

The History of Medicine

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Published 7 November 2016

Preface

This paper was written in order to examine the order of discovery of the significant developments in the history of medicine. It is part of my efforts to put the study of social and cultural history and social change on a scientific basis capable of rational analysis and understanding. This has resulted in a hard copy book *How Change Happens: A Theory of Philosophy of History, Social Change and Cultural Evolution* and a number of websites such as [How Change Happens](#) and [How Change Happens Rochelle Forrester's Social Change, Cultural Evolution and Philosophy of History website](#). There are also papers on [Academia.edu](#), [Figshare](#), [Mendeley](#), [Vixra](#) and [Social Science Research Network](#) websites and other papers on the [Discovery of Agriculture](#), [the Discovery of the Atomic World and the Constituents of Matter](#), and on [Guttman Scale Analysis and its use to explain Cultural Evolution and Social Change](#). Other papers by Rochelle Forrester include, [Rochelle's Philosophy Website](#), and works on Epistemology and the Philosophy of Perception such as [Sense Perception and Reality](#) and on [Slideshare](#), [Issuu](#) and [Scribd](#) and Rochelle Forrester is a member of the [International Network for Theory of History](#).

Abstract

This paper was written to study the order of medical advances throughout history. It investigates changing human beliefs concerning the causes of diseases, how modern surgery developed and improved methods of diagnosis and the use of medical statistics. Human beliefs about the causes of disease followed a logical progression from supernatural causes, such as the wrath of the Gods, to natural causes, involving imbalances within the human body. The invention of the microscope led to the discovery of microorganisms which were eventually identified as the cause of infectious diseases. Identification of the particular microorganism causing a disease led to immunization against the disease. Modern surgery only developed after the ending of the taboo against human dissection and the discovery of modern anesthesia and the discovery of the need for anti-septic practices. Modern diagnostic practices began with the discovery of x-rays and the invention of medical scanners. Improved mathematics, especially in probability theory, led to statistical studies which led to a much greater ability, to identify the causes of disease, and to evaluate the effectiveness of treatments. These discoveries all occurred in a necessary and

inevitable order with the easiest discoveries being made first and the harder discoveries being made later. The order of discovery determined the course of the history of medicine and is an example of how social and cultural history has to follow a particular course determined by the structure of the world around us.

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Introduction

Illness and injury are as old as humankind. Stone Age human remains show evidence of diseases such as arthritis, tuberculosis, inflammations, dental problems, leprosy bone tumours, scurvy, spinal tuberculosis, cleft spine, osteomyelitis, sinusitis and various congenital abnormalities and injuries. These diseases show in human skeletal remains and if more complete human remains were available, it is likely a much greater range of disease would be apparent. Given that human beings do not like pain, death and suffering there was a clear need to try and find a cure for diseases and injuries.

The curing and prevention of disease often involves an explanation of the cause of the disease. In the absence of knowledge of germs, bacteria and viruses and of human anatomy and physiology stone age humans ascribed disease, injuries and death to supernatural forces, just as other inexplicable events such as storms, earthquakes and volcanic eruptions were considered to be caused by supernatural forces. This led to the need for a method of influencing the supernatural forces which required a person with knowledge of the supernatural world who could communicate with and placate the gods or spirits that caused the disease and injury. Priests, shamans, witch doctors and medicine men were often responsible for protecting the health of Stone Age humans by means of appropriate rituals and spells. A cave painting of what is considered to be a Stone Age medicine man dating from around 15,000 BCE is on the cave walls of the *Les Trois Freres* cave in the Pyrenees.

Stone Age medicine men would most likely have supplemented their spells and rituals with the use of various herbs, roots, leaves and animal parts and other medicines. Given the body's natural tendency to heal itself and placebo effects, it would have been difficult for pre-historic healers to work out whether their spells and herbs were actually working. Only in recent times with modern written records, statistical techniques and double blind studies involving control groups, can it be reasonably clear if a particular medicine is working.

The earliest clear example of a surgical operation is trepanning which involves boring a hole into the skull. This operation was first carried out in Neolithic times using stone tools. Some of the patients survived as shown by healing around the holes and some skulls even had several holes bored in them, indicating repeated operations. It is not clear why such a painful operation was carried out, but it may have been to allow evil spirits that were causing migraines, epilepsy or madness to escape from the patient's skull. It is also likely other surgical operations, such as the lancing of abscesses and the sewing up of wounds with bone or flint needles, were performed, but there is no clear evidence of this.

When nomadic hunter-gatherers first began to settle in permanent villages, which grew into towns and then cities, new health problems arose. Large numbers of people concentrated in small areas meant disease would quickly spread through populations. The domestication of animals resulted in many diseases spreading from animals to humans such as measles, smallpox and tuberculosis from cattle and flu from pigs and dogs. However a further result from living in cities was the development of writing which allowed a more organized medical profession and the possibility of accurate recording of symptoms and remedies.

Writing began in Mesopotamia before 3,000 BCE when it was invented by the ancient Sumerians. The Sumerians wrote on clay tablets and one such tablet contains lists of drugs, chemical substances and plants used for medical purposes. Magic and religion however played a major role in Mesopotamian medicine as injury and disease were considered to be caused by Gods, demons, evil spirits and witchcraft. Numerous magic spells, incantations and sacrifices were available to combat particular diseases and

correct recitation was necessary for an effective cure. Whether a patient would survive or not could be divined by examining the liver of a sacrificed sheep or goat. The Code of Hammurabi, a law code made by a Babylonian King, sets out medical fees for various services and penalties for errors made by the doctor. Services referred to involved, the opening of an abscess, the treatment of broken limbs, eyes and intestinal complaints.

Our knowledge of ancient Egyptian medicine comes from certain medical papyri and from the embalming of Egyptian dead. The papyri contain various descriptions of magic spells designed to drive out the demon causing a particular disease and of various prescriptions, including the dosage for particular diseases. Drugs used included castor oil, hartshorn, bile and fat from animals and copper sulphate. Treatment was prescribed for wounds and bruises and surgical instruments appear to have been used and broken bones were treated with splints.

The Egyptian practice of embalming and the favourable conditions of Egypt for the natural preservation of bodies shows us some of the diseases the Egyptians suffered from. Arthritis and inflammation of the periosteum and osteomyelitis were common. Spinal deformations and spinal tuberculosis, gout and virulent osteomas have been found in Egyptian mummies. Tooth decay was as common as in modern times and there is good evidence of kidney stones and gall stones, appendicitis and stomach and intestinal troubles. The lower classes in particular suffered from infectious diseases such as plague, smallpox, typhus, leprosy, malaria, amoebic dysentery and cholera and various parasitic diseases.

Egyptian physician's knowledge of anatomy was not extensive despite the practice of embalming. This is because embalming was carried out by specialist technicians and not by physicians. Knowledge of internal organs was largely limited to an awareness of their outward appearance.

Chinese Medicine

The earliest Chinese medicine, in common with most other ancient civilizations, assumed disease and illness were caused by the gods or by demons. The correct remedies for illness involved ritual exorcisms and appeals to the Gods.

A more naturalistic explanation of illness developed with the belief in Yin and Yang. The Yin and Yang principles were considered to control everything and their interaction controlled the functioning of the human body. Yin was feminine, soft, cold, moist, receptive, dark, and associated with water, while Yang was masculine, dry, hot, creative, bright, and associated with fire. Human health depended on a balance between Yin and Yang. Further factors effecting disease were wind, rain, twilight and brightness of day so there was a total of six disease making influences. Any of these six influences could upset the balance of Qi, which was a vital spirit similar to breath or air, which existed throughout the human body.

Chinese knowledge of anatomy was very limited due to a strict prohibition on the dissection of the human body. Chinese belief concerning the inner organs was largely erroneous. They believed there were five "firm" organs that acted as receiving organs and lay opposite five "hollow" organs who served the purpose of evacuation. The firm organs were the heart, spleen, lungs, liver and kidneys. The heart was considered to be the place of wisdom and judgement while the liver and the lungs were associated with the soul. The male's right kidney was seen as the source of sperm and its connection with the passage of urine was not understood. The hollow organs were the bladder, gall bladder, colon, small intestine and the stomach.

Chinese doctors attempted to make a diagnosis by studying the state of the pulse. This practice known as sphygmology involved attempting to recognize some very subtle variations in the pulse. There

were considered to be 51 different varieties of pulse which were to be taken in 11 different areas of the body. Chinese doctors were attempting to obtain far more information from the pulse, than it could possibly provide.

Acupuncture, aimed to restore the balance of Yin and Yang, and involved inserting needles into particular parts of the body. There were 388 areas of the body into which the needles could be inserted and they needed to be inserted at the correct time, based upon the weather, the time of day and the phases of the moon. The needles were left in anything from five to fifteen minutes. Acupuncture does appear to be effective for pain relief as the needles seem to make the body produce endorphins, the body's own natural painkillers. Claims have been made that acupuncture can cure many diseases including muscle, bone, respiratory and digestive disorders. A further Chinese treatment was Moxa which involved inflicting a slight burn on the skin. It was considered to be a treatment for a vast range of complaints such as diarrhoea, abdominal pains, anaemia, vertigo, nose bleeding, gout, toothaches and headaches.

Indian Medicine

Indian medicine began with the belief that illness was caused by the Gods or by demons and was a punishment for bad behaviour. Over time however other beliefs arose such as that which considered good health required a balance being kept between the elements of air, bile and mucous.

India developed surgery to a higher standard, than any of the other ancient civilizations. This was because the prohibition on human dissection which existed in Europe, China and the Arab world did not exist in India. This enabled the Indian physicians to obtain a good knowledge of human bones, muscles, blood vessels and joints. A wide variety of surgical operations was carried out, including cosmetic surgery on people who had been mutilated as part of a legal punishment. An adulterous wife could have her nose cut off as a punishment and Indian surgeons learnt how to repair the damage and replace the nose.

India is a land of many diseases and Indian doctors were familiar with 1,120 different diseases. They guessed the connection between malaria and mosquitoes, noticed that the plague was foreshadowed by the death of large numbers of rats and that flies could infect food causing intestinal disease. They were also aware that cleanliness could help in the prevention of disease.

Greco-Roman Medicine

Greek medicine derived its earliest beliefs and practices from Egypt and West Asia. Greek medicine later spread around the Mediterranean during Roman times and was to form the basis of the medical knowledge of Medieval Europe. Our knowledge of Greek medicine mainly comes from the Hippocratic writings and from Galen writing in the second century CE.

