 70 percent remission rate) in the treatment of severe depression, some acute psychotic states, and mania. Its effectiveness had not been demonstrated in dysthymia, substance abuse, anxiety, or personality disorder. The report stated that ECT does not have a long-term protective effect against suicide and should be regarded as a short-term treatment for an acute episode of illness, to be followed by continuation therapy in the form of drug treatment or further ECT at weekly to monthly intervals.

A 2004 large multicentre clinical follow-up study of ECT patients in New York—describing itself as the first systematic documentation of the effectiveness of ECT in community practice in the 65 years of its use—found remission rates of only 30 to 47 percent, with 64 percent of those relapsing within six months. However, when patients with co-morbid personality disorders or who were suffering from schizoaffective disorder were removed from the analysis, the remission rates climbed to 60-70%.

## **Degree of effectiveness**

All systematic published reviews of the literature have concluded that ECT is effective in the treatment of depression. In 2003, The UK ECT Review group published a systematic review and meta-analysis comparing ECT to placebo and antidepressant drugs. This meta-analysis demonstrated a large effect size for ECT versus placebo, and versus antidepressant drugs. In 2006, research psychiatrist Colin A. Ross reviewed the placebo-controlled trials one-by-one and found that no single study showed a significant difference between real and placebo ECT at one month post-treatment. Dr. Ross was highly critical of other published reviews, which concluded that ECT is effective, and Ross stated that these reviews often relied primarily on studies that were not placebo-controlled. However, Dr. Ross's analysis does not include a statistical synthesis in contrast to the well conducted meta-analytic evidence presented by the UK ECT review group in 2003.

## **Adverse effects**

Aside from effects in the brain, the general physical risks of ECT are similar to those of brief general anesthesia; the United States' Surgeon General's report says that there are "no absolute health contraindications" to its use. Immediately following treatment the most common adverse effects are confusion and memory loss. The state of confusion usually disappears after a few hours. It can be tolerated by pregnant women who are not suffering major complications. It can be used with diabetic or obese patients, and with caution in those whose cancers are in remission or under control. It can be used in some immunocompromised patients. It must be used very cautiously in people with epilepsy or other neurological disorders because by its nature it provokes small tonic-clonic seizures, and so would likely not be given to a person whose epilepsy is not well-controlled. Some patients experience muscle soreness after ECT. This is due to the muscle relaxants given during the procedure and rarely due to muscle activity. The death rate due to ECT is around 4 per 100,000 procedures.

## **Effects on memory**

It is the purported effects of ECT on long-term memory that give rise to much of the concern surrounding its use. The acute effects of ECT can include amnesia, both retrograde (for events occurring before the treatment) and anterograde (for events occurring after the treatment). However, the vast majority of these effects are short lived. Memory loss and confusion are more pronounced with bilateral electrode placement rather than unilateral, and with outdated sine-wave rather than brief-pulse currents. The vast majority of modern treatment uses brief pulse currents. Research by Harold Sackeim has shown that excessive current causes more risk for memory loss, and using right-sided electrode placement may reduce verbal memory disturbance.

Retrograde amnesia is most marked for events occurring in the weeks or months before treatment, with one study showing that although some people lose memories from years prior to treatment, recovery of such memories was "virtually complete" by seven months

post-treatment, with the only enduring loss being memories in the weeks and months prior to the treatment. Anterograde memory loss is usually limited to the time of treatment itself or shortly afterwards. In the weeks and months following ECT these memory problems gradually improve, but some people have persistent losses, especially with bilateral ECT. One published review summarizing the results of questionnaires about subjective memory loss found that between 29% and 55% of respondents believed they experienced long-lasting or permanent memory changes. In 2000, American psychiatrist Sarah Lisanby and colleagues found that bilateral ECT left patients with more persistently impaired memory of public events as compared to RUL ECT.

Some studies have found that patients are often unaware of cognitive deficits induced by ECT. For example, in June 2008, a Duke University study was published assessing the neuropsychological effects and attitudes in patients after ECT. Forty-six patients participated in the study, which involved neuropsychological and psychological testing before and after ECT. The study documented substantial cognitive impairment after ECT on a variety of memory tests, including "verbal memory for word lists and prose passages and visual memory of geometric designs." The study further found that a significant number of patients believed that their memory had improved after ECT despite the fact that neuropsychological testing clearly showed the opposite. As stated by the researchers, "Indeed, there was a slight trend towards [patients reporting] improved memory functioning, despite the objective neuropsychological data indicating significantly lower recognition and delayed recall." Based on their findings, the authors issued the following recommendation:

"When ECT is provided to adolescents, the potential impact of such cognitive changes should be discussed with the patients and their parents or guardians in terms of implications for not only the patient's emotional functioning but cognitive functioning as well, particularly upon his or her academic performance. In summary, we argue that an individual cost-benefit analysis should be made in light of the implications of the potential benefits versus costs of ECT upon improving emotional functioning and the impact that potential memory changes may have on real-world functioning and quality of life."

Severe memory loss from ECT is described in an autobiographical book, *Doctors of Deception: What They Don't Want You to Know about Shock Treatment*.

### **Controversy over long-term effects on general cognition**

According to prominent ECT researcher Harold Sackeim, "despite over fifty years of clinical use and ongoing controversy", until 2007 there had "never been a large-scale, prospective study of the cognitive effects of ECT." In this first-ever large-scale study (347 subjects), Sackeim and colleagues found that at least some forms (namely bilateral application and outdated sine-wave currents) of ECT "routine[ly]" lead to "adverse cognitive effects," including global cognitive deficits and memory loss, that persist for up to six months after treatment, suggesting that the induced deficits may be permanent. The authors also warned that their findings did not suggest that right-unilateral ECT did not

also lead to chronic cognitive deficits. However, the several limitations of this study include the lack of a depressed control group with which to compare memory decay over 6 months. The measure of autobiographical memory used, the Columbia Autobiographical Short-Form (AMI-SF) is not capable of showing memory improvement, with scores at followup expressed as percentages of baseline.

Harold Sackeim can be seen in a videotaped deposition briefly discussing the findings of this study and why, in his opinion, earlier studies had failed to find evidence of long-term harm from ECT. Despite over fifty years of clinical use, Sackeim states that prior to 2001, "the field itself never really had an opportunity to have a discussion about patients who have complaints about long-term memory loss." In this video clip, Sackeim also reveals that at a California ECT conference with 200 practitioners present, when polled as to whether they think ECT can lead to chronic cognitive deficits, two-thirds raised their hands. Sackeim says this was "almost a watershed moment for the field", and was the "first time *publicly* that the field itself said 'no' to the position that it can't happen."

In July 2007, a second study was published concluding that ECT routinely leads to chronic, substantial cognitive deficits, and the findings were not limited to any particular forms of ECT. The study, led by psychiatrist Glenda MacQueen and colleagues, found that patients treated with ECT for bipolar disorder show marked deficits across multiple cognitive domains. According to the researchers, "Subjects who had received remote ECT had further impairment on a variety of learning and memory tests when compared with patients with no past ECT. This degree of impairment could not be accounted for by illness state at the time of assessment or by differential past illness burden between patient groups." Despite the findings of chronic, global cognitive deficits in post-ECT patients, MacQueen and colleagues suggest that it is "unlikely that such findings, even if confirmed, would significantly change the risk–benefit ratio of this notably effective treatment."

Six months after the publication of the Sackeim study documenting routine, long-term memory loss after ECT, prominent ECT researcher Max Fink published a review in the journal *Psychosomatics* concluding that patient complaints of memory loss after ECT are "rare" and should be "characterized as somatoform disorders, rather than as evidence of brain damage, thus warranting psychological treatment for such disorders." Based on his findings, Fink suggests that, "Instead of endorsing these reports as the direct consequence of ECT, especially in patients who have recovered from their depressive illness, lost their suicidal drive, and have improved social functioning, is it not more useful to accept the complaint as a somatoform disorder, explore the basis in the individual's history and experience, and offer appropriate supportive treatment?"

Most recent reviews of the literature and other articles continue to characterize ECT as safe and effective. For example, in June 2009, Portuguese researchers published a review on the safety and efficacy of ECT in an article entitled, *Electroconvulsive Therapy: Myths and Evidences*. In their review, the researchers conclude that ECT is an "efficient, safe and even life saving treatment for several psychiatric disorders." In 2008, Yale researchers published a review on the safety and efficacy of ECT in elderly patients.

According to the authors, "ECT is well established as a safe and effective treatment for several psychiatric disorders." And in a June 2009 article published in the *Journal of ECT*, Iranian researchers observe that, "Despite the wide consensus over the safety and efficacy of electroconvulsive therapy (ECT), it still faces negative publicity and unfavorable attitudes of patients and families."

Psychiatrist Peter Breggin, chief editor of the journal *Ethical Human Psychology and Psychiatry*, is a leading critic of ECT who believes the procedure is neither safe nor effective. In a published article reviewing the findings of Harold Sackeim's 2007 study on the cognitive effects of ECT, Breggin accuses Max Fink and other pro-ECT researchers of having a history of "systematically covering up damage done to millions of [ECT] patients throughout the world." He disagrees with the position that findings of chronic, global cognitive deficits should have no bearing on the risk-benefit ratio of ECT, and he believes it's important to address the "actual impact of these losses on the lives of individual patients." In a section of his paper entitled *Destroying Lives*, Dr. Breggin writes, "Even when these injured people can continue to function on a superficial social basis, they nonetheless suffer devastation of their identities due to the obliteration of key aspects of their personal lives. The loss of the ability to retain and learn new material is not only humiliating and depressing but also disabling. Even when relatively subtle, these activities can disrupt routine activities of living."

A study published in 2004 in the *Journal of Mental Health* reported that 35 to 42% of patients responding to a questionnaire reported ECT resulted in loss of intelligence. The study also reported, "There is no overlap between clinical and consumer studies on the question of benefit."