The earliest Greek medicine was based on religion. Asclepius, the son of Apollo, was able to cure disease and patients sleeping at his shrines would see the God in their dreams and receive advice on appropriate treatments. Around the sixth century BCE Greek medicine began to change with a greater emphasis on rational explanations of disease involving natural rather than supernatural causes. The Hippocratic writings, probably written by a number of authors, suggested liquids were the vital element in all living things. The human body contained four fluids or humors, phlegm, yellow bile, black bile and blood. Disease was caused by an imbalance of these fluids in the body. Such an imbalance could be caused by the weather or by extreme behaviour such as over eating or excessive drinking. The medical

practice of bleeding, which was to persist for several thousand years, originated from the belief there was an excess of blood which could be cured by releasing some blood from the body. Correct diet, bathing, exercise, sleep and sex would prevent illness. According to Hippocrates sex should be more frequent in winter and older men should have sex more frequently than younger men. He considered epilepsy was caused by an excess of phlegm. Hippocrates however tells us little about infectious diseases and anatomy as the dissection of bodies was taboo as it was considered to be a violation of the sanctity of the human body.

The classical era taboo on human dissection led to some quite erroneous views of the human body. Aristotle considered the heart was where the soul was located and was the center of thought, sense perception and controlled bodily movements. He considered the brain cooled the heart and the blood. There was however a brief period in Alexandria where due to the ancient Egyptian practice of embalming and the more recent Platonic view that the soul and not the body, was sacred, human dissection was allowed. Herophilus and Erasistratus carried out dissections that led them to discover the nerves leading to the brain. They discovered there were two different types of nerves, one, dealing with sense perception and the other with body movement. When studying the brain they discovered the cerebrum and the cerebellum and suggested the heavily folded human brain indicated humans higher intelligence compared to animals. They considered the lungs took in air that was then transferred to the arteries, the veins held blood and the heart worked like a bellows. After making significant discoveries that could only be made by human dissection, the taboo against dissection rose again delaying further progress until the 16th century. Until then, knowledge of the interior of the human body could only be guessed at from its external behaviour or by comparison with animal anatomy.

Two further theories created by the ancient Greeks were the methodic theory and the pneumatic theory. The methodic theory considered disease to be caused by a disturbance of atoms in the body and treatment involved manipulating the body by massage, bathing or exercise. The pneumatic theory considered breath to be a crucial factor in human health.

The high point of Greco-Roman medical knowledge came with Galen in the second century CE. Galen's two main areas of study were anatomy and physiology. As human dissection was illegal his anatomical studies were based on dissections of animals, particularly the Barbary ape. He did however have the assistance of his study of gladiator's wounds, a human skeleton he had seen in Alexandria and of human bodies exhumed by natural events, such as floods. Galen's work on the bone structure and muscular system were a significant advance on anything else in antiquity. His belief in Aristotle's idea that everything had a purpose led him to assume every bone, muscle and organ had a particular function and he set out to describe each bone, muscle and organ and their particular function. He described the human skeleton and muscular system with some accuracy. He put an end to Aristotle's idea that the mind was located in the heart, locating it in the brain. Galen discovered seven pairs of cranial nerves, the sympathetic nervous system and he distinguished between the sensory and motor nerves. However he also found things that did not exist. The *rete mirabile* (wonderful network) is located under the brain of many hoofed animals but is not found in humans. Yet Galen's claim that it exists in humans was accepted for some thirteen centuries.

Galen's physiology, his concept of how the human body worked, began with a vital spirit, *pneuma* taken into the body by breathing. The *pneuma* entered the lungs where it met some blood before passing into the left ventricle of the heart. The blood then flowed into the arteries and spread through the body feeding the flesh. When food entered the body it converted into blood in the liver, some of the blood then entered the veins and spread through the body and was feed into the flesh. Other blood flowed from

the liver into the right ventricle of the heart from where some of the blood entered the lungs to absorb the *pneuma*. Some of the blood in the right ventricle however passed directly into the left ventricle and from there flowed into the arteries. One problem for Galen, was that he was unable to discover how blood moved from the right ventricle to the left ventricle, which were divided by a solid muscular wall. He eventually concluded there must be tiny holes in the wall, so small they could not be seen by the human eye. Galen's system correctly realized the heart caused blood to flow through the body and that the arteries contained blood. Previously Erasistratus suggested the arteries only contained air, as the arteries of a dead body do not contain blood. Galen did not realize that the blood circulated and his suggestion of minute holes in the wall between the right and left ventricles of the heart was wrong.

Galen's pathology, his concept of illness, brought together Hippocrates theory of the four humors and Aristotle's idea of the four elements, air, fire, earth and water. Blood was considered to be warm and moist, yellow bile warm and dry, black bile cold and dry and phlegm cold and moist. Blood is associated with the heart, yellow bile with the liver, black bile with the spleen and phlegm with the brain. The following table shows how Galen brought the two ideas together.

Humor	Element	Organ	Qualities
Phlegm	Water	Brain	Cold & Wet
Blood	Air	Heart	Hot & Wet
Yellow bile	Fire	Liver	Hot & Dry
Black bile	Earth	Spleen	Dry & Cold

The table indicates the symptoms of the disease, the cause of the disease and the cure for the disease. If the patient has the symptom of being hot and perspiring, this is the quality of being hot and wet; this suggests there is an imbalance in the blood, so that bleeding is the cure. If they have a hot and dry fever, this suggests the yellow bile is out of balance, so that vomiting up the yellow bile is the cure. The humors could also affect a person's personality. An excess of phlegm would make one phlegmatic, of blood, one would be sanguine, of yellow bile, one would be choleric and of black bile, one would be melancholic.

An imbalance in the humors in particular organs could result in illness. Excessive phlegm in the bowels resulted in dysentery and an excess in the lungs caused tuberculosis. Cancer was caused by a massive imbalance in the humors. Stroke was caused by an excess of blood, jaundice by excessive yellow bile and depression by too much black bile.

Dark Ages

The fall of the Roman Empire marked the beginning of the Dark Ages in Europe. The later stages of the Roman Empire were a period of epidemic disease and population decline. The population of cities in particular was to fall and the cities paved roads, drains, aqueducts and public baths soon fell into disrepair. The decline of the cities was accompanied by a decline in classical learning which was opposed

by the new Christian church. In 391 CE a Christian mob set fire to the great library of Alexandria and murdered the pagan philosopher Hypatia. The last pagan school of learning, the academy in Athens was closed in 529 CE by order of the Emperor Justinian.

Medicine was not to escape the general decline of learning which accompanied the fall of the Roman Empire and the arrival of Christianity. There was a return to the belief that the cause of much illness was supernatural. Illness was a punishment from God for people's sins. The curing of such disease by medical practices was contrary to God's will. The only appropriate treatment was prayer and penitence. Diseases might also be caused by witchcraft, possession by demons or spells made by elves and pixies. Some of the old learning did survive, ironically in Christian monasteries where monks copied and translated classical writings. Their work mixed superstition and religion with classical learning and knowledge. Bede, (born 673 CE) an English monk famous for his *Ecclesiastical History of the English People* and one of the most learned men of the Dark Ages, also wrote on medical matters. He referred to Hippocrates and the theory of the four humors and prescribed bleeding as the appropriate treatment for hot fevers caused, as he believed by an excess of blood. But he also considered magic incantations and the wearing of magic amulets as the way to deal with spells made by pixies. There are also stories of miraculous cures such as a leper sleeping where a saint died and being cured when waking the next morning.

Not much had changed by the 12th century CE when Hildegard of Bingen began to bring together classical medical beliefs with 12th century religious beliefs. She considered the imbalance of the four humors resulted from man's ejection from the Garden of Eden. The eating of the forbidden fruit destroyed the balance of the four humors in the human body. Sin was to cause the imbalance of the humors and was therefore the cause of disease. Some of her medical beliefs could not be regarded as scientific or rational. Her cure for jaundice was to tie a live bat, first to the patient's back and then to the patient's stomach. Failing eyesight, caused by excessive lust, was to be cured by placing the skin of a fish's bladder over the patient's eyes when he goes to sleep, but it had to be taken off by midnight.

Arab medicine

The Moslem prophet Mohammed was born in 570 CE and he and his successors were to conquer an empire extending from Spain to India. The early Moslems had a tolerant attitude to Christian and Jewish minorities who were allowed to freely practice their religions. The origins of Arabian medicine lay with a heretical Christian sect known as the Nestorians. The Nestorians under threat of persecution from orthodox Christians fled eastwards toward present day Iraq and Iran. They brought with them classical texts from a range of authors including Hippocrates, Aristotle and Galen which they proceeded to translate into Arabic. At this time the Arab world had a positive attitude to new ideas and was happy to adopt the ideas of classical scholars like Aristotle and Galen.

The first great Arab medical authority was Rhazes who was born in 854 CE. Rhazes believed illness had nothing to do with evil spirits or God and that classical authorities were not above criticism. He was in frequent disagreement with Galen. He considered Galen's cure for asthma consisting of a mixture of owl's blood and wine did not work as he had tried it and found it to be useless. He questioned the belief that disease could be diagnosed by studying the patient's urine and was the first medical authority to understand the difference between measles and smallpox. Rhazes gave a full description of diseases he encountered giving his diagnosis, prognosis and treatment. His understanding of the workings of the human body were however, hindered by the Islamic prohibition on dissections of the human body.

Arabian medicine's second great authority was Avicenna (980-1037) whose book the *Cannon of Medicine* was to become the leading medical work in both Europe and the Middle East for some 600 years. Avicenna's *Cannon* includes many of the ideas of Hippocrates, Aristotle and Galen but also includes many of Avicenna's own ideas. The *Cannon* deals with a range of diseases and describes their diagnosis, prognosis and treatment. Avicenna accepted Hippocrates and Galen's theory of the four humors. Treatments included bleeding, enemas and purges while diagnosis included examining the pulse and urine. Over 700 drugs were recognized by Avicenna and the *Cannon* provided instructions on how they were to be prepared, which drugs should be used for which illness and their effects. Wounds were dealt with by cauterizing, a treatment that dates back to Ancient Egypt.

Surgery in the Arab world was not respected and surgeons were usually craftsmen. One exception to this is Albucasis (936-1013) who practiced in Cordoba in southern Spain. Albucasis wrote a book called *Tasrif* or the *Collection* which provided full accounts of surgery practiced at the time. The *Collection* was to become the standard book on surgery during medieval times. The book prescribes a range of surgical procedures including trepanning, dentistry, mastectomy and lithotomy and advocates cauterization as a treatment for a wide range of problems.

Medieval European medicine

European medicine began to move away from the supernatural explanations of disease with the founding of a medical school at Salerno. The school was probably founded in the ninth century and reached its greatest heights between the tenth and thirteenth centuries. Anatomy was taught at Salerno based on the dissection of pigs whose internal organs were thought to be similar to those of humans. *Passionarius*, a book written by Gariopontus, one of the teachers at the school, was based upon classical Greek learning while the arrival in Salerno of Constantine the African around 1075 with many Arab medical works was to greatly improve the medical knowledge at Salerno and eventually all Europe. Constantine was to spend the remainder of his life translating the Arabic texts into Latin and so bring the classical Greek authors, upon whose work Arabic medicine was based, to Europe.

The translation of Arabic medical texts into Latin continued in early medieval times so that the works of Hippocrates, Aristotle, Galen, Rhazes, Avicenna and Albucasis became well known. They soon assumed a status of great authority and their initial impact was to help free medicine from supernatural and magical explanations and cures. Their status however was eventually to hold back the improvement of European medicine as new ideas contrary to those of the Greek and Arab writers had great difficulty in obtaining acceptance.

New medical schools at Montpellier, Bologna, Paris and Padua were founded that significantly increased medical knowledge. The knowledge of anatomy improved with the occasional human dissection being performed as post-mortem examinations for judicial purposes and with occasional dissections of the bodies of executed criminals. Anatomy was also improved by Mondino de Luzzi or Mundinus who taught at Bologna. His book *Anothomia* brought a new level of knowledge of anatomy, although he did repeat many of the errors of Galen. Mundinus however did most of his dissections himself, unlike other teachers who sat on a high chair somewhat above the body reading a book supposedly describing the dissection, but probably only loosely related to it. Guy de Chaulias, the leading surgeon of the 14th century was a pupil of Mundinus.

The most dramatic medical event of the 14th century in Europe was the arrival of the Black Death. It originated in China killing up to two thirds of the population and then spread along trade routes

to Europe and the Arab world. It killed half the population of Cairo and between a quarter and a third of the population of Europe. The medical authorities in Europe had no solution to the Black Death. The idea of a contagious disease was beyond the understanding of medical knowledge in either the Arab or European world during the 14th century. The Arabs considered the Black Death was caused by evil spirits; the Europeans blamed everything from the Jews to Gods punishment for human's sins. Jews were accused of poisoning wells and entire Jewish communities were wiped out by vengeful Christians. Flagellants travelled around Europe whipping themselves for their sins hoping this would appease God. Conventional medicine of the time had no answers; bleeding, cauterizing and cleaning the air with incense were all tried and failed. Quarantining worked to some extent but the best advice was to run like the wind. The failure of conventional medicine during the Black Death led to a revival of supernatural explanations of disease.

The Renaissance

A revolution was to take place in medicine at the time of the Renaissance. It was to involve the breaking of the stranglehold classical and Arabic thought, especially Galen and Avicenna, had on medicine and its replacement by a belief in observation and experiment. One of the principal proponents of the new beliefs was Paracelsus who attacked academic learning, especially Galen and Avicenna and advocated learning from experience. His own ideas however were not much of an improvement on the classical learning. He rejected the humoral theory, but considered everything was made out of sulphur, mercury and salt. Sulphur caused inflammability, mercury volatility and salt solidity in substances. He also believed in the "doctrine of signatures" the idea that assumed plants capable of healing visibly showed their healing qualities. Heart shaped lilac leaves would cure heart disease and yellow celandine would cure jaundice.

However Paracelsus's interest in alchemy led him to some significant discoveries. He noticed the anaesthetic effects of ether and tincture of morphine which he called laudanum. He recognised that particular substances had their own individual qualities and that compounds including those substances often had some of those same qualities. He considered that each disease needed to be cured by its own remedy. The main value of Paracelsus's ideas, were in his iconoclastic attack on classical medical learning, which was held in vastly excessive reverence in Paracelsus's time. After Paracelsus it became easier to criticise established medical learning and for new ideas to be accepted.

A contemporary of Paracelsus, Fracastorius, suggested contagious disease was caused by tiny seeds invading the human body. The seeds were too small to be seen with the human eye and could find their way into the body from the air, from bodily contact or from infected clothes or bed linen. Once they had entered the human body they could multiply causing people to fall ill. Fracastorius also considered each disease was caused by its own particular seed leading Fracastorius to clearly distinguish between such contagious diseases as smallpox, measles, the plague, syphilis and typhus. Previously contagious diseases were sometimes considered to be versions of the same disease with varying degrees of intensity. Fracastorius's theory is virtually identical to the germ theory of disease but in the 16th century, without microscopes, he was unable to prove the theory. Physicians preferred other theories, such as the humoral theory, which while also unprovable at least had the support of tradition and ancient authority.

The study of anatomy was to undergo a revolution at the hands of Vesalius. Vesalius was able to dissect human corpses and this enabled him to provide a generally accurate picture of the human body.

Previously anatomy had suffered from the prohibition on human dissection that extended back to classical times, so that knowledge of human anatomy was based on animal dissections. Before Vesalius the accepted authority was Galen whose anatomical studies were based on animal dissection and whose work had acquired such a status that to question it could involve accusations of heresy.

Vesalius was able to obtain human corpses for dissection, as public authorities were prepared to allow the dissection of the corpses of executed criminals. Some physicians had previously dissected the corpses of criminals, but such was the reputation of Galen that they had not noticed or not dared to point out that the dissection of humans showed that much of what Galen had said was wrong. Vesalius's strength was that he was prepared to rely on his observations and where these contradicted Galen he was prepared to say Galen was wrong.

Vesalius's great work was the *De Humani Corporis Fabrica* usually called the *Fabrica*. It consisted of seven books, the first dealing with the skeleton, the second with the muscular system, the third with the veins and arteries, the fourth with the nervous system, the fifth with the abdominal organs, the sixth with the heart and lungs and the seventh with the brain. The *Fabrica* especially books 1 and 2 were illustrated with high quality drawings showing the various human parts in considerable detail. In book 1 Vesalius emphasises that the bones supported the human body, played an important role in movement and provided protection for other parts of the body. The illustrations in book 2 show the muscles in the order in which a person dissecting a body would see them. The upper layer of muscles, are shown then the layer below them and then the next layer and so on. Book 3 gives a good description of the arteries and veins and book 7 describes some of the structure of the brain for the first time.

The book corrected certain of Galen's errors. It questioned Galen's suggestion that blood flowed from the right ventricle of the heart to the left ventricle. Vesalius also showed that *the rete mirabile* did not exist, that the liver was not divided into five lobes, that the uterus had multiple chambers and that the pituitary was directly connected to the nose. Vesalius's expose of such errors by Galen resulted in some criticism of Vesalius's work from physicians who considered any questioning of Galen to be outrageous.

Vesalius did make some errors. His descriptions of the visceral organs (the liver, the kidney and the uterus) were based upon those of pigs and dogs. He failed to notice the pancreas, the ovaries and the adrenal glands. His description of female organs was poor, probably due to there being fewer female bodies available for dissection. Nevertheless the book still represented an enormous advance in human knowledge of anatomy.

Circulation of the Blood

Classical physicians were aware of the existence of the heart, but had little idea of its function in the human body. They realised when the heart stopped beating life would stop which led them to believe the heart had a significant role during and at the end of life. They considered the heart was where the soul was located when a person was living and the soul left the body when a person died.

Classical physicians had little understanding of the relationship between the heart and the blood. They did not know how blood got to the heart, how it got from the right ventricle to the left ventricle or what happened after it left the heart. They believed the heart provided a "vital spirit" to blood passing through the heart. They also believed the arteries did not contain blood as when a person or animal dies, the heart stops pumping blood into the arteries, which then contract and drive their blood into the veins. This only leaves air in the arteries of a dead person or animal and classical physicians only dissected dead bodies and so never discovered blood in the arteries. The veins in dead bodies are full of blood, especially

the veins connected to the liver. This led classical physicians to believe that the liver created blood which was passed through the veins to the rest of the body. It was also believed that the body somehow absorbed the blood.

Galen, who had the opportunity to observe the internal organs of living human beings while acting as physician to injured gladiators had a better understanding of the heart and blood. He understood the arteries contained blood in living people and that the heart was a pump which pushed blood from the right ventricle of the heart into the lungs which then flowed into the left ventricle and from there into the arteries. This circulation from the right ventricle to the lungs and then to the left ventricle was known as the pulmonary transit. Galen however still believed that the liver created the blood, but also that it pumped the blood to the rest of the body and that blood was passed directly from the right ventricle to the left ventricle of the heart. The irony is that Galen's work on the pulmonary transit, which was at least partly right, was largely not noticed, while other work which was quite erroneous like the humoral theory was treated as holy writ.

The idea of the pulmonary transit was revived by the Arab physician Ibn al-Nafis in the 13th century when he suggested that all the blood went from the right ventricle to the lungs and then to the left ventricle and none travelled directly from the right ventricle to the left ventricle. In the 16th century the same idea was suggested by Michael Servetus and accepted by Realdo Colombo. Colombo also suggested the heart could act as a pump and discovered the presence of valves in the veins which ensured that the blood could move only in a single direction from the right ventricle to the lungs and then to the left ventricle.

The classical ideas concerning the heart and blood were beginning to be challenged in the 16th century. Ideas of the pulmonary transit, the heart acting as a pump and valves in the veins ensuring blood flowed only one way questioned the classical orthodoxy still largely accepted in Renaissance Europe. Into this environment William Harvey proposed his ideas of the continuous circulation of the blood.

Harvey had been carrying out dissections on a wide range of living animals and it is from his observations of their living organs that he was able to understand how the blood circulates through the human body. His book *De Motu Cordis* begins by explaining the structure of the heart and what it does. The heart consists of two upper parts called the auricles and two lower parts called the ventricles. The left auricle and the left ventricle were separated from the right auricle and the right ventricle by an impenetrable muscular wall. The question of whether the auricles or the ventricles beat first was difficult to resolve as hearts would often beat too fast for normal observation to provide an answer. Harvey answered the question by observing the hearts of cold blooded animals like fish which beat slowly and then confirmed it by observing the slow beating hearts of dying warm blooded animals. He observed the auricles beat first, pushing blood into the ventricle which contracted pushing blood out of the heart.