*Doctors of Deception: What They Don't Want You to Know About Shock Treatment* reports before-and-after IQ testing of persons receiving ECT, including the author, that show 30 to 40 point losses.

A recent opinion article by a neuropsychologist and a psychiatrist in Dublin suggests that ECT patients who experience cognitive problems following ECT should be offered some form of cognitive rehabilitation. The authors say that the failure to attempt to rehabilitate patients may be partly responsible for the negative public image of ECT. The article speculates on what aspects of such rehabilitation might be useful, without reviewing the literature on its presence or absence.

## **Effects on brain structure**

Considerable controversy exists over the effects of ECT on brain tissue although a number of mental health associations, including the American Psychiatric Association, have concluded that there is no evidence that ECT causes structural brain damage. A 1999 report by the United States Surgeon General states, "The fears that ECT causes gross structural brain pathology have not been supported by decades of methodologically sound research in both humans and animals". However, the word "gross" is a synonym for major, leaving the possibility open for real brain damage which the US Surgeon

General considers minor. However, not all experts agree that ECT does not cause brain damage, and two studies have been published since 2007 finding that at least some forms of ECT may result in *widespread, persisting, generalized cognitive dysfunction*, which might support claims that ECT causes brain damage.

A leading critic of ECT, psychiatrist Peter Breggin has published books and journalistic reviews of the literature purporting to show that ECT routinely causes brain damage as evidenced by a considerable list of studies in humans and animals. In particular, Dr. Breggin asserts that animal and human autopsy studies have shown that ECT routinely causes '*widespread pinpoint hemorrhages and scattered cell death.*' According to Dr. Breggin, the 1990 APA task force report on ECT ignored much of the scientific literature pointing out the negative effects of electroshock therapy. For example, in 1952 Hans Hartelius conducted and published an animal study on cats entitled *Cerebral Changes Following Electrically Induced Convulsions* in which a double-blind microscopic pathology examination showed that it was possible to distinguish the 8 shocked animals from the 8 non-shocked animals with remarkable accuracy based on statistically significant structural changes to the brain, including vessel wall changes, gliosis, and nerve cell changes. Based on the detection of shadow cells and neuronophagia, Hartelius determined that there was irreversible damage to neurons associated with electroshock.

Proponents argue that the addition of hyperoxygenation and refinement in technique in the last thirty years has made ECT safe, and a majority of published reviews in recent decades have reflected this position. In a 2004 study designed to evaluate whether modern ECT techniques lead to identifiable brain damage, twelve monkeys underwent daily electroshock for six weeks under conditions meant to simulate human ECT; the animals were then sacrificed and their brains were compared to monkeys undergoing anesthesia alone. According to the researchers, "None of the ECT-treated monkeys showed pathological findings."

There are recent animal studies that have documented significant brain damage after an electroshock series. For example, in 2005, Russian researchers published a study entitled, *Electroconvulsive Shock Induces Neuron Death in the Mouse Hippocampus: Correlation of Neurodegeneration with Convulsive Activity*. In this study, the researchers found that after an electroshock series, there was a significant loss of neurons in parts of the brain and particularly in defined parts of the hippocampus where up to 10% of neurons were killed. The researchers conclude that "the main cause of neuron death is convulsions evoked by electric shocks." In 2008, Portuguese researchers conducted a rat study aimed at answering the question of whether an electroshock series causes structural changes in vulnerable parts of the brain. According to the authors, "This study answers positively the question of whether repeated administration of ECS seizures can cause brain lesions. Our data are consistent with findings from other animal models and from human studies in showing that neurons located in the entorhinal cortex and in the hilus of the dentate gyrus are particularly vulnerable to repeated seizures." However, they question the applicability of their own research with respect to Electroconvulsive therapy in humans: "An important caveat of our results is that it is unclear to what extent they are relevant to the use of electroconvulsive therapy in psychiatry, because the protocol employed in this

study is different from that used clinically. Evidence from previous studies (Gombos et al., [1999]; Vaidya et al., [1999]) and from our pilot experiments indicates that treating rats either with five to ten widely spaced ECS (at 24- or 48-hr schedules) or with two stimulations only 2 hr apart does not lead to loss of hippocampal neurons".

Many expert proponents of ECT maintain that the procedure is safe and does not cause brain damage. Dr. Charles Kellner, a prominent ECT researcher and former chief editor of the *Journal of ECT* states in a recent published interview that, "There are a number of well-designed studies that show ECT does not cause brain damage and numerous reports of patients who have received a large number of treatments over their lifetime and have suffered no significant problems due to ECT." Dr. Kellner cites specifically to a study purporting to show an absence of cognitive impairment in eight subjects after more than 100 lifetime ECT treatments. One of the authors of the cited study, Harold Sackeim, published a large-scale study less than a month after this interview concluding that the type of ECT used in the eight patients receiving the 100 lifetime treatments, bilateral sine wave, routinely leads to persistent, global cognitive deficits (discussed supra). Dr. Kellner states that, "Rather than cause brain damage, there is evidence that ECT may reverse some of the damaging effects of serious psychiatric illness."

### **Effects in pregnancy**

If steps are taken to decrease potential risks, ECT is generally accepted to be relatively safe during all trimesters of pregnancy, particularly when compared to pharmacological treatments. Suggested preparation for ECT during pregnancy includes a pelvic examination, discontinuation of nonessential anticholinergic medication, uterine tocodynamometry, intravenous hydration, and administration of a nonparticulate antacid. During ECT, elevation of the pregnant woman's right hip, external fetal cardiac monitoring, intubation, and avoidance of excessive hyperventilation are recommended. Much of the medical literature in this area is composed of case studies of single or twin pregnancies, and although some have reported serious complications, the majority have found ECT to be safe. ECT is not performed on the fetus.

### **Administration**

Informed consent is sought before treatment. Patients are informed about the risks and benefits of the procedure. Patients are also made aware of risks and benefits of other treatments and of not having the procedure done at all. Depending on the jurisdiction the need for further inputs from other medical professionals or legal professionals may be required. ECT is usually given on an in-patient basis. Prior to treatment a patient is given a short-acting anesthetic such as methohexital, etomidate, or thiopental, a muscle relaxant such as succinylcholine (succinylcholine), and occasionally atropine to inhibit salivation.

Both electrodes can be placed one on the same side of the patient's head. This is known as unilateral ECT. Unilateral ECT is used first to minimize side effects (memory loss). When electrodes are placed on both sides of the head, this is known as bilateral ECT. In bifrontal ECT, an uncommon variation, the electrode position is somewhere between

bilateral and unilateral. Unilateral is thought to cause fewer cognitive effects than bilateral but is considered less effective. In the USA most patients receive bilateral ECT. In the UK almost all patients receive bilateral ECT.

The electrodes deliver an electrical stimulus. The stimulus levels recommended for ECT are in excess of an individual's seizure threshold: about one and a half times seizure threshold for bilateral ECT and up to 12 times for unilateral ECT. Below these levels treatment may not be effective in spite of a seizure, while doses massively above threshold level, especially with bilateral ECT, expose patients to the risk of more severe cognitive impairment without additional therapeutic gains. Seizure threshold is determined by trial and error ("dose titration"). Some psychiatrists use dose titration, some still use "fixed dose" (that is, all patients are given the same dose) and others compromise by roughly estimating a patient's threshold according to age and sex. Older men tend to have higher thresholds than younger women, but it is not a hard and fast rule, and other factors, for example drugs, affect seizure threshold.

## **ECT machines**

Most modern ECT machines deliver a brief-pulse current, which is thought to cause fewer cognitive effects than the sine-wave currents which were originally used in ECT. A small minority of psychiatrists in the USA still use sine-wave stimuli. Sine-wave is no longer used in the UK or Ireland. Typically, the electrical stimulus used in ECT is about 800 milliamps and has up to several hundred watts, and the current flows for between one and 6 seconds. In the USA, ECT machines are manufactured by two companies, Somatics, which is owned by psychiatrists Richard Abrams and Conrad Swartz, and Mecta. The Food and Drug Administration has classified the devices used to administer ECT as Class III medical devices. Class III is the highest-risk class of medical devices. In the UK, the market for ECT machines was long monopolized by Ectron Ltd, although in recent years some hospitals have started using American machines. Ectron Ltd was set up by psychiatrist Robert Russell, who together with a colleague from the Three Counties Asylum, Bedfordshire, invented the Page–Russell technique of intensive ECT.

## **Variations in international practice**

There is wide variation in ECT use between different countries, different hospitals, and different psychiatrists. International practice varies considerably from widespread use of the therapy in many western countries to a small minority of countries that do not use ECT at all, such as Slovenia. Guidelines on the use of ECT are stringent in the USA and the UK. Modern standards are not always followed throughout the world and not all countries that use ECT have written technical standards. The use of both anesthesia and muscle relaxants is universally recommended in the administration of ECT. If anesthesia and muscle relaxants are not used the procedure is called unmodified ECT. In a minority of countries such as Japan, India, and Nigeria, ECT may be used without anesthesia. WHO has called for a worldwide ban on unmodified ECT and the topic is currently being debated in countries like India. The practice has been recently abolished in Turkey's largest psychiatric hospital. A major difficulty for developing countries in eliminating

unmodified ECT is a lack of trained anesthesiologists available to administer the procedure. A small minority of countries never seek consent before administering ECT. This significantly uneven application of ECT around the world continues to make ECT a controversial procedure.

Sarah Hall reports, "ECT has been dogged by conflict between psychiatrists who swear by it, and some patients and families of patients who say that their lives have been ruined by it. It is controversial in some European countries such as the Netherlands and Italy, where its use is severely restricted".