The classical theory considered blood was made by the liver, flowed through the heart and was absorbed by the body. Harvey calculated the amount of blood that flowed through the heart of a dog. He calculated the number of heart beats per minute, which was the number of times the heart pumped blood out into the body. He also calculated the quantity of blood that was pumped with each heart beat and concluded that the heart pumped blood weighing three times the weight of the whole body each hour. The question arose as to where all this blood came from, and where did it all go. Blood equivalent to three times a person's body weight per hour could not come from food and drink consumed. No one could eat or drink that much per hour. Nor could that quantity of blood be absorbed by the body every hour. Veins, arteries and tissues would explode with that quantity of blood being poured into them every hour. Harvey

suggested the solution to this problem was that blood was not being created by the liver or absorbed by the body, but that the same blood was constantly circulating around the body.

Galen had suggested that the blood moved in both directions in the veins and arteries. Harvey showed that valves in the veins ensured that blood moved in only one direction. He showed that blood in the veins always moved towards the heart, by pressing a vein, blood accumulated in the vein on the side of the compression away from the heart. The side of the compression close to the heart would be emptied of blood as the blood flowed to the heart and away from the compression point. When an artery was pressed the blood built up on the side of the compression closest to the heart. This indicated the blood flowed in a single direction, in the veins towards the heart, and in the arteries away from the heart.

The consequences of the blood all flowing in one direction and the same blood constantly be circulated, without blood being created by the liver or absorbed by the body was a revolution in physiology. New ideas often receive considerable criticism and Harvey's idea of constantly circulating blood was attacked for daring to disagree with Galen. One rational criticism of Harvey's theory was that Harvey could not show how blood flowing out of the heart to the arteries could connect to the veins and flow back into the heart. Harvey suggested tiny connections, too small to be seen with the naked eye, linked the arteries and the veins but he could not prove their existence. This problem was solved by Marcello Malpighi, in 1661, when using a microscope he was able to observe the existence of capillaries linking the arteries and the veins which allowed blood to flow from the arteries to the veins so that the idea of the circulation of the blood was complete.

Jenner and vaccination

Smallpox goes back at least to Ancient Egypt and was in Greece in the classical period and was present in Ancient China and India. The symptoms of the disease were described by Al-Razi in 910 CE and involved blisters filled with puss appearing on the eyes, face, arms and legs. Twenty to forty percent of those who caught smallpox died from it and the survivors were covered with disfiguring scars. In London in the 17th and 18th centuries a third of the people had smallpox scars and the majority of cases of blindness were caused by smallpox.

It had been observed that people who survived smallpox did not usually catch it again. The idea developed that if a mild case of smallpox could be produced it would protect a person from future smallpox attacks. In the East dust from a smallpox scab was blown into the nose to induce a mild case of smallpox to create immunity from future attacks. In Ottoman Turkey smallpox material was rubbed into small cuts made in a person's arm. These methods of conferring immunity from smallpox were made known in England in the early 18th century but were ignored.

The practice of deliberately giving a person a mild case of smallpox began in England in the early 18th century with Lady Mary Montagu. The practice became known as variolation and Lady Montagu who had learnt about the practice in Turkey had her own daughter variolated in the presence of newspaper reporters which ensured substantial publicity. Lady Montagu then persuaded the Prince and Princess of Wales to have their children variolated which ensured even more publicity. Variolation also took place in America where Zabdiel Boylston, a Boston physician, heard of variolation from an African slave and faced with a smallpox epidemic variolated 244 people of whom only 6 died. Surgeons however demanded patients go through a 6 week period of bleeding, purging and dieting before variolation which limited the popularity of the practice and resulted in patients being weakened before variolation took place.

Variolation turned out to be quite dangerous with modern estimates that 12% of patients died; a lower death rate than the 20-40% who might die in a smallpox epidemic, but certainly not a perfect treatment for the problem of smallpox.

A better treatment was to come with Edward Jenner, who while training as a surgeon in 1768, heard that milkmaids who had contacted cowpox were immune from smallpox. Cowpox resulted in lesions on the milkmaids hands, but had no other symptoms. Later Jenner met a Mr Frewster who in 1765 had presented a paper to the London medical society on the ability of cowpox to prevent future smallpox attacks. The paper was never published but reminded Jenner of what he had heard of cowpox from the milkmaids. Cowpox is part of a family of animal poxes, including horsepox, cowpox, swinepox and smallpox all caused by the orthopox virus. All the animal pox diseases can infect humans and an infection from anyone of them will protect people from all the other animal poxes. In December 1789 Jenner began a series of experiments. He inoculated three people including his son with swinepox and later variolated them with smallpox and none of them produced the rash that usually came from variolation with smallpox. Swinepox seemed to protect them from smallpox. Later in 1796 Jenner put cowpox into a healthy 8 year old boy and after he developed normal cowpox symptoms variolated him with smallpox. The boy did not develop any of the symptoms that normally occurred with variolation with smallpox. Jenner then took fluid from the boy's cowpox pustule and used it to inoculate some more children and fluid from their cowpox pustules was used to inoculate some more children. Two of these were later variolated with smallpox, but did not develop any of the symptoms that normally occurred with variolation, confirming the initial experiment. The experiment showed that cowpox could provide protection against smallpox without any of the risks of variolation. The practice of cowpox inoculations, which began to be called vaccination, was soon done throughout the British Empire, the United States and Europe although there was some opposition to it. The opposition gradually disappeared and eventually late in the twentieth century smallpox was completely eliminated.

The discovery of anaesthesia

A vital component of modern surgical operations is the use of anaesthesia. Without anaesthesia operations would be excruciatingly painful and as a result many patients chose not to have operations. The pain of having limbs amputated could result in patients dying of shock and forced surgeons to perform operations with extreme speed. The best surgeons could amputate a limb in less than a minute. The state of mind of a person awaiting surgery would be similar to that of a person about to be tortured or executed. When London hospital was built in 1791, and was to act as a model for other hospitals, the design took into account the lack of effective anaesthetics. The operating room was on the top floor, partly to allow sunlight through a skylight to illuminate the operation, but also so the patient's screams would not travel through the hospital and could be muffled by extra heavy doors. When an operation was to commence hospital staff would go to the top floor and assist in holding the patient down and if necessary in gagging the patient.

The problem with an effective aesthetic that will allow major surgery is that it must place the patient in a state where the central nervous system is depressed to an extent where painful stimuli cause no muscular or other reflexes. This is far beyond ordinary sleep as obviously performing surgery on a sleeping person will wake them. Effective surgical anaesthesia must place the patient in a state close to that of death.

In the past various attempts were made to reduce or eliminate pain during surgical procedures. Dioscorides, a Greek physician in the early Roman Empire, used drugs such as henbane and mandrake root to relieve pain. These drugs continued to be used into medieval times. Arab physicians seemed to have used drugs such as opium and hyoscyamus. Alcohol was often used but was probably more effective at making the patient easier to hold down than in relieving pain. Soporific sponges, involving the inhalation of drugs such as opium, mandragora and hyoscyamus were used from around the ninth century. However modern experiments with such sponges suggest they had no aesthetic effect at all. The use of soporific sponges was discontinued in the seventeenth century. It may well be due to the lack of effectiveness of pre-modern anaesthetics that their use was not widespread. Egyptian papyri and the Code of Hammurabi describe surgery without mention of anaesthetics. Only one Chinese surgeon, one Indian surgeon and a few Greek, Roman and Arab surgeons seem to have made any attempt to relieve pain during surgery. Pre-modern attempts to relieve pain during surgical operations seem to have been of little or no effect.

The first step in the development of modern anaesthetics was the discovery of ether. In 1275, the Spanish alchemist Raymundus Lullius produced ether by mixing alcohol with sulfuric acid. Paracelsus used ether to relieve pain in 1605 in some of his medical patients but not in surgery as he was not a surgeon.

Nitrous oxide, soon to be known as laughing gas, was discovered by Joseph Priestly in 1772. Priestley however did not realise nitrous oxide could act as an anaesthetic. Others however soon discovered both nitrous oxide and ether had an intoxicating effect when inhaled and soon “ether frolics” and “laughing gas parties” became a popular source of amusement. It was soon observed that minor injuries such as bruises received at the frolics and parties were not accompanied by any pain. In addition Humphrey Davy discovered that nitrous oxide relieved the pain of an inflamed gum and jaw and suggested nitrous oxide could be used in surgery. Similar observations concerning nitrous oxide were made by William Barton in the United States. In 1842 ether was used to painlessly extract a tooth, by a dentist, Dr Elija Pope, acting on the suggestion of William Clark a chemistry student who had participated in ether frolics.

The first use of ether for surgical purposes was by Crawford Long in Georgia, USA in 1842. Long had attended ether frolics and had noticed bruises he had received while under the influence of ether had involved no pain. Realising that ether had stopped the pain he used it in various surgical operations and in obstetrical procedures. He did not however publish his work until 1849.

A dentist, Horace Wells, while attending a nitrous oxide party in 1844 noticed a person injuring his legs without suffering any pain. Realising nitrous oxide could serve as a dental anaesthetic Wells had one of his own decaying teeth removed by another dentist while he was under the influence of nitrous oxide. Wells experienced no pain and was soon performing dentistry using nitrous oxide on his own patients. However when he attempted a public demonstration at Massachusetts General Hospital he used insufficient gas and the demonstration was not a success.

The public demonstration at Massachusetts General Hospital had been arranged by Wells former dentistry partner William Morton. Morton, who had possibly seen Long operate in Georgia, became interested in ether as an anaesthetic and had discussed it with Charles Jackson, a doctor in Harvard’s medical faculty and at Massachusetts General Hospital. Intending to patent the anaesthetic Morton and Jackson disguised the ether by mixing it with aromatic oils and called it Letheon. They then arranged public demonstrations of the use of Letheon, in 1846, for pulling teeth and for an operation removing a tumour from a patients jaw. Both the dentistry and the operation were carried out painlessly. Jackson and

Morton however were forced to withdraw the patent for Letheon and reveal that Letheon was really ether by pressure from the surgeons involved in the operations. By the end of 1846 news of the use of ether as an anaesthetic had travelled across the Atlantic and in December 1846 it was used in an operation in London.