### **United States**

In the United States, a survey of psychiatric practice in the late 1980s found that an estimated 100,000 people received ECT annually, with wide variation between metropolitan statistical areas. Accurate statistics about the frequency, context and circumstances of ECT in the United States are difficult to obtain because only a few states have reporting laws that require the treating facility to supply state authorities with this information. One state which does report such data is Texas, where in the mid-1990s ECT was used in about one third of psychiatric facilities and given to about 1,650 people annually. Usage of ECT has since declined slightly; in 2000–01 ECT was given to about 1,500 people aged from 16 to 97 (in Texas it is illegal to give ECT to anyone under sixteen). ECT is more commonly used in private psychiatric hospitals than in public hospitals, and minority patients are underrepresented in the ECT statistics. In the United States, ECT is usually given three times a week; in the UK, it is usually given twice a week. Occasionally it is given on a daily basis. A course usually consists of 6–12 treatments, but may be more or fewer. Following a course of ECT some patients may be given continuation or maintenance ECT with further treatments at weekly, fortnightly or monthly intervals. A few psychiatrists in the USA use multiple-monitored ECT (MMECT) where patients receive more than one treatment per anesthetic. Electroconvulsive therapy is not a required subject in US medical schools and not a required skill in psychiatric residency training. Privileging for ECT practice at institutions is a local option, no national certification standards are established, and no ECT-specific continuing training experiences are required of ECT practitioners.

### **United Kingdom**

In the United Kingdom in 1980, an estimated 50,000 people received ECT annually, with use declining steadily since then to about 12,000 per annum. It is still used in nearly all psychiatric hospitals, with a survey of ECT use from 2002 finding that 71 percent of patients were women and 46 percent were over 65 years of age. Eighty-one percent had a diagnosis of mood disorder; schizophrenia was the next most common diagnosis. Sixteen percent were treated without their consent. In 2003, the National Institute for Clinical Excellence, a government body which was set up to standardize treatment throughout the National Health Service in England and Wales, issued guidance on the use of ECT. Its use was recommended "only to achieve rapid and short-term improvement of severe symptoms after an adequate trial of treatment options has proven ineffective and/or when

the condition is considered to be potentially life-threatening in individuals with severe depressive illness, catatonia or a prolonged manic episode". The guidance received a mixed reception. It was welcomed by an editorial in the British Medical Journal but the Royal College of Psychiatrists launched an unsuccessful appeal. The NICE guidance, as the British Medical Journal editorial points out, is only a policy statement and psychiatrists may deviate from it if they see fit. Adherence to standards has not been universal in the past. A survey of ECT use in 1980 found that more than half of ECT clinics failed to meet minimum standards set by the Royal College of Psychiatrists, with a later survey in 1998 finding that minimum standards were largely adhered to, but that two-thirds of clinics still fell short of current guidelines, particularly in the training and supervision of junior doctors involved in the procedure. A voluntary accreditation scheme, ECTAS, was set up in 2004 by the Royal College, but as of 2006 only a minority of ECT clinics in England, Wales, Northern Ireland and the Republic of Ireland have signed up.

### ***Mechanism of action***

The aim of ECT is to induce a therapeutic clonic seizure (a seizure where the person loses consciousness and has convulsions) lasting for at least 15 seconds. Although a large amount of research has been carried out, the exact mechanism of action of ECT remains elusive. The main reasons for this are that the human brain can not be studied directly before and after ECT and therefore scientists rely on animal models of depression and ECT, with major limitations. While animal models are acknowledged to model merely aspects of depressive illness, human and animal brains are very similar at a molecular level, enabling detailed study of the molecular mechanisms involved in ECT

There is a vast literature on the effects of Electroconvulsive Shock (ECS) in animals. In animal models of depression, particularly "Learned helplessness" and "Social defeat", there is evidence of pruning of normally dense synaptic connections in the hippocampus, a richly connected area deep in the temporal lobe which is vital in controlling both mood and memory. ECS has been shown to increase levels of Brain-derived neurotrophic factor (BDNF) and Vascular Endothelial Growth Factor (VEGF) in the rodent hippocampus. This reverses the toxic effects of depression on this area of the brain, increasing both new synapse formation and the formation of new brain cells (hippocampal neurogenesis). Both these effects have been noted to be present in antidepressant-treated animals, however they are neither necessary nor sufficient for antidepressant response. ECT is a more robust inducer of these neuroplastic effects than antidepressants. Electroconvulsive Therapy (ECT) has also been shown to increase serum brain-derived neurotrophic factor (BDNF) in drug resistant depressed patients. This suggests a common molecular mechanism of action, albeit in need of much further study.

## ***Legal status***

### **Informed consent**

It is widely acknowledged internationally that obtaining the written, informed consent of the patient is important before ECT is administered. The World Health Organization, in its 2005 publication "Human Rights and Legislation WHO Resource Book on Mental Health," specifically states, "ECT should be administered only after obtaining informed consent."

In the US, this doctrine places a legal obligation on a doctor to make a patient aware of: the reason for treatment, the risks and benefits of a proposed treatment, the risks and benefits of alternative treatment, and the risks and benefits of receiving no treatment. The patient is then given the opportunity to accept or reject the treatment. The form states how many treatments are recommended and also makes the patient aware that the treatment may be revoked at anytime during a course of ECT. The Surgeon General's Report on Mental Health states that patients should be warned that the benefits of ECT are short-lived without active continuation treatment in the form of drugs or further ECT, and that there may be some risk of permanent, severe memory loss after ECT. The report advises psychiatrists to involve patients in discussion, possibly with the aid of leaflets or videos, both before and during a course of ECT.

To demonstrate what he believes should be required to fully satisfy the legal obligation for informed consent, one psychiatrist, working for an anti-psychiatry organisation, has formulated his own consent form using the consent form developed and enacted by the Texas Legislature as a model.

In the UK, in order for consent to be valid it requires an explanation in "broad terms" of the nature of the procedure and its likely effects. One review from 2005 found that only about half of patients felt they were given sufficient information about ECT and its adverse effects and another survey found that about fifty percent of psychiatrists and nurses agreed with them.

A 2005 study published in the *British Journal of Psychiatry* described patients' perspectives on the adequacy of informed consent before ECT. The study found that, "About half (45–55%) of patients reported they were given an adequate explanation of ECT, implying a similar percentage felt they were not." The authors also stated:

"Approximately a third did not feel they had freely consented to ECT even when they had signed a consent form. The proportion who feel they did not freely choose the treatment has actually increased over time. The same themes arise whether the patient had received treatment a year ago or 30 years ago. Neither current nor proposed safeguards for patients are sufficient to ensure informed consent with respect to ECT, at least in England and Wales."

## **Involuntary ECT**

Procedures for involuntary ECT vary from country to country depending on local mental health laws. Legal proceedings are required in some countries, while in others ECT is seen as another form of treatment that may be given involuntarily as long as legal conditions are observed. Involuntary electroshock contravenes the principle of autonomy in medical ethics. The maxim of autonomy is "Voluntas aegroti suprema lex." This rule states that the will of the patient is supreme. It implies that a patient has the right to consent to, or to refuse a medical treatment, such as ECT. Persons considered not to be of sound mind are in many jurisdictions considered incapable of giving true consent. In such a case, the patient's "assent" may be sought; opinions are divided as to whether this should be routinely done, or whether a patient who is not competent to consent to therapy should retain the right to refuse it.

Citizens in western societies often undergo emergency medical procedures when they have lost the capacity to consent (such as neurosurgery after head injury). Under these circumstances, the principles of beneficence and non-maleficence must be adhered to.

### **United States**

In most states in the USA, a judicial order following a formal hearing is needed before a patient can be forced to undergo involuntary ECT. Patients may be represented by legal counsel at the hearing. Oregon Revised Statutes allow for involuntary ECT with the signature of a physician independent of the patient's facility, and no judicial order or legal counsel are required. According to the Surgeon General's Report on Mental Health, "As a rule, the law requires that such petitions are granted only where the prompt institution of ECT is regarded as potentially lifesaving, as in the case of a person in grave danger because of lack of food or fluid intake caused by catatonia." However, there are legal loopholes that thwart strict adherence to this principle. For example, an American citizen was being forced to undergo ECT against his will in 2009, even though his life was not in danger. In this March 17, 2009 video, the man, his mother, and advocates, speak out against his forced ECT. The description of the video states that "Though Sandford, 54, is not charged with any crime, he has received over 40 such rounds of shocks on an outpatient basis so far – even after his original mental problems have long since subsided and he has repeatedly asked for the shocks to stop. Over the objections of Sandford, his mother and friends, his legal conservator at Lutheran Social Service of MN (LSSMN) has gone to court and succeeded in mandating a continuation of the procedure." Twin Cities Indymedia asserts "Like all other USA states, Minnesota has [legal] loopholes allowing [its] citizens to receive electroshock over their expressed wishes."

### **Great Britain**

Until 2009 in England and Wales, the Mental Health Act 1983 allowed the use of ECT on detained patients whether or not they had capacity to consent to it, so long as the treatment was likely to alleviate or prevent deterioration in a condition and was authorized by a psychiatrist from the Mental Health Act Commission's panel. However,

following amendments which took effect in 2009, ECT may not be given to a patient who has capacity to refuse to consent to it, irrespective of his or her detention under the Act, although treatment may still be given to capacious patients in an emergency under Section 62 of the Act. If the treating psychiatrist thinks the need for treatment is urgent they may start a course of ECT before authorization. About 2,000 people a year in England and Wales are treated without their consent under the Mental Health Act. In Scotland the Mental Health (Care and Treatment) (Scotland) Act 2003 also gives patients with capacity the right to refuse ECT.

## ***History***



A psychotron, apparatus for administering elektroshocks

As early as the 16th century, agents to produce seizures were used to treat psychiatric conditions. In 1785, the therapeutic use of seizure induction was documented in the London Medical Journal. Convulsive therapy was introduced in 1934 by Hungarian neuropsychiatrist Ladislav J. Meduna who, believing mistakenly that schizophrenia and epilepsy were antagonistic disorders, induced seizures with first camphor and then metrazol (cardiazol). Within three years metrazol convulsive therapy was being used worldwide. In 1937, the first international meeting on convulsive therapy was held in Switzerland by the Swiss psychiatrist Muller. The proceedings were published in the American Journal of Psychiatry and, within three years, cardiazol convulsive therapy was being used worldwide. Italian Professor of neuropsychiatry Ugo Cerletti, who had been using electric shocks to produce seizures in animal experiments, and his colleague Lucio Bini developed the idea of using electricity as a substitute for metrazol in convulsive therapy and, in 1937, experimented for the first time on a person. Sherwin B. Nuland, having discussed the matter with a first-hand observer in the 1970s, gave the following description of the results of the first use of ECT on a person:

"They thought, 'Well, we'll try 55 volts, two-tenths of a second. That's not going to do anything terrible to him.' So they did that. [...] This fellow — remember, he wasn't even put to sleep — after this major grand mal convulsion, sat right up, looked at these three fellows and said, 'What the fuck are you assholes trying to do?' Well, they were happy as could be, because he hadn't said a rational word in the weeks of observation."

ECT soon replaced metrazol therapy all over the world because it was cheaper, less frightening and more convenient. Cerletti and Bini were nominated for a Nobel Prize but did not receive one. By 1940, the procedure was introduced to both England and the US. In Germany and Austria it was promoted by Friedrich Meggendorfer. Through the 1940s and 1950s the use of ECT became widespread. ECT is the only form of shock treatment still performed by modern medicine.

In the early 1940s, in an attempt to reduce the memory disturbance and confusion associated with treatment, two modifications were introduced: the use of unilateral electrode placement and the replacement of sinusoidal current with brief pulse. It took many years for brief-pulse equipment to be widely adopted. Unilateral ECT has never been popular with psychiatrists and is still only given to a minority of ECT patients. In the 1940s and early 1950s ECT was usually given in "unmodified" form, without muscle relaxants, and the seizure resulted in a full-scale convulsion. A rare but serious complication of unmodified ECT was fracture or dislocation of the long bones. In the 1940s psychiatrists began to experiment with curare, the muscle-paralysing South American poison, in order to modify the convulsions. The introduction of suxamethonium (succinylcholine), a safer synthetic alternative to curare, in 1951 led to the more widespread use of "modified" ECT. A short-acting anesthetic was usually given in addition to the muscle relaxant in order to spare patients the terrifying feeling of suffocation that can be experienced with muscle relaxants.

The steady growth of antidepressant use along with negative depictions of ECT in the mass media led to a marked decline in the use of ECT during the 1950s to the 1970s. The

Surgeon General stated there were problems with electroshock therapy in the initial years before anesthesia was routinely given and, *these now antiquated practices contributed to the negative portrayal of ECT in the popular media*. The New York Times described the public's negative perception of ECT as being caused mainly by one movie, "For Big Nurse in *One Flew Over the Cuckoo's Nest*, it was a tool of terror, and in the public mind *shock therapy* has retained the tarnished image given it by Ken Kesey's novel: dangerous, inhumane and overused".

In 1976, Dr. Blatchley demonstrated the effectiveness of his constant current, brief pulse device ECT. This device eventually largely replaced earlier devices because of the reduction in cognitive side effects, although some ECT clinics in the US still use sine-wave devices. The 1970s saw the publication of the first American Psychiatric Association task force report on electroconvulsive therapy (to be followed by further reports in 1990 and 2001). The report endorsed the use of ECT in the treatment of depression. The decade also saw criticism of ECT. Specifically critics pointed to shortcomings such as noted side effects, the procedure being used as a form of abuse, and uneven application of ECT. The use of ECT declined until the 1980s, "when use began to increase amid growing awareness of its benefits and cost-effectiveness for treating severe depression". In 1985 the National Institute of Mental Health and National Institutes of Health convened a consensus development conference on ECT and concluded that, whilst ECT was the most controversial treatment in psychiatry and had significant side-effects, it had been shown to be effective for a narrow range of severe psychiatric disorders.

Due to the backlash noted previously, national institutions reviewed past practices and set new standards. In 1978, The American Psychiatric Association released its first task force report in which new standards for consent were introduced and the use of unilateral electrode placement was recommended. The 1985 NIMH Consensus Conference confirmed the therapeutic role of ECT in certain circumstances. The American Psychiatric Association released its second task force report in 1990 where specific details on the delivery, education, and training of ECT were documented. Finally in 2001 the American Psychiatric Association released its latest task force report. This report emphasizes the importance of informed consent, and the expanded role that the procedure has in modern medicine.

### ***Patient experience***

The APA ECT taskforce guidelines report findings that most patients find ECT no worse than going to the dentist, and many found it less stressful than the dentist. They report that other research finds that most patients would voluntarily receive ECT again if needed.

NICE ECT guidelines report that some individuals consider ECT to have been a beneficial and lifesaving treatment, while others reported feelings of terror, shame and distress, and found it positively harmful and an abusive invasion of personal autonomy, especially when administered without their consent.

## Individual positive depictions

Kitty Dukakis, wife of politician Michael Dukakis, reports in a *Newsweek* article mostly positive effects from electroconvulsive therapy, and regards memory loss as an acceptable price to pay for relief from depression.

For me, the memory issues are real but manageable. Things I lose generally come back. Other memories I prefer to lose, including those about the depression I was suffering. But there are some memories—of meetings I have attended, people's homes I have visited—that I don't want to lose but I can't help it. They generally involve things I did two weeks before and two weeks after ECT. Often they are just wiped out....I have learned ways to partly compensate for whatever loss I still experience. I call my sister Jinny, Michael and my kids, asking what my niece Betsy's phone number is, what we did yesterday and what we are planning to do tomorrow. I apologize prior to asking. I wonder when they are going to run out of patience with "Kitty being Kitty." I hate losing memories, which means losing control over my past and my mind, but the control ECT gives me over my disabling depression is worth this relatively minor cost. It just is.

American psychotherapist Martha Manning's autobiographical *Undercurrents* acknowledges the downside of treatment: "I felt like I'd been hit by a truck for a while, but that was, comparatively speaking, not so bad," as well as the upside: "Afterwards, I thought, do regular people feel this way all the time? It's like you've not been in on a great joke for the whole of your life."

In his autobiographical book *Electroboy*, American writer Andy Behrman describes undergoing ECT as a treatment for bipolar disorder while under house-arrest: "I wake up thirty minutes later and think I am in a hotel in Acapulco. My head feels as if I have just downed a frozen margarita too quickly. My jaws and limbs ache. But I am elated."

Curtis Hartmann, a lawyer in western Massachusetts, stated: "ECT, a treatment of last resort for severe, debilitating depression, is all that has ever worked for me. I awaken about 20 minutes later, and although I am still groggy with anesthesia, much of the hellish depression is gone. It is a disease that for me, literally steals me from myself—a disease that executes me and then forces me to stand and look down at my corpse. Thankfully, ECT has kept my monster at bay, my hope intact".

Beverly Callard is a British actress, best known for her role as Liz McDonald in *Coronation Street*. In her recently published autobiography titled "Unbroken", she describes her experience with ECT for severe depression, stating that the treatment was responsible, in part for her recovery.

## Individual negative depictions

### Depictions of severe long-term, permanent memory loss

Ernest Hemingway, American author, committed suicide shortly after ECT at the Mayo Clinic in 1961. He is reported to have said to his biographer, "Well, what is the sense of ruining my head and erasing my memory, which is my capital, and putting me out of business? It was a brilliant cure but we lost the patient...."

In a letter to the editor published in the *Washington Post* in December, 2000, registered nurse Barbara C. Cody wrote that her life was forever changed by 13 outpatient ECTs she received in 1983. She wrote,

"Shock 'therapy' totally and permanently disabled me. EEGs [electroencephalograms] verify the extensive damage shock did to my brain. Fifteen to 20 years of my life were simply erased; only small bits and pieces have returned. I was also left with short-term memory impairment and serious cognitive deficits. ... Shock 'therapy' took my past, my college education, my musical abilities, even the knowledge that my children were, in fact, my children. I call ECT a rape of the soul."

Similarly, writer Johnanton Cott claims to have completely lost 15 years of memory in *On the Sea of Memory: A Journey from Forgetting to Remembering*.

Despite former patients having reported devastating, permanent amnesia and cognitive impairment since ECT was first invented, the first lawsuit for ECT amnesia, Marilyn Rice v. John Nardini, was not brought until 1975; dozens of suits followed. While there have been a few settlements, including one for half a million dollars, no former patient had won a case until 2005. In a 2005 South Carolina court proceeding, Peggy S. Salters became the first ECT survivor to win a jury verdict and compensation. Ms. Salters sued Palmetto Baptist Medical Center in Columbia, as well as the three doctors responsible for her care, for an intensive course of outpatient ECT that she received in 2000, at age 55 years old, that caused her to lose all memories of the past 30 years of her life, including all memories of her husband of three decades, then deceased, and the births of her three children. She held a Masters of Science in nursing and, prior to the ECT, had a long career as a psychiatric nurse; but, as a result of the ECT, lost her knowledge of nursing skills and was unable to return to work. The jury awarded Salters \$635,177 in compensation for her inability to work. The judgement was upheld upon appeal in an unpublished opinion.

### Accounts of severe cognitive diminishment

Liz Spikol, the senior contributing editor of *Philadelphia Weekly*, wrote of her ECT in 1996,

"Not only was the ECT ineffective, it was incredibly damaging to my cognitive functioning and memory. But sometimes it's hard to be sure of yourself when everyone

'credible' — scientists, ECT docs, researchers — are telling you that your reality isn't real. How many times have I been told my memory loss wasn't due to ECT but to depression? How many times have I been told that, like a lot of other consumers, I must be perceiving this incorrectly? How many times have people told me that my feelings of trauma related to the ECT are misplaced and unusual? It's as if I was raped and people kept telling me not to be upset—that it wasn't that bad."