Jackson, Morton and Wells all claimed to be the discoverer of surgical anaesthesia and in 1847 the United States Congress became involved in trying to sort out who was the true discoverer of anaesthesia. Congress eventually dismissed Wells and Morton's claims and decided it was between Jackson and Long. The American Medical Association, in 1872, gave the credit to Wells, while in 1913 the electors of the New York University Hall of Fame named Morton as the discoverer of surgical anaesthesia. The American College of Surgeons, in 1921, decided Long should be credited with the discovery.

Attempts were soon made to use ether in obstetrics but it was found to be unsuitable. Ether often produced vomiting patients, irritated lungs and a bad smell. Chloroform had been discovered independently in 1831 by Samuel Guthrie in New York, by Eugene Soubeiran in Paris and by Liebig. Initially its anaesthetic quality was not recognised but Guthrie's daughter had become unconscious for several hours after tasting it. In 1847 Sir James Simpson while looking for an anaesthetic to use in obstetrics tried chloroform on himself and having found it to be an effective anaesthetic began using it in surgical operations. Its use was soon extended to obstetrics provoking considerable opposition from the Calvinist Church in Scotland on the grounds the Bible stated "In sorrow thou shalt bring forth children" showed women must suffer when giving birth. The Calvinist church opposition disappeared when Queen Victoria gave birth to her eighth child under the influence of chloroform. However chloroform was soon discovered to have its own problems as it could cause liver damage and five times as many people died under chloroform as died under ether.

The method of application of the anaesthetic developed over time. Long had simply poured ether into a towel for his patient to inhale. Morton used an inhaler made up of a round glass bottle with two holes and a mouth piece. Air passed through one hole into the bottle which contained a sponge soaked in the ether which was then inhaled by the patient through the mouth piece which was attached to the other hole. Morton's inhaler did not allow the anaesthetist to have control over the amount of anaesthetic. Soon John Snow, who had provided the chloroform to Queen Victoria, created an improved inhaler which provided a 4% mix of chloroform in air. Joseph Clover produced a further improved inhaler in which the chloroform and air mixture was prepared in advance and held in an air tight bag. Sir Francis Shipway created an apparatus which allowed the anaesthetist to control a mixture of varying amounts of chloroform, ether and oxygen for inhalation by the patient.

A significant improvement in the provision of anaesthetics occurred with the introduction of the anaesthetic directly into the windpipe or trachea. This was first attempted by Frederick Trendelenburg, in 1869, who inserted the anaesthetic through a tube he inserted into a hole he had cut into the patient's windpipe. Sir Ian Macewan achieved the same result without cutting into the windpipe, in 1880, by inserting a metal pipe down the throat and into the windpipe. This allowed the development of endotracheal anaesthesia which was important for operations on the mouth and the jaw and for many modern cardiac and pulmonary operations. Endotracheal anaesthesia was further improved, in 1919, when Sir Ian Magill put tubes through the conscious patient's nose and mouth and down into the windpipe by anaesthetizing the throat with cocaine before inserting the tubes.

General anaesthetics were often not necessary for minor operations. A local anaesthetic which worked on a particular part of the body and avoided the small risk of death and several hours of recovery

time involved with general anaesthetics was sought. Peruvian Indians knew about the anaesthetic qualities of the coca plants and in the nineteenth century cocaine was obtained from the plant. In 1872 Alexander Bennett observed that cocaine had anaesthetic properties and in the 1880's Carl Koller experimented with cocaine using it to anaesthetize frog's eyes. Soon cocaine began to be used as a local anaesthetic for eyes, the mouth, nose and throat and in the urethra. The use of cocaine was extended by injecting it into the nerves relating to the area to be operated on and eventually into the epidural space around the spinal cord which allowed a larger area to be anaesthetized. The use of cocaine as a local anaesthetic has discontinued with its replacement by novocaine which was synthesized as an aesthetic after 1905.

The Germ Theory of Disease

The first person to see micro-organisms was Anthony Leeuwenhoek (1632-1723) a Dutch draper who was an expert maker of microscopes. His microscopes gave a degree of magnification which was not exceeded until the 19th century. He used his microscopes for observing a wide variety of phenomena. In 1675 and 1676 he looked at drops of rain water and found tiny animals within the water. Those animals would have included what we now call bacteria and other micro-organisms. In 1683 Leeuwenhoek looked at plaque from his own teeth and found it contained large numbers of small animals. Later samples of plaque did not contain the small animals, which Leeuwenhoek suspected was because his drinking of hot coffee killed the little animals. Leeuwenhoek also looked at scrapings from his tongue when he was sick and at the decay in the roots of a rotten tooth he had removed. In both cases he found vast numbers of the little animals. The presence of these animals in such great numbers in places of illness and decay raised the question as to whether the animals arose from the decay or whether they were attracted to it or whether they caused the decay. The question of whether the small animals were spontaneously generated from decaying materials or were attracted to it was the subject of much controversy. Francesco Redi (1626-1698) kept boiled meat in sealed containers and when maggots failed to appear suggested this showed there was no spontaneous generation. However in 1748 John Needham repeated the experiment and found small animals in the meat which he considered proved spontaneous generation. Lazzaro Spallanzoni suggested Needham had failed to seal his containers properly so that the small animals arrived on the meat through the air, rather than being spontaneously generated by the meat. Supporters of spontaneous generation argued that sealing the containers prevented some gaseous substance, necessary for spontaneous generation, from reaching the meat and so preventing the generation of the living organisms.

Whether micro-organisms caused the diseases they were so often found with, was investigated by Agostino Bassi. In 1835 he showed that the silkworm disease, muscarine, was caused by bacteria. When he inoculated healthy silkworms with the bacteria, he produced the sickness in the silkworms. This suggested that other diseases may be caused by bacteria.

The questions of spontaneous generation and whether micro-organisms played any role in causing disease were eventually settled by Louis Pasteur. He was to show that fermentation in wine, putrefaction of meat and infection in human disease all involved the same process and were all caused by the activities of micro-organisms. The micro-organisms were generated not by decaying matter but were continually present in the air and when they were present in great numbers and were of unusual strength they could cause matter to decay and human beings to fall ill.

Pasteur began with fermentation in wine. At the time chemists such as Wohler and Justus von Liebig suggested fermentation was solely a chemical process with living organisms playing no role in the

process. Fermentation in wine was a problem as sometimes the fermentation went wrong and soured the wine. Pasteur showed that fermentation was caused by micro-organisms in yeast and that round yeast cells produced good wine, but long yeast cells created lactic acid which caused the wine to go sour. Pasteur showed that if the wine was heated it would kill the yeast and stop any of the wine going sour.

Pasteur next began to investigate putrefaction in meat with an experiment that allowed air to reach boiled meat via an undulating u shaped tube. The meat did not putrefy and Pasteur considered this was because the dust particles containing the micro-organisms were caught on the low bend of the tube as they could not travel up the tube due to gravity. The micro-organisms did not reach the meat even though it was exposed to air so the meat did not putrefy. This showed it was not air that caused putrefaction, but micro-organisms in the air.

Pasteur then began to investigate diseases in living organisms, first with silkworms and then anthrax which affects sheep and cattle and occasionally humans. Pasteur showed the disease killing silkworms were two different sorts of micro-organisms which caused two different diseases in the silkworms. In relation to anthrax it was already known that the blood of cattle, which had died from anthrax, contained micro-organisms and that these micro-organisms were the cause of the disease. Robert Koch had discovered the anthrax bacteria, had cultured it, and injected it into animals which had immediately died. He also found that anthrax micro-organisms could sometimes form spores, which were tiny organisms resistant to a range of environmental conditions. The spores were formed when the temperature was right and oxygen was present. Once the spores were formed they could survive for a considerable time and re-infect other animals making the disease difficult to control. Pasteur, with some difficulty, then produced an anthrax vaccine which he used to inoculate sheep which were later injected with the anthrax bacteria. The sheep did not develop anthrax and Pasteur had found a vaccine for anthrax.

Pasteur's last great achievement was to discover a vaccine for rabies. Rabies normally occurs in humans after they have been bitten by a rabid dog with the symptoms appearing between 10 days and several months after the dog bites took place. Pasteur studied the tissues of rabid dogs but could not find a micro-organism that could have caused rabies. He decided the organism was too small to be detected with a microscope. Pasteur considered the micro-organism entered the body through the bite wound and over time moved to the brain, explaining the period of time between the bite and the arrival of symptoms. After some time Pasteur was able to produce a vaccine for rabies which was able to be injected in the period after the dog bite and before the onset of symptoms.

Pasteur's work had followed a logical path. He had first shown that fermentation was caused by micro-organisms, and that those micro-organisms originated in the air rather than from the fermenting matter and that micro-organisms also caused putrefaction and infectious disease. He then showed how the diseases in both animals and people could be cured by vaccination. Pasteur's work established the germ theory of disease and put an end to other theories of disease such as the humoral theory.

Robert Koch, after isolating the anthrax bacteria, began using an improved microscope with a light condenser and an oil immersion lens. This enabled him to see bacteria that had previously been too small to be seen even with the best microscopes available. He also used new aniline dyes which helped him to distinguish between different types of bacteria. Koch also found a way of producing pure cultures of different types of bacteria by placing the bacteria on a solid culture medium, in place of the liquid culture medium then currently used, which only worked well with bacteria that moved in the blood stream. With his improved microscope and better techniques for creating pure cultures of bacteria Koch began to search for a tuberculosis bacterium, in the tissue of humans who had died of tuberculosis. Using a microscope equipped with the oil immersion lens and condenser that was five times as powerful as

Leeuwenhoek's microscopes he was able to find a tiny bacterium which he called the tubercle bacillus. The tubercle bacillus was much smaller than the anthrax bacteria and was too small to be found without the use of his new improved microscope. To prove the tubercle bacillus caused tuberculosis Koch needed to isolate it in a pure culture and to inject it into various animals. If it produced tuberculosis in those animals that would prove the tubercle bacillus was the cause of tuberculosis. After some difficulty he was able to produce a pure culture of the tubercle bacilli. He then injected this into animals which soon became sick and when he examined their diseased tissues he found they had tuberculosis. Koch had found the cause of tuberculosis giving hope that a cure would eventually become possible.

If Pasteur established the germ theory of disease, it was Koch who was to turn bacteriology into a science. Koch formalized the methods for studying micro-organisms and proving their relationship with particular diseases. To prove an organism was the cause of a disease Koch proposed the following criteria, which came to be known as Koch's postulates:

1. The organism must be present in every case of the disease.
2. It must be possible to prepare a pure culture, maintainable over repeated generations.
3. The disease must be reproduced in animals using the pure culture, several generations removed from the organism originally isolated.
4. The organism must be able to be recovered from the inoculated animal and be re-produced again in a pure culture.

Clearly the third and fourth postulates can only apply to diseases which apply to animals as well as humans and the postulates were not able to be applied to all micro-organisms for example viruses. Nevertheless the postulates provided a set of procedures for the investigation of diseases which were to establish the causes of a range of diseases which opened up the possibility of finding cures and treatments for the diseases. Between 1879 and 1906 the micro-organisms causing many diseases were discovered. The diseases involved included gonorrhoea (1879), typhoid fever (1880), suppuration (1881), glanders (1882), tuberculosis (1882), pneumonia (1882 and 1883), erysipelas (1883), cholera (1883), diphtheria (1883-4), tetanus (1884), cerebrospinal meningitis (1887), food poisoning (1888), soft chancre (1889), influenza (1892), gas-gangrene (1892), plague (1894), pseudo-tuberculosis of cattle (1895), botulism (1896), bacillary dysentery (1898), paratyphoid fever (1900) syphilis (1905), and whooping cough (1906). The discovery of the micro-organism causing the disease did not always result in effective treatments.

Anti-septics

The increase in surgery produced by the use of anaesthetics simply highlighted another problem, the death of large numbers of patients due to infection. Patients dying from infection had long been a problem both in obstetrics and surgery. It was in obstetrics that the first understanding of the causes of infection arose, but it was in surgery that the solution to the problem was achieved.

Some doctors and surgeons sensed that a lack of cleanliness may be the cause of infection. Charles White in 1773 in Manchester suggested the cleaning of the surgery room, clothing and articles in contact with the patients but did not refer to cleansing of surgeons and others involved in operations. Alexander Gordon (1752-1799) suggested infection was carried from infected patients to uninfected patients. He suggested the cleansing of surgeons but did not realise that infected matter was involved in the spread of disease.

In the mid nineteenth century Ignaz Semmelweis was working at the maternity clinic at Vienna General Hospital. He noticed that the section of the hospital used for training medical students in obstetrics had a much higher rate of mortality, around 13% than the section used to train midwives, which was around 2-3%. Explanations considered for the variations in the mortality rates included that the poor single mothers and prostitutes in the hospital were less embarrassed when treated by women. Semmelweis noticed that the puerperal fever which killed many of the women immediately after they had given birth seemed to be the same disease that had killed the surgeon Jakob Kolletschka who died after cutting his finger in a post mortem. Later Semmelweis realised that medical students going to their section of the maternity clinic came from anatomy classes involving dissections and the handling of diseased body parts. Little attempt was made to clean up between the anatomy classes and the work done in the maternity clinic. Semmelweis suspected the students coming from the anatomy classes were bringing infection into the maternity clinic so he ordered students to wash and scrub in a chlorine solution before entering the maternity clinic. Within a month the mortality rate in the students section dropped to 2% the same as for the midwives section. Despite his success Semmelweis became very unpopular with the medical students, his immediate superior and even the patients who felt he was suggesting they were dirty. Semmelweis left Vienna for a hospital in Budapest where he instituted similar hygienic reforms and again the mortality rate dropped dramatically. He published a paper on his discoveries, which was ignored, and then a book which was also ignored. Semmelweis then began to behave erratically writing angry letters to those who criticised his work. He was soon induced or forced to enter a mental hospital and within two weeks was dead in circumstances that may have amounted to murder.

Joseph Lister was a surgeon in Glasgow who noticed that the mortality rate for compound bone fractures where the bone was exposed to the air were much higher than for broken bones where there was no exposure to the air. Broken bones exposed to the air often developed gangrene which was usually blamed on “miasma” or bad air. Lister did some experiments on frogs legs and concluded that gangrene was a form of rotting, involving the decomposition of organic material. He also read Pasteur’s work which suggested that putrefaction was the rotting of organic material caused by bacteria in the air. Lister accepted Pasteur’s idea that it was not the air that caused the gangrene but bacteria in the air.

The question was how to destroy the bacteria both in the air and in the wounds. Carbolic acid or phenol had been isolated in the 1830’s through coal tar distillation. It was used to clean sewers and after various experiments with crude carbolic, which killed tissue, Lister began to use carbolic acid. He would dress wounds in lint soaked with carbolic acid and sprayed the air in the operating room with carbolic acid. Lister published his work in 1867 in a paper entitled *On the Antiseptic Principle in the Practice of Surgery*. The mortality rates from Lister’s amputation operations fell from 45% to 15%, but despite this some doctors still refused to believe that bacteria existed or could cause infection. However the results of using Lister’s methods soon became obvious and they began to be used throughout Europe. Over time he refined his procedures getting rid of the carbolic spray and putting greater emphasis on using heat to sterilize dressings and instruments. There was also a move from anti-septic measures which destroyed germs in wounds to aseptic measures which ensures that everything that touches the wound such as instruments and the surgeon’s hands are free from germs. Towards the end of the 19th century sterilized gowns, masks, caps and rubber gloves were introduced for surgical operations.

Antibiotics

Scientists experimenting with bacteria had on various occasions noticed that penicillin and other biological organisms could inhibit the growth of bacteria. In 1875 John Tyndall had observed penicillin had killed bacteria in some of his test tubes. In 1877 Pasteur had noted anthrax bacilli grew in sterile urine but the addition of “common bacteria” stopped the growth. In 1885 Arnaldo Canteri noted certain bacterial strains killed tubercle bacilli and reduced fever in the throat of a tubercular child. In 1896 a French medical student noted that animals inoculated with penicillin and a virulent bacterium did better than animals inoculated with the virulent bacteria only. In 1925 D A Gratia noted that penicillin could kill anthrax bacilli.

Alexander Fleming was experimenting with bacteria in 1928 when he observed bacteria in his petri dish had been killed by the *Penicillium* mould. Fleming began experimenting with the mould and soon isolated the substance that killed the bacteria. He called the substance penicillin and then tested its effectiveness against other bacteria. He found penicillin could kill a range of bacteria but there were some bacteria it did not affect. He injected it into animals and found that it did not do them any harm. Fleming then published his results in 1929 and then in a briefer report in 1932. Fleming’s work was largely ignored and he then turned his research interests elsewhere. The prevailing scientific view at the time was that anti-bacterial drugs would not work against infectious disease and would be too toxic to use on humans. This belief was to change after 1935 when it was found that Prontosil could destroy streptococcal infection when given intravenously. Research on penicillin only began again in 1940, in Oxford, when Howard Florey and Ernest Chain discovered that penicillin was an unstable simple molecule. They were able to stabilize it by freeze drying it in a water solution. This produced a powder that was tested on mice and did not harm them and cured them of streptococci. It was also discovered that penicillin could travel through the body to attack infections wherever they were. Their results were published in August 1940 and Florey, Chain and their colleagues began to manufacture penicillin as fast as possible. The first human test of penicillin was on a badly ill policeman. The policeman improved until he seemed on the verge of total recovery when the supply of penicillin ran out and the policeman relapsed and died. More penicillin was manufactured and tested on humans and was found to regularly clean up infections. It was found to be effective against most forms of pus forming cocci and against tetanus, anthrax, syphilis and pneumonia. The manufacture of penicillin was greatly expanded when the United States began to produce it and new manufacturing techniques involving deep fermentation were developed. This involved submerging the mould below the surface of the culture medium. Eventually semisynthetic penicillins and penicillins that could be swallowed were produced.

Eventually a systematic search began for other anti-biotics. Howard Florey outlined the procedure to be followed which involved the investigation of micro-organisms to find out which ones produced an anti-bacterial substance, the isolation of that substance, testing the substance for toxicity, testing it in animal experiments and then testing it on people. The search for new anti-biotics was to produce a substantial number of new anti-biotics including streptomycin developed in 1944 which was effective against tuberculosis. Chloramphenicol, developed in 1949, was effective against typhoid fever. Anti-biotics were eventually found that could act against every bacteria that causes diseases in humans. Some of those bacteria are now developing resistance to anti-biotics and the development of new anti-biotics is inhibited by the extreme cost, running into hundreds of millions of dollars, of obtaining United States government approval for the drugs. Nevertheless anti-biotics have saved hundreds of millions of lives.

Medical Statistics

The use of statistics in medicine to determine the cause of disease or the success of a treatment has a relatively short history. In the past the causes of disease and the success of treatments were usually decided by physicians personal experience with patients, which, assuming that physicians had similar experiences, led to accepted beliefs as to the efficacy of treatments and the causes of disease. The beliefs would be recorded in authoritative medical texts and would in many cases become a sort of medical dogma. Disputing the dogma could involve accusations of unorthodox opinions that could lead to bad practices that could endanger patients' lives.

The idea of doing trials, to test the effectiveness of medical treatments, was suggested by the scientist, Johannes van Helmont and the philosopher George Berkeley. The first known trial to assess the cause of a disease seems to have been done by James Lind in an attempt to discover the cause of scurvy. Scurvy was killing large numbers of sailors on long sea voyages. Lind took 12 scurvy sufferers and divided them into 6 groups of 2 and each group was given a different dietary supplement. The two sailors given oranges and lemons rapidly recovered and the others did not. Lind eventually published his findings, and although there remained some confusion for some time, eventually lemon juice became standard on long sea voyages.

One question, much debated in the 18th century, was whether smallpox inoculation was a good thing. In England inoculation was generally favoured, in France it was opposed. Various calculations were made as to the death rate from smallpox which was considered to be around one in ten, excluding fatalities of those under 2 years old. Other calculations were 1 in 12 and 1 in 7. This was compared to the death rate from inoculation which James Jurin, secretary of the Royal Society, calculated at 1 in 91. The Swiss mathematician, Daniel Bernoulli calculated that inoculation increased the average life expectancy by two years. A further problem was that people inoculated with smallpox could spread it to others and this was not taken into account in calculating death rates from inoculation. If people who were inoculated could be isolated for a period, then the figure might not be too high, but then if people who got smallpox naturally were isolated that would reduce the death rate from normal smallpox. An additional problem was that the rate of smallpox infection varied considerably from large cities where nearly everyone would, sooner or later get smallpox and the small towns and villages where most people in the 18th century lived, and many people could live their lives without getting smallpox. Modern estimates of the death rate from inoculation are as high as 12%, not much better than the death rate from normal smallpox infection.