### **Involuntary or other problems in administrating ECT**

In 2007, a judge canceled a two-year-old court order that allowed the involuntary electroshock of Simone D., a psychiatric patient at Creedmoor Psychiatric Center in the state of New York. Although Simone spoke only Spanish, she rarely received access to staff fluent in her language. Simone previously had 200 electroshocks. However, she communicated that she did not want more electroshock. Simone stated, "Electroshock causes more pain. I suffer more from shock treatment! "

In 2008, David Tarloff, a psychiatric patient who had received electroshock, assaulted two therapists in the city of New York. Tarloff injured one therapist and killed the other. One of the therapists was Kent Shinbach, a psychiatrist who had an interest in electroconvulsive therapy. "It is not clear whether Dr. Shinbach played any role in Mr. Tarloff's shock therapy". However, Tarloff told investigators that Shinbach had given Tarloff psychiatric treatment at a psychiatric facility initially in 1991.

### **Bad but vague descriptions**

In an interview with *Houston Chronicle* in 1996, Melissa Holliday, a former extra on *Baywatch* and model for *Playboy* stated the ECT she received in 1995, "ruined her life." She went on to state, "I've been through a rape, and electroshock therapy is worse. If you haven't gone through it, I can't explain it."

## Chapter 25

# Oxygen Therapy



Oxygen piping and regulator, for oxygen therapy, mounted on the wall of an ambulance



Oxygen Regulator for portable D-Cylinder, usually carried in an ambulance's resuscitation kit

**Oxygen therapy** is the administration of oxygen as a medical intervention, which can be for a variety of purposes in both chronic and acute patient care. Oxygen is essential for cell metabolism, and in turn, tissue oxygenation is essential for all normal physiological functions.

Room air only contains 21% oxygen, and increasing the fraction of oxygen in the breathing gas increases the amount of oxygen in the blood. It is often only required to raise the fraction of oxygen delivered to 30–35% and this is done by use of a nasal cannula. When 100% oxygen is needed, it may be delivered via a tight-fitting face mask, or by supplying 100% oxygen to an incubator in the case of infants. Oxygen can be administered in other ways, including specific treatments at raised air pressure, such as hyperbaric oxygen therapy.

High blood and tissue levels of oxygen can be helpful or damaging, depending on circumstances and oxygen therapy should be used to benefit the patient by increasing the supply of oxygen to the lungs and thereby increasing the availability of oxygen to the body tissues, especially when the patient is suffering from hypoxia and/or hypoxaemia.

## ***Indications for use***

Oxygen is used as a medical treatment in both chronic and acute cases, and can be used in hospital, pre-hospital or entirely out of hospital, dependant on the needs of the patient and the views of the medical professional advising.

### **Use in chronic conditions**

A common use of supplementary oxygen is in patients with chronic obstructive pulmonary disease (COPD), a common long term effect of smoking, who may require additional oxygen to breathe either during a temporary worsening of their condition, or throughout the day and night. It is indicated in COPD patients with  $\text{PaO}_2 \leq 55\text{mmHg}$  or  $\text{SaO}_2 \leq 88\%$  and has been shown to increase lifespan.

### **Use in acute conditions**

Oxygen is widely used in emergency medicine, both in hospital and by emergency medical services or advanced first aiders.

In the pre-hospital environment, high flow oxygen is definitively indicated for use in resuscitation, major trauma, anaphylaxis, major haemorrhage, shock, active convulsions and hypothermia.

It may also be indicated for any other patient where their injury or illness has caused hypoxaemia, although in this case oxygen flow should be moderated to achieve target oxygen saturation levels, based on pulse oximetry (with a target level of 94-98% in most patients, or 88-92% in COPD patients).

For personal use, high concentration oxygen is used as home therapy to abort cluster headache attacks, due to its vaso-constrictive effects.

## ***Storage and sources***



Gas cylinders containing oxygen to be used at home. When in use a pipe is attached to the cylinder's regulator and then to a mask that fits over the patient's nose and mouth.



A home oxygen concentrator *in situ* in an emphysema patient's house. The model shown is the DeVILBISS LT 4000.

Oxygen can be separated by a number of methods, including chemical reaction and fractional distillation, and then either used immediately or stored for future use. The main types sources for oxygen therapy are:

1. Liquid storage - Liquid oxygen is stored in chilled tanks until required, and then allowed to boil (at a temperature of 90.188 K ( $-182.96\text{ }^{\circ}\text{C}$ )) to release oxygen as a gas. This is widely used at hospitals due to their high usage requirements, but can also be used in other settings.
2. Compressed gas storage - The oxygen gas is compressed in a gas cylinder, which provides a convenient storage, without the requirement for refrigeration found

with liquid storage. Large oxygen cylinders hold 6,500 litres (230 cu ft) and can last about two days at a flow rate of 2 litres per minute. A small portable M6 (B) cylinder holds 164 or 170 litres (5.8 or 6.0 cu ft) and weighs about 1.3 to 1.6 kilograms (2.9 to 3.5 lb). These tanks can last 4–6 hours when used with a conserving regulator, which senses the patient's breathing rate and sends pulses of oxygen. Conserving regulators may not be usable by patients who breathe through their mouths.

3. Instant usage - The use of an electrically powered oxygen concentrator or a chemical reaction based unit can create sufficient oxygen for a patient to use immediately, and these units (especially the electrically powered versions) are in widespread usage for home oxygen therapy and portable personal oxygen, with the advantage of being continuous supply without the need for additional deliveries of bulky cylinders.

## ***Delivery***

Various devices are used for administration of oxygen, from whichever source. In most cases, the oxygen will first pass through a pressure regulator, used to control the high pressure of oxygen delivered from a cylinder (or other source) to a lower pressure. This lower pressure is then controlled by a flowmeter, which may be preset or selectable, and this controls the flow in a measure such as litres per minute (lpm). The typical flowmeter range for medical oxygen is between 0 and 15 lpm with some units able to obtain up to 25 liters per minute. Many wall flowmeters using a "thorpe tube" style design are able to be dialed to "flush" which is beneficial in emergency situations.

## Supplemental oxygen



A patient wearing a simple face mask

Many patients require only a supplementary level of oxygen in the room air they are breathing, rather than pure or near pure oxygen, and this can be delivered through a number of devices dependant on the situation, flow required and in some instances patient preference.

A nasal cannula (NC) is a thin tube with two small nozzles that protrude into the patient's nostrils. It can only comfortably provide oxygen at low flow rates, 2-6 litres per minute (LPM), delivering a concentration of 24-40%.

There are also a number of face mask options, such as the simple face mask, often used at between 6 and 12 LPM, with a concentration of oxygen to the patient of between 28% and 50%. This is closely related to the more controlled air-entrainment masks, also known as Venturi masks, which can accurately deliver a predetermined oxygen concentration to the trachea up to 40%.

In some instances, a partial rebreathing mask can be used, which is based on a simple mask, but featuring a reservoir bag, which increases the provided oxygen rate to 40-70% oxygen at 5 to 15 LPM.

## **High flow oxygen delivery**

In cases where the patient requires a flow of up to 100% oxygen, a number of devices are available, with the most common being the non-rebreather mask (or reservoir mask), which is similar to the partial rebreathing mask except it has a series of one-way valves preventing exhaled air from returning to the bag. There should be a minimum flow of 10 L/min. The delivered FIO<sub>2</sub> of this system is 60-80%, depending on the oxygen flow and breathing pattern. High flows of warmed and humidified air/oxygen blends can also be delivered via a nasal cannula, allowing the patient to continue to talk, eat and drink while still receiving the therapy.

In specialist applications such as aviation, tight fitting masks can be used, and these also have applications in anaesthesia, carbon monoxide poisoning treatment and in hyperbaric oxygen therapy

## **Positive pressure delivery**

Patients who are unable to breathe on their own will require positive pressure to move oxygen in to their lungs for gaseous exchange to take place. Systems for delivering this vary in complexity (and cost), starting with a basic pocket mask adjunct which can be used by a basically trained first aider to manually deliver artificial respiration with supplemental oxygen delivered through a port in the mask.

Many emergency medical service and first aid personnel, as well as hospitals, will use a bag-valve-mask (BVM), which is a malleable bag attached to a face mask (or invasive airway such as an endotracheal tube or laryngeal mask airway), usually with a reservoir bag attached, which is manually manipulated by the healthcare professional to push oxygen (or air) in to the lungs. This is the only procedure allowed for initial treatment of cyanide poisoning in the UK workplace.

Automated versions of the BVM system, known as a resuscitator or pneupac can also deliver measured and timed doses of oxygen direct to patient through a facemask or airway. These systems are related to the anaesthetic machines used in operations under general anaesthesia that allows a variable amount of oxygen to be delivered, along with other gases including air, nitrous oxide and inhalational anaesthetics.

## **As a drug delivery route**

Oxygen therapy can also be used as part of a strategy for delivering drugs to a patient, with the usual example of this being through a nebulizer mask, which delivers nebulizable drugs such as salbutamol or epinephrine into the airways by creating a vapor-mist from the liquid form of the drug.

## **Filtered oxygen masks**

Filtered oxygen masks have the ability to prevent exhaled, potentially infectious particles from being released into the surrounding environment. These masks are normally of a closed design such that leaks are minimized and breathing of room air is controlled through a series of one-way valves. Filtration of exhaled breaths is accomplished either by placing a filter on the exhalation port, or through an integral filter that is part of the mask itself. These masks first became popular in the Toronto (Canada) healthcare community during the 2003 SARS Crisis. SARS was identified as being respiratory based and it was determined that conventional oxygen therapy devices were not designed for the containment of exhaled particles.,, Common practices of having suspected patients wear a surgical mask was confounded by the use of standard oxygen therapy equipment. In 2003, the HiOx<sup>80</sup> oxygen mask was released for sale. The HiOx<sup>80</sup> mask is a closed design mask that allows a filter to be placed on the exhalation port. Several new designs have emerged in the global healthcare community for the containment and filtration of potentially infectious particles. Other designs include the ISO-O<sub>2</sub> oxygen mask, the Flo<sub>2</sub>Max oxygen mask, and the O-Mask. The use of oxygen masks that are capable of filtering exhaled particles is gradually becoming a recommended practice for pandemic preparation in many jurisdictions.

Because filtered oxygen masks use a closed design that minimizes or eliminates inadvertent exposure to room air, delivered oxygen concentrations to the patient have been found to be higher than conventional non-rebreather masks, approaching 99% using adequate oxygen flows. Because all exhaled particles are contained within the mask, nebulized medications are also prevented from being released into the surrounding atmosphere, decreasing the occupational exposure to healthcare staff and other patients.

## ***Negative effects***

Many EMS protocols indicate that oxygen should not be withheld from any patient, while other protocols are more specific or circumspect. However, there are certain situations in which oxygen therapy is known to have a negative impact on a patient's condition.

Oxygen should never be given to a patient who is suffering from paraquat poisoning unless they are suffering from severe respiratory distress or respiratory arrest, as this can increase the toxicity. (Paraquat poisoning is rare - for example 200 deaths globally from 1958–1978). Oxygen therapy is not recommended for patients who have suffered pulmonary fibrosis or other lung damage resulting from bleomycin treatment.

High levels of oxygen given to infants causes blindness by promoting overgrowth of new blood vessels in the eye obstructing sight. This is retinopathy of prematurity (ROP).

Oxygen has vasoconstrictive effects on the circulatory system, reducing peripheral circulation and was once thought to potentially increase the effects of stroke. However, when additional oxygen is given to the patient, additional oxygen is dissolved in the plasma according to Henry's Law. This allows a compensating change to occur and the

dissolved oxygen in plasma supports embarrassed (oxygen-starved) neurons, reduces inflammation and post-stroke cerebral edema. Since 1990, hyperbaric oxygen therapy has been used in the treatments of stroke on a worldwide basis. In rare instances, hyperbaric oxygen therapy patients have had seizures. However, because of the aforementioned Henry's Law effect of extra available dissolved oxygen to neurons, there is usually no negative sequel to the event. Such seizures are generally a result of oxygen toxicity, although hypoglycemia may be a contributing factor, but the latter risk can be eradicated or reduced by carefully monitoring the patient's nutritional intake prior to oxygen treatment.

Oxygen first aid has been used as an emergency treatment for diving injuries for years. Recompression in a hyperbaric chamber with the patient breathing 100% oxygen is the standard hospital and military medical response to decompression illness. The success of recompression therapy as well as a decrease in the number of recompression treatments required has been shown if first aid oxygen is given within four hours after surfacing. There are suggestions that oxygen administration may not be the most effective measure for the treatment of decompression illness and that heliox may be a better alternative.

### **Chronic obstructive pulmonary disease**

Care needs to be exercised in patients with chronic obstructive pulmonary disease, such as emphysema, especially in those known to retain carbon dioxide (type II respiratory failure). Such patients may further accumulate carbon dioxide and decreased pH (hypercapnation) if administered supplemental oxygen, possibly endangering their lives. This is primarily as a result of ventilation–perfusion imbalance. In the worst case, administration of high levels of oxygen in patients with severe emphysema and high blood carbon dioxide reduces respiratory drive to the point of precipitating respiratory failure, and eventual death. However the risk of the loss of respiratory drive are far outweighed by the risks of withholding emergency oxygen, and therefore emergency administration of oxygen is never contraindicated. Transfer from field care to definitive care, where oxygen use can be carefully calibrated, typically occurs long before significant reductions to the respiratory drive.

A recent study has shown that titrated oxygen therapy (controlled administration of oxygen) may be more appropriate for COPD patients, and less of a danger to them. The study also showed that other, non-COPD patients, may also, in some cases, benefit more from titrated therapy. However, the results are not conclusive, and may have no statistical relevance when adjusted for proper protocol usage.

### **Fire risk**

Highly concentrated sources of oxygen promote rapid combustion. Fire and explosion hazards exist when concentrated oxidants and fuels are brought into close proximity; however, an ignition event, such as heat or a spark, is needed to trigger combustion. Oxygen itself is not the fuel, but the oxidant. Combustion hazards also apply to

compounds of oxygen with a high oxidative potential, such as peroxides, chlorates, nitrates, perchlorates, and dichromates because they can donate oxygen to a fire.

Concentrated O<sub>2</sub> will allow combustion to proceed rapidly and energetically. Steel pipes and storage vessels used to store and transmit both gaseous and liquid oxygen will act as a fuel; and therefore the design and manufacture of O<sub>2</sub> systems requires special training to ensure that ignition sources are minimized.

Hospitals in some jurisdictions, such as the UK, now operate “no- smoking” policies, which although introduced for other reasons, supports the aim of keeping ignition sources away from medical piped oxygen. Other recorded sources of ignition of medically prescribed oxygen include candles, aromatherapy, medical equipment, cooking, and unfortunately, deliberate vandalism. Smoking pipes, cigars and cigarettes are of special concern. This does not entirely eliminate the risk of injury with portable oxygen systems, especially if compliance is poor.

### ***Oxygen therapy while on aircraft***

In the United States, most airlines restrict the devices allowed on board aircraft. As a result passengers are restricted in what devices they can use. Some airlines will provide cylinders for passengers with an associated fee. Other airlines allow passengers to carry on approved portable concentrators. However the lists of approved devices varies by airline so passengers need to check with any airline they are planning to fly on. Passengers are generally not allowed to carry on their own cylinders. In all cases, passengers need to notify the airline in advance of their equipment.

## Chapter 26

# Vision Therapy

**Vision therapy**, also known as **visual training**, **vision training**, or **visual therapy**, is a broad group of techniques aimed at correcting and improving binocular, oculomotor, visual processing, and perceptual disorders."

### ***Historical development***

Various forms of visual therapy have been used for centuries. The concept of vision therapy was introduced in the late nineteenth century for the non-surgical treatment of misaligned eyes (strabismus). This early and traditional form of vision therapy is what is now known as 'orthoptics' - although this term does not limit the work of Orthoptists who today often work beyond the realm of strabismus. Collaboration of some Eye care professionals with educators and neuroscientists produced an expansion of vision therapy into the treatment of other eye coordination (binocular) deficits as well as dysfunctions in visual focusing, perception, tracking and motor skills.

As a result of this expansion and ensuing confusion over what the term "vision therapy" includes, there is some controversy as to the use of vision therapy for individuals with learning disorders.

### ***Current definitions in clinical practice***

Vision Therapy encompasses a wide variety of non-surgical methods which some have divided into two broad categories based on their clinical acceptance and general practice by eyecare professionals:

- 1) **Orthoptic Vision Therapy**, also known as orthoptics.

It may be prescribed to patients with problems of visual related skills required for reading, eye strain, visually-induced headaches, strabismus and/or diplopia. It is commonly practiced by optometrists and behavioral optometrists - however, more specialized problems are co-managed between orthoptists and ophthalmologists.

- 2) **Behavioral Vision Therapy**, or **Visual Integration Vision Therapy** (also known as behavioral or developmental optometry).

Behavioural Vision Therapy does not limit itself to disorders of the visual system. For example, Behavioral Optometrists hold that the sensitivity of a professional athlete's peripheral vision on the playing field may have enhanced responsiveness to fast moving objects with vision therapy, beyond the normal realm general improvement with practicing their sport. Ophthalmologists and orthoptists do not endorse these exercises as having clinically significant validity for improvements in vision. Usually, they see these perceptual-motor activities being in the sphere of either speech therapy, occupational therapy or physical therapy.

### ***Orthoptic visual therapy***

Orthoptics aims to treat binocular vision disorders such as strabismus, and diplopia. Key factors involved include: Eye Movement Control, Simultaneous Focus at Far, Sustaining Focus at Far, Simultaneous Focus at Near, Sustaining Focus at Near, Simultaneous Alignment at Far, Sustaining Alignment at Far, Simultaneous Alignment at Near, Sustaining Alignment at Near, Central Vision (Visual Acuity) and Depth Awareness.

Some of the exercises used are:

- Near point of convergence exercises (i.e. "pencil push-ups"),
- Base-out prism reading, stereogram cards, computerized training programs are used to improve fusional vergence.
- The wearing of convex lenses
- The wearing of concave lenses
- "Cawthorne Cooksey Exercises" also employ various eye exercises, however, these are designed to alleviate vestibular disorders, such as dizziness, rather than eye problems.
- Antisuppression exercises - this is being less commonly practiced, although occasionally it may be used.

There is widespread acceptance of orthoptic therapy indications for:

- Convergence insufficiency. Patients who experience eyestrain, "tired" eyes, or diplopia (double vision) while reading or performing other near work, and who have convergence insufficiency may benefit from orthoptic treatment. Patients whose outward drift occurs at distance rather than at near distance are less ideal candidates for treatment.
- Intermittent exotropia. This is often linked to convergence insufficiency.

Convergence insufficiency is a common binocular vision disorder characterized by asthenopia, eye fatigue and discomfort. Asthenopia may be aggravated by close work and is thought by some to contribute to reading inefficiency. In 2005, the Convergence Insufficiency Treatment Trial (CITT) published two large, randomized clinical studies examining the efficacy of orthoptic vision therapy in the treatment of symptomatic convergence insufficiency. Although neither study examined reading efficiency or comprehension, both demonstrated that in-office vision therapy was more effective than

"pencil pushups" (a commonly prescribed home-based treatment) for improving the symptoms of asthenopia and the convergence ability of the eyes. The design and results of at least one of these studies has been met with some reservation, questioning the conclusion as to whether intensive office-based treatment programs are truly more efficacious than a properly implemented home-based regimen. The CITT has since published articles validating its research and treatment protocols. Its most recent publication suggested that home-based computer therapy combined with office based vision therapy is more effective than pencil pushups or home-based computerised therapy alone for the treatment of symptomatic convergence insufficiency.