The difficulty in calculating accurate death rates for inoculation and for normal smallpox infection, how to introduce into the figures people who caught smallpox from those who were inoculated and how to deal with the widely varying rates of smallpox infection between urban and rural areas gives some idea of the difficulty in working out whether inoculation was a good thing or a bad thing. The whole debate eventually became irrelevant when vaccination with cowpox, a quite safe form of immunization became available at the end of the 18th century. A further illustration of the problem of accurate statistical analysis of medical treatments is contained in the work of Pierre Louis in the first half of the nineteenth century. Louis conducted several trials to test bloodletting as a treatment for various inflammatory diseases. He concluded from his trials that bleeding resulted in patients recovering earlier, than if there was no bleeding and that if bleeding is done, patients bleed earlier during the course of the disease recovered more quickly than those bleed later. However the way Louis conducted the trial was not ideal.

Those bleed earlier during the illness were on average 8 years and 5 months younger than those bleed later, which could explain the faster recovery. A further criticism of Louis's study was that the numbers involved in his trial were insufficient so there was a wide margin of error in his results so they were not reliable.

A more successful use of statistics to discover the cause of disease occurred in the mid-19th century when John Snow discovered the cause of cholera. Cholera was like many infectious diseases, assumed to be caused by miasma or bad air caused by putrefaction. Snow suspected that cholera could be transmitted by personal contact and through polluted water supplies. He examined the sources of the water supplies in London and compared it to mortality rates from cholera. Areas with clean water supplies, due to water being taken from the Thames above sewage outfalls, or with filtered water, or with water passed through settlement ponds, showed much lower rates of cholera than areas using unfiltered and unpounded water taken from below sewage outlets. Areas with clean water had a death rate of 10 per 10,000 from cholera, areas with polluted water had a death rate of 110 per 10,000 from cholera.

Snow also investigated the cholera levels for households in the same areas, where the water supplies came from two separate companies, one of which supplied clean water to its customers and the other which supplied polluted water. Those customers obtaining clean water had 5 cholera deaths per 10,000, those obtaining polluted water had 71 cholera deaths per 10,000. The 5 cholera deaths per 10,000 could have been caused by visiting houses, pubs and cafes with polluted water and people who had fallen sick with cholera.

Snow's final study concerned a small area around Broad Street in London where 500 people died of cholera in ten days. Snow suspected a water pump supplying drinking water in the centre of the area could be responsible so he asked the local authority to remove the handle from the pump. This was done and the cholera outbreak ended. More particularly Snow showed certain groups within the Broad Street area, people in a workhouse and those working in a brewery who did not use water from the pump had an unusually low cholera death rate. He also showed that certain individuals from outside the Broad street area who drank water from the pump also died of cholera within the ten day period.

Snow's three studies provided powerful evidence that polluted water caused cholera but his findings were initially rejected. Two inquiries considered cholera still came from bad air and another study which concluded that the death rate from cholera rose as one moved from highlands to sea level also suggested bad air was to blame. Eventually, when miasmatic theories of disease lost creditability with the rise of the germ theory of disease, Snow's explanation of cholera was accepted.

The first truly scientific randomised control test was that conducted on the drugs streptomycin and PAS as a treatment for tuberculosis. Tuberculosis was in the mid twentieth century, the most common fatal infectious disease in the western world. Its cause, the tubercle bacillus, had been identified by Robert Koch in 1885, but no effective treatment had been found for it. Antibiotics like penicillin did not work against it, as it had an impermeable waxy coat that protected it from antibiotics.

A new drug called streptomycin had been discovered in America in 1944 which seemed to work against tuberculosis germs. It inhibited the growth of tuberculosis bacillus on agar plates and was successful at curing tuberculosis in guinea pigs and when tried on a human patient with five courses of treatment between November 1944 and April 1945, cured the human patient. A second drug which showed promise as a tuberculosis treatment was PAS. It had been noted that Aspirin resulted in the tuberculosis bacilli absorbing increased amounts of oxygen and it was considered that a similar drug to Aspirin might block the supply of oxygen to the tubercle bacilli. PAS was tried and was shown to cause an improvement in the condition of tuberculosis patients.

Immediately after World War II Britain was short of money and could afford only a very small amount of streptomycin. The Tuberculosis Trial Committee, encouraged by one of its members Austin Bradford Hill, recognised there was not enough streptomycin to provide to all patients, decided to conduct a random control test with the streptomycin, providing streptomycin to one set of patients and comparing the results with another set of patients not receiving the drug. There was enough streptomycin to provide to 55 patients and the results of the treatment were compared with 52 patients who received the usual treatment provided for tuberculosis patients. Which patients received the streptomycin and which received the usual tuberculosis treatment was decided completely at random to avoid any conscious or unconscious bias in the allocation of patients to either group.

Six months after the trial had begun it was found that only four patients had died from the group given streptomycin while fourteen had died from the group receiving the conventional treatment. Streptomycin seemed to be an effective treatment with significantly fewer deaths in the group receiving the streptomycin. However a follow up investigation three years later revealed 32 of the group using the streptomycin had died compared to 35 in the group not receiving the drug. After three years the group using the streptomycin was only slightly better off than the group not using it. What had happened was that over the period of treatment some of the tubercle bacilli had become resistant to the streptomycin and when this happened patients who initially seemed to be getting better, worsened and often died. The test revealed that not only did streptomycin not work in the longer term but that there was a problem of the bacilli becoming resistant to the streptomycin which, if it could be overcome could mean that streptomycin could still be an effective treatment for tuberculosis. If the drugs had simply be provided to doctors for treating patients it would have taken much longer to work out why it was not working.

A further trial was conducted which combined streptomycin with PAS with the aim of overcoming the problem of resistance from the tubercle bacilli. In the second trial resistance to streptomycin developed in only 5 patients compared to 33 in the first trial. The combination of the two drugs proved to be an effective treatment for tuberculosis and survival rates for tuberculosis patients went up to 80%. Eventually other drugs such as isoniazid and rifampicin were introduced and it was found that combining three drugs resulted in survival rates approaching 100%.

Random controlled trials were also found to be effective in proving the causes of certain diseases. After World War II the great majority of the adult population smoked and lung cancer deaths were rapidly increasing. Bradford Hill, Edward Kennaway, Percy Stock and Dr Richard Doll were asked to investigate whether smoking was a cause of the increasing number of lung cancer deaths. Smoking was only one possible explanation, others such as increased air pollution especially from motor vehicles were considered to be as likely or more likely the cause of increased lung cancer deaths, than smoking. The asphaltting of roads was considered to be another possible cause of the escalating lung cancer deaths. Given that most adults smoked it was difficult to find a suitable control group of non-smokers. The investigation was conducted by creating a detailed questionnaire which patients suspected of having lung cancer completed. The questionnaire was also completed by patients who had other cancers and also by patients in hospital for reasons other than cancer to act as two control groups. It was found that 99.7% of the lung cancer patients smoked against 95.8% of the control group patients. This was not a great difference but it was also found that 4.9% of the lung cancer patients smoked 50 cigarettes a day as opposed to only 2% of the control group patients. The lung cancer rate amongst those smoking 50 cigarettes a day was over double for lung cancer patients than for the control group. The more people smoked the greater their chances of getting lung cancer.

The study conducted by Doll and Bradford Hill had looked at lung cancer patients and looked back in time at their smoking habits. They then decided to do a study of healthy people investigating their smoking habits and then observing how their health developed in the future. Doll and Bradford Hill decided to do the study on doctors, 40,000 of whom filled in and returned their questionnaire. Two and a half years later enough doctors had died for Doll and Bradford Hill to be able to show that the more the doctors smoked the greater the likelihood they had died of lung cancer. It was eventually found that doctors smoking 25 cigarettes per day were 25 times as likely to develop lung cancer compared to non-smokers.

The success of the random control tests on streptomycin and in showing that smoking caused lung cancer led to random control tests becoming standard practice to test new drugs and to identify the causes of disease. The testing has had its undesirable side with the testing costs running to hundreds of millions of dollars and so discouraging the production of new drugs and some studies of disease showing a relationship between environmental factors and the disease without giving any real indication of a cause and effect relationship.

Diagnostic Technology

The twentieth century has seen the development of a series of new technologies that have enabled physicians to see inside the human body. The technologies began with X-Rays, and then CT scanners, PET scanners and MRI scanners were developed. These technologies all allowed physicians to see inside the body from the outside while other technologies such as endoscopy allowed physicians to invade the body with tiny cameras to observe the state of the interior of patients bodies.

X-Rays were first discovered by Wilhelm Roentgen in 1895. Roentgen was experimenting with a Crookes tube, a glass tube with the air removed to create a vacuum and with electrodes to allow the production of an electric current within the tube. The electric current, consisting of a stream of electrons known as cathode rays, would cause phosphorescent material within the tube to glow. When experimenting with a Crookes tube, the German physicist, Phillip Leonard has noticed that cathode rays could travel through an aluminium sheet he had placed over a window in the Crookes tube and turn slips of paper covered with barium platinocyanide salts, fluorescent. Lenard sent a Crookes tube to Roentgen for Roentgen to study the cathode rays. Roentgen repeated Lenard's experiments and found the cathode rays were escaping from the Crookes tube just as Lenard had found. Roentgen thought that the cathode rays might be passing through the walls of the Crookes tube as well as through the aluminium covered window in the tube. When conducting the experiment Roentgen noticed a screen coated with barium platinocyanide, a yard away from the Crookes tube, turned fluorescent. This could not be caused by cathode rays which only travel a few inches in the air. Roentgen moved the screen further away from the Crookes tube and the screen still turned fluorescent when he turned on the electric current in the Crookes tube. Roentgen placed objects like a book and a deck of cards between the Crookes tube and the screen and the screen still lit up when he turned on the current in the Crookes tube. Further experiments revealed, that the ray causing the screen to light up, could penetrate a wide range of materials such as wood and flesh. Roentgen had no idea what the ray was so he called it an X-ray. When a human hand was placed in front of a photographic plate and exposed to X-rays, the plate showed the bones in the human hand. However the X-rays did not easily pass through metals and could not pass through lead at all.