### ***Behavioural visual therapy***

Behavioral vision therapy is practiced primarily by optometrists who specialize in this field. Behavioural VT aims to treat problems including difficulties of visual attention and concentration, which may manifest themselves as an inability to sustain focus or to shift focus from one area of space to another.

This includes vision therapy for: Peripheral Vision, Color Perception, Gross Visual-Motor, Fine Visual-Motor, and Visual Perception.

Some of the exercises involve the use of:

- Marsden balls
- Rotation trainers
- Syntonics
- Balance board/beams
- Saccadic fixators
- Directional sequencers

Major optometric organizations, including the American Optometric Association, the American Academy of Optometry, the College of Optometrists in Vision Development, and the Optometric Extension Program, support the assertion that non-strabismic visual therapy does not directly treat learning disorders, but rather addresses underlying visual problems which are claimed to affect learning potential.

Major organizations, including the International Orthoptic Association and the American Academy of Ophthalmology have alternatively so far concluded that there is no current validity for clinically significant improvements in vision with Behavioural Vision Therapy, therefore they do not practice it.

Advocates cite a number of indications for the use of non-strabismic vision therapy. Some assert that poor eye tracking affects reading skills, and that improving tracking can improve reading.

## **Efficacy of behavioural visual therapy**

In 1988, a review of 238 scientific articles was published in the *Journal of the American Optometric Association* widely defined vision therapy as "a clinical approach for correcting and ameliorating the effects of eye movement disorders, non-strabismic binocular dysfunctions, focusing disorders, strabismus, amblyopia, nystagmus, and certain visual perceptual (information processing) disorders." - and thereby did not discriminate between orthoptic and behavioural visual therapy. The paper was positive about vision therapy generally: "It is evident from the research that there is scientific support for the efficacy of vision therapy in modifying and improving oculomotor, accommodative, and binocular system disorders, as measured by standardized clinical and laboratory testing methods for patients of all ages for whom it is properly undertaken and employed."

A more recent (2005) review concluded less positively that: "*Less robust, but believable, evidence indicates visual training may be useful in developing fine stereoscopic skills and improving visual field remnants after brain damage. As yet there is no clear scientific evidence published in the mainstream literature supporting the use of eye exercises in the remainder of the areas reviewed, and their use therefore remains controversial.*"

In 2006, noted neurologist Oliver Sacks published a case study about "Stereo Sue", a woman who had regained her stereo vision, absent for 48 years, after undergoing vision therapy. The article was published in *The New Yorker* magazine, which is fact-checked but not peer-reviewed, very few details were given of the exact therapies used and the article discussed only one case of stereo rehabilitation. However, the woman described by Sacks, Susan Barry, a neurobiology professor at Mt. Holyoke College, subsequently published a book, "Fixing My Gaze." The book discusses multiple case histories and details the therapy procedures and the science underlying them.

A systematic review of the literature on the effects of vision therapy on visual field defects published in 2007 concluded that it was unclear to what extent patients benefited from vision restoration therapy (VRT) as "no study has given a satisfactory answer." The authors concluded that *scanning compensatory therapy* (SCT) seemed to provide a more successful rehabilitation, and simpler training techniques, therefore they recommended SCT until the effects of VRT could be defined.

A 2008 review of the literature concluded that "there is a continued paucity of controlled trials in the literature to support behavioural optometry approaches. Although there are areas where the available evidence is consistent with claims made by behavioural optometrists ... a large majority of behavioural management approaches are not evidence-based, and thus cannot be advocated."

Other than for strabismus (such as intermittent exotropia) and convergence insufficiency, the consensus among *ophthalmologists*, *orthoptists* and *pediatricians* is that non-strabismic visual therapy lacks documented evidence of effectiveness. In 1998, the American Academy of Pediatrics, American Academy of Ophthalmology, and American

Association for Pediatric Ophthalmology and Strabismus issued a policy statement regarding the use of vision therapy specifically for the treatment of *learning problems* and *dyslexia*. According to the statement: "No scientific evidence exists for the efficacy of eye exercises ('vision therapy')... in the remediation of these complex pediatric neurological conditions." More recently, in 2004, the American Academy of Ophthalmology released a position statement asserting that there is no evidence that vision therapy retards the progression of *myopia*, no evidence that it improves visual function in those with *hyperopia* or *astigmatism*, or that it improves *vision lost through disease processes*. This was also supported by the International Orthoptic Association.

The Joint Statement mentioned above was criticised at the time by Merrill Bowan, a vision therapy enthusiast, for being biased, with the author of a rebuttal concluding "The AAP/AAO/AAPOS paper contains errors and internal inconsistencies. Through highly selective reference choices, it misrepresents the great body of evidence from the literature that supports a relationship between visual and perceptual problems as they contribute to classroom difficulties.". The author also states that the Joint Statement presents an unsupported opinion by implication that Optometrists claim that vision therapy cures the learning problem. A similar criticism could be levelled at the 2004 American Academy of Ophthalmology paper which implies that vision therapy is claimed to treat "vision lost through disease processes". There is a common theme that critics of vision therapy seem to do by placing vision therapy under the same banner with alternative therapies. By implication, the lack of evidence for the alternative therapies is cited as a lack of evidence for vision therapy. No supporting evidence is given that vision therapy is actually used to treat eye disease or vision lost through disease processes.

Some optometrists take a slightly different view. In 1999 a joint statement by the American Academy of Optometry, the American Optometric Association, the College of Optometrists in Vision Development and Optometric Extension Program Foundation reported: "Many visual conditions can be treated effectively with spectacles or contact lenses alone; however, some are most effectively treated with vision therapy....Research has demonstrated that vision therapy can be an effective treatment option for *ocular motility problems, non-strabismic binocular disorders, strabismus, amblyopia, accommodative disorders (and) visual information processing disorders.*"

Although skeptics assert that vision therapists may have a financial bias in proclaiming the efficacy of the practice, proponents and advocates of vision therapy claim that other eye professionals have a similar bias in rejecting its claims. In either case, most insurance companies do not cover vision therapy services, partly because of the lack of support for vision therapy in evidence-based literature.

## ***Eye exercises***

The eye exercises used in vision therapy can generally be divided into two groups; those employed for "strabismic" outcomes and those employed for "non-strabismic" outcomes, to improve eye health.

Some of the exercises used are

- Near point of convergence exercises (i.e. "pencil push-ups"),
- Base-out prism reading, stereogram cards, computerized training programs are used to improve fusional vergence.
- The wearing of convex lenses
- The wearing of concave lenses
- "Cawthorne Cooksey Exercises" also employ various eye exercises, however, these are designed to alleviate vestibular disorders, such as dizziness, rather than eye problems.
- Antisuppression exercises - this is no longer commonly practiced, although occasionally it may be used.

The eye exercises used in **Behavioural Vision Therapy**, also known as Developmental Optometry is practiced primarily by Behavioural Optometrists. Behavioural Vision Therapy therapy aims to treat problems including difficulties of **visual attention and concentration**, which may manifest themselves as an inability to sustain focus or to shift focus from one area of space to another.

Some of the exercises used are:

- Marsden balls
- Rotation trainers
- Syntonics
- Balance board/beams
- Saccadic fixators
- Directional sequencers

Ophthalmologists and orthoptists do not endorse these exercises as having clinically significant validity for improvements in vision. Usually they see these perceptual-motor activities being in the sphere of either speech therapy, occupational therapy or physical therapy.

## **Orthoptists, optometrists and ophthalmologists**

Orthoptists, optometrists and ophthalmologists primarily use eye exercises that relate to strabismus treatments.

Physical therapy

- To reduce muscle contracture in an eye muscle palsy; assess action following ocular muscle surgery or botox injection.

Fusional Amplitude and Relative Fusional Amplitude training

- Designed to alleviate convergence insufficiency. The CITT study (Convergence Insufficiency Treatment Trial) was a randomized, double blind multi-centre trial (high level of reliability) indicates that Orthoptic Vision Therapy is an effective method of treatment of convergence insufficiency (CI). Both optometry and ophthalmology were co-authors of this study.
- Designed to alleviate intermittent exotropia or other less common forms of strabismus.

The consensus among Ophthalmologists, Orthoptists and Pediatricians is that "visual training" in non-strabismic **Behavioural Vision therapy** lacks documented scientific evidence of effectiveness. Although Ophthalmologists and Orthoptists believe that exercises can improve binocular vision control, they believe it does not purely improve monocular visual acuity such as that in amblyopia (rather, occlusion is the therapy of choice), change a person's refractive error, improve general physical fitness or agility or improve intelligence. It is probable that they do not change the accommodative/convergence ratio or enable someone to develop the ability for stereopsis. It is likely that they do not change the amplitude of accommodation to postpone or delay presbyopia.

### **Behavioral Optometrists**

Practitioners in Behavioral optometry (also known as *Functional optometrists* or *optometric vision therapists*) practice methods that have been characterized as a complementary alternative medicine practice. A review in 2000 concluded that there were insufficient controlled studies of the approach and a 2008 review concluded that "a large majority of behavioural management approaches are not evidence-based, and thus cannot be advocated."

### **Other forms**

Do-it-yourself eye exercises are claimed by some to improve visual acuity by reducing or eliminating refractive errors. Such claims rely mainly on anecdotal evidence, and are not generally endorsed by orthoptists, ophthalmologists or optometrists.

## Chapter 27

# Hormone Replacement Therapy (Menopause)

**Hormone replacement therapy (HRT)** is a system of medical treatment for surgically menopausal, perimenopausal and to a lesser extent postmenopausal women. It is based on the idea that the treatment may prevent discomfort caused by diminished circulating estrogen and progesterone hormones. It involves the use of one or more of a group of medications designed to artificially boost hormone levels. The main types of hormones involved are estrogens, progesterone or progestins, and sometimes testosterone. It often referred to as "treatment" rather than therapy.