X-rays were found to have a number of uses such as in crystallography, astronomy and in microscopic analysis, but their most important use has been in medicine. X-rays can provide a photograph

of the inside of the human body. X-rays have a shorter wave length than light so they can penetrate materials opaque to light. X-Rays can more easily penetrate materials of low density such as skin and muscle, but cannot penetrate materials of higher density, such as bone, bullets and kidney stones.

The use of x-rays in medicine was greatly extended by the employment of contrasting media such as barium salts and iodine solutions. Barium makes it possible to obtain x-rays of the large and small intestine and the stomach and the oesophagus. Iodine allows an x-ray picture of the kidneys and bladder and also the carrying out of angiographs. Angiography provides a view of the blood within the arteries and veins which will disclose blockages and other problems within the arteries and veins. The use of catheters allows contrast materials to be injected into the heart allowing x-rays of the internal structures of the heart. X-rays can be used to detect tumours, cancers and cysts.

A further enhancement of x-ray technology came with the development of CT or CAT scanners. The CT scanner uses x-rays, photon detectors and computers to create cross section images or tomograms of the human body. In 1963 Allan Cormack invented an improved x-ray machine using computers, an algorithm and tomograms. In 1972 Godfrey Hounsfield invented the CT or computerized tomography scanner. It allowed many x-rays to be taken, from multiple angles of thin slices of the human body and detectors opposite the x-ray tubes would collect the data, which was converted into digital data, which was then converted by an algorithm, a set of mathematical instructions, by a computer into x-ray pictures. The CT scanner could give three dimensional views of the body and provides much better resolution than ordinary x-ray images. It can show soft tissues and liquid parts of the brain and can show tumours as small as one or two millimetres in size. CT scanners have gone through a series of improvements involving various different generations of scanners. In the earlier scanners the x-ray beam lacked the width and the number of detectors to cover the complete area of interest requiring multiple sweeps to produce a suitable image. In subsequent scanners a wider x-ray beam and more detectors were used to shorten scanning times.

Endoscopy, also known as laparoscopy, involves inserting an instrument into the body either through the body's natural entrances or through a small hole surgically cut in the body. The instrument is used to observe the internal structures of the body and can also be used for surgery with tiny instruments at the end of the endoscope being manipulated by the surgeon through the endoscope.

Endoscopy goes back to the late nineteenth century but was not widely used as the views it provided of the interior of the body were too poor for practical use. Harold Hopkins, a physicist, heard about the problems with endoscopes and remembered that although light normally travelled in a straight line it could in certain circumstances be made to travel around corners by the use of curved glass. Hopkins considered that tens of thousands of flexible glass fibres operating together may be able to cause light to go around corners. He made an experimental endoscope and published his results in 1954. Basil Hirschowitz, a South African, working in the United States, read about Hopkins ideas and created his own endoscope. Several hundred thousand fibres were wound together and to stop light jumping from one fibre to another which could cause the loss of the image a technique of coating each fibre with a glass coating was developed. The endoscope allowed investigation of much of the interior of the body and some surgery on the interior of the body without having to make substantial incisions into the body.

Photography through an endoscope was not very satisfactory due to inadequate illumination and because the optical system was not good enough. Hopkins investigated the problem and found that an endoscope consisting of a glass tube containing thin lenses of air gave improved light transmission around eighty times stronger than conventional endoscopes made of an air tube containing thin lenses of glass. This allowed the taking of photographs through the endoscope and allowed greatly expanded surgical

possibilities through the endoscope. Endoscopy can be used for surgery by instruments such as lasers or wire loop cautery devices attached to the head of the endoscope and controlled by the surgeon through the endoscope.

Modern Surgery

Surgery, before the introduction of anaesthetics and anti-septic and aseptic practises, was limited to a narrow range of operations, of which limb amputation was by far the most common. The quickest operations only were possible without anaesthetics and the mortality rates from infection were enormous before anti-septic practices were introduced. The introduction of gowns, masks, rubber gloves and the sterilization of instruments dramatically cut the death rate in surgery.

Abdominal surgery only became possible with anaesthetics and anti-septics. Christian Billroth (1829-94) pioneered operations in this area. Operations to remove the appendix and to close a perforated gastric ulcer began to be performed in the late 19th century. Brain surgery began with Sir William Macewan (1848-1924) in Glasgow and Macewan also developed operations to deal with bone diseases such as rickets.

Plastic surgery was to make great progress in the 20th century, two New Zealanders Harold Gilles and Archibald McIndoe leading the way. Plastic surgery dates back to ancient times and was practiced in pre-British India and Renaissance Europe when it was used to deal with the terrible damage caused by syphilis. During World War I Harold Gilles carried out plastic surgery on the badly disfigured faces of soldiers and sailors. He developed an operation whereby a skin flap was sliced from the upper arm, one end of the flap remaining attached to the arm and the other end was moulded over the nose and then sewn down. After several weeks the skin sewn to the face would take and the skin attached to the arm could be cut and sewn into place on to the face. When the injured had no facial skin at all Gilles took the flap of skin from the abdomen rolling it over the chest and sewing one end to the face. Holes would be cut in the skin for the nose, eyes and mouth. When that end had taken Gilles cut the end still attached to the abdomen and then sewed that into place on the face. This system involved two operations as if the skin was completely removed from the donor area before it had taken on the face it would die due to lack of blood supply. These techniques were further developed by Archibald McIndoe while operating on air force pilots injured in World War II.

The first experiments with organ transplants had been made by Alexis Carrel early in the 20th century. He carried out various transplant operations on animals discovering the problem of rejection where the transplanted organ was rejected by the receiving animal's body. The problem of rejection was investigated by Peter Medawar when he observed skin grafts taken from a donor would last for ten days before rejection, while a subsequent skin graft from the same donor was instantly rejected. When the body suffers an infection from bacteria or viruses initially it takes time to identify the invading organism before the immune system attacks the invading organism. In the event of a subsequent attack by the same organism the organism is immediately attacked because the immune system recognises it as foreign material due to its previous contact with the virus or bacteria. The way in which the first rejection takes some time but a second rejection of the same material occurs immediately led Medawar to realise that it was the immune system rejecting the transplant in the same way as it attacked invading bacteria and viruses.

Organ transplant required a practical surgical technique which was developed by Joseph Murray who improved on techniques experimented with by Alexis Carrel on animals. The technique involved the sewing together of small blood vessels which allowed the attaching of the transplanted organs blood

supply to those of the recipient so that it could receive the recipient's blood. The first attempts at organ transplant were kidney transplants. This was because humans had two kidneys, but only need one so living donors were readily available. Kidney transplants were also relatively straightforward operations the main job being to connect the transplanted organ's blood supply to the recipient's blood supply.

Kidney transplants did however require the prior invention of the kidney dialysis machine. The dialysis machine was invented by Wilhelm Kolff, a Dutch physician in 1941. The dialysis machine performs the work of the kidneys when the kidneys fail. This mainly involves removing waste material from the blood. The dialysis machine is needed during transplants to keep people alive before the operation and for a period of time after the operation, often ten days or so, until the donated kidney begins to work.

A workable surgical technique and the dialysis machine allowed kidney transplants to be performed and the first operation was performed in 1954 by Joseph Murray on a patient whose identical twin supplied the donated kidney. The operation was a success with no rejection problems as the donated kidney came from an identical twin so that the recipient's immune system did not treat the donated kidney as foreign material. When however kidney transplants were attempted using close relatives as donors, the donated organs were rejected by the recipient's immune system resulting in the death of the recipient.

A drug, known as 6-mp, had been developed by George Hitchings and Gertrude Elion as a treatment for leukaemia. 6-mp worked by stopping the cancer cell from dividing by appearing to be a chemical necessary for the cancer cells' division, but which was slightly different so that it stopped the cancer cell from dividing and so killed the cancer cell. 6-mp was tried to stop the immune system rejecting transplanted organs by stopping the division of cells in the immune system. 6-mp was tried on rabbits and found to stop the rabbits' immune system attacking foreign material, but leaving the rabbits' immune system otherwise working. Hitchings and Elion also developed a new drug azathioprine that was an improved version of 6-mp. Azathioprine was tried on people but with poor results until high doses of steroids in short bursts were given to patients with the azathioprine. This had the desired effect of preventing the immune system attacking the transplanted organ while still leaving the immune system able to work against ordinary infections. Eventually another drug cyclosporine was developed which had the same effect and transplant operations for other organs such as the lungs, liver, bone marrow and hearts were developed.

Improvements in medicine and sanitation led to people living longer and an increasing exposure to the diseases of old age. Arthritis became much more common in the twentieth century than previously. Arthritis of the hip was particularly a problem causing constant and serious pain to patients and greatly reducing mobility. The pain was caused by the rubbing of bone against bone in the hip due to the erosion of cartilage between the bones.

Some attempts had been made to provide artificial hips in the 1930's and 1940's but none had been particularly successful. A major difficulty was that the hip has to maintain the weight of the body as well as being completely mobile. John Charnley looked at the problem and came up with three innovations that were to lead to a practical artificial hip. He redesigned the socket, he cemented the artificial hip to the bones with acrylic cement and he lubricated the joint first with Teflon and then when that failed with polyethylene. Charnley's new artificial hip was an outstanding success and the hip replacement operation was to become a common operation in the late 20th century.

The heart is the most complex organ in the body and for the first half of the twentieth century surgeons did not touch it believing that to do so would kill their patient. In the 1930's and 1940's operations were carried out on the aorta and the pulmonary artery to ease symptoms caused by heart

problems, but the heart itself was not touched. In the late 1940's surgeons began to widen heart valves through a hole cut in the wall of the heart while the heart was still working. However, much heart surgery, known as open-heart surgery, was only possible with the heart being stopped. If the heart was stopped some means of maintaining the blood supply to the body was necessary or the patient would die. John Gibbon and his wife Mary Hopkins began work on a machine that could perform the work of the heart and lungs in the 1930's. The machine needed to be able to add oxygen and remove carbon dioxide from the blood and to pump the blood through the body. The machine needed valves to ensure the blood all flowed in one direction and had to use glass tubes as plastic had yet to be invented. The Second World War delayed progress, but a heart-lung machine was created in the early 1950's. Early results were not promising but the machine was taken over and improved by the Mayo Clinic. Donald Melrose, in England, and Viking Bjork, in Sweden, also