### **Overview**

HRT is available in various forms. It generally provides low dosages of one or more estrogens, and often also provides either progesterone or a chemical analogue, called a progestin. Testosterone may also be included. In women who have had a hysterectomy, an estrogen compound is usually given without any progesterone, a therapy referred to as "unopposed estrogen therapy". HRT may be delivered to the body via patches, tablets, creams, troches, IUDs, vaginal rings, gels or, more rarely, by injection. Dosage is often varied cyclically, with estrogens taken daily and progesterone or progestins taken for about two weeks every month or two; a method called "sequentially combined HRT" or scHRT. An alternate method, a constant dosage with both types of hormones taken daily, is called "continuous combined HRT" or ccHRT, and is a more recent innovation. Sometimes an androgen, generally testosterone, is added to treat diminished libido. It may also treat reduced energy and help reduce osteoporosis after menopause.

HRT is often given as a short-term relief (often one or two years, usually less than five) from menopausal symptoms (hot flashes, irregular menstruation, fat redistribution etc.). Younger women with premature ovarian failure or surgical menopause may use hormone replacement therapy for many years, until the age that natural menopause would be expected to occur.

Attitudes towards HRT changed in 2002 following the announcement by the Women's Health Initiative of the National Institutes of Health that those receiving the treatment (Prempro) in the main part of their study had a larger incidence of breast cancer, heart attacks and strokes. The WHI findings were reconfirmed in a larger national study done

in the UK, known as The Million Women Study. As a result of these findings, the number of women taking hormone treatment dropped precipitously. As a result of these findings, the Women's Health Initiative recommended that women with normal rather than surgical menopause should take the lowest feasible dose of HRT for the shortest possible time to avoid these risks.

### ***Risks and benefits***

Proprietary mixtures of conjugated equine estrogens (CEE, Premarin is one such CEE), estrogens derived from the urine of pregnant horses, have been a common prescribed form of HRT, as well as progestins. As the most common and longest-prescribed type of HRT, the majority of studies of HRT involve CEE. More recent forms of drug delivery have been researched, including suppositories, subdermal implants, skin patches and gels rather than pills or injections, which allow more local effect, lower doses, fewer side effects and a constant rather than cyclical level of hormones within the blood.

Comparisons between a pill and transdermal patch suggests that when estrogens are taken orally the risks of thrombophlebitis and pulmonary embolism are increased, an effect which is not seen in with transdermal administration (this effect refers only to patches that contain estradiol for hormone replacement, and has no bearing on the patches used for birth control, which contain ethinyl estradiol). Transdermal drugs enter the bloodstream directly and unlike oral estrogens are not modified by the liver before being absorbed (modification by the liver is believed to be the reason for the increased risks). Once considered protective of the cardiovascular system, the large-scale, randomized, placebo controlled studies in the Women's Health Initiative found that conventional hormone therapy with CEE actually increased the risk of heart disease, strokes, emboli and breast cancer while offering only mild protection against osteoporosis and colorectal cancer. Unopposed estrogen (the supplementation of endogenous estrogens without a progestagen) can also result in endometrial hyperplasia, a precursor to endometrial cancer. The extensive use of high-dose estrogens for birth control in the 1970s is thought to have resulted in a significant increase in the incidence of this type of cancer.

HRT may also be effective at reversing the effects of aging on muscle and/or promoting reverse cholesterol transport (RCT) via the induction of cholesterol ABC transporters.

Women have also pursued alternative interventions which do not involve estrogen supplementation. Due to the risks and potential problems of progestins and equine estrogens, a number of alternative therapies have been presented, including lifestyle changes and phytoestrogens (plants and food supplements believed to alleviate the symptoms of menopause due to estrogen-like compounds). However, systemic reviews of the research on phytoestrogens demonstrated that these compounds are not effective. Bioidentical hormone replacement therapy has also been inaccurately promoted as a panacea and an alternative to conventional HRT, but bioidentical hormones are derived from the same sources as nonbioidentical molecules, have been used in FDA-approved drugs for many years, lack a research base demonstrating their risks or benefits, are expected to have the same risks and benefits as conventional HRT, and frequently

associated with the expensive, unnecessary and potentially dangerous practice of compounding .

### ***Bioidentical hormone replacement therapy***

Bioidentical hormone replacement therapy refers to the use of hormones that are chemically identical to those produced in a woman's body, though they are also associated with the practices of pharmaceutical compounding and saliva testing to determine, and adjust a woman's hormone levels (the latter two practices are extremely controversial - compounding has not demonstrated any benefits and presents risks of uncertain dosing, potency and possible contamination; saliva testing is considered to have no merit due to the natural fluctuations in hormone levels and the lack of support for a specific dosage of hormones being ideal). Proponents also claim that BHRT can offer advantages beyond those typical of traditional HRT, though there is no evidence to support these claims. The United States Food and Drug Administration states that BHRT is expected to present the same risks and benefits of non-bioidentical HRT, but that traditional products have been researched to quantify these risks and benefits, and are produced by manufacturers with stringent purity and potency standards.

### ***Results of the WHI hormone replacement therapy studies***

Clinical medical practice changed rapidly and dramatically with the results of the two parallel WHI studies of postmenopausal HRT. Prior studies were much smaller, and many were studies of women who were electively taking hormones. This self-selected group tended to be composed of women who were more health-conscious, which was a possible factor to explain why these women tended to be healthier than the average. The WHI studies were the first large, double-blind, placebo-controlled clinical trials of HRT in healthy, postmenopausal women. The WHI estrogen-plus-progestin trial and estrogen-alone trial were both halted early (in July 2002 and February 2004 respectively) because preliminary study results indicated that the health risks of the conjugated equine estrogen and progestin exceeded benefits.

The first report on the halted WHI estrogen-plus-progestin study came out in July 2002. It followed over 16 000 women for an average of 5.2 years, half of which taking a placebo, the other half taking PremPro, a combination of the progestin medroxyprogesterone acetate and conjugated equine estrogens. The study found statistically significant increases in rates of breast cancer, coronary heart disease, strokes and pulmonary emboli. The study also found statistically significant decreases in rates of hip fracture and colorectal cancer. "A year after the study was stopped in 2002, an article was published indicating that estrogen plus progestin also increases the risks of dementia." The conclusion of the study was that the HRT combination presented risks that outweighed its measured benefits. The results were almost universally reported as risks and problems associated with HRT in general, rather than with PremPro, the specific proprietary combination of conjugated equine estrogen and progestin studied.

The increase in risks of coronary heart disease in the PremPro arm of the study varied according to age and years since the onset of menopause. Women aged 50 to 59 using HRT showed a small trend towards lower risk of coronary heart disease, as did women who were within five years of the onset of menopause.

The adverse cardiovascular outcomes may only apply to oral dosing with the progestin and equine estrogens in Prempro, while other types of HRT such as topical estradiol and estriol may not produce the same risks. Results from other studies suggest that when estrogen is administered orally, liver function is altered and the risk of blood clots is increased.

The WHI preliminary results in 2004 found a non-significant trend in the estrogen-alone clinical trial towards a reduced risk of breast cancer and a 2006 update concluded that use of estrogen-only HRT for 7 years does not increase the risk of breast cancer in postmenopausal women who have had a hysterectomy. The results of the WHI estrogen-alone trial suggest that the progestin used in the WHI estrogen-plus-progestin trial increased the risk for breast cancer above that associated with estrogen alone.

After the increased clotting found in the first WHI results was reported in 2002, a large number of women who had been taking the proprietary mixtures of equine estrogens and progestins studied (Prempro) ceased filling their prescriptions. The number of Prempro prescriptions filled was abruptly cut almost in half. A number of women started taking alternatives to Prempro, such as bioidentical hormones. A sharp drop in breast cancer rates was observed following these changes, and held steady in subsequent years.

### ***Recent findings***

According to a 2007 presentation at an American Academy of Neurology meeting, hormone therapy taken soon after menopause may help protect against dementia, even though it raises the risk of mental decline in women who do not take the drugs until they are older. Dementia risk was 1% in women who started HRT early, and 1.7% in women who didn't, (e.g. women who didn't take it seem to have had—on average—a 70% higher relative risk of dementia). This is consistent with research that hormone therapy improves executive and attention processes in postmenopausal women. It is also supported by research upon monkeys that were given ovariectomies to imitate the effect of menopause and then estrogen therapies. This showed replacement treated compared to nontreated monkeys had long term improved prefrontal cortex executive abilities on the Wisconsin card sort task.

Another recent randomized controlled trial found HRT may actually prevent the development of heart disease and reduce the incidence of heart attack in women between 50 and 59, but not for older women. The mechanism may have something to do with the contradictory effects of increasing propensity for clotting, versus improving both "good" and "bad" cholesterol concentrations in the blood (which would have a protective effect). Followup studies are being performed which are intended to confirm these findings. The increased risk of breast cancer remains.

A recent large well-designed randomized controlled trial recently showed that increased breast cancer risk applies only to those women who take progesterone analogues (as was done in the WHI) but not to those taking progesterone itself

## ***Contraindications***

### **Absolute contraindications**

- Undiagnosed vaginal bleeding
- Severe liver disease
- Pregnancy
- Coronary artery disease (CAD)
- Venous thrombosis
- Well-differentiated and early endometrial cancer (once treatment for the malignancy is complete, is no longer an absolute contraindication.) Progestins alone may relieve symptoms if the patient is unable to tolerate estrogens.

### **Relative contraindications**

- Migraine headaches
- Personal history of breast cancer
- History of uterine fibroids
- Atypical ductal hyperplasia of the breast
- Active gallbladder disease (cholangitis, cholecystitis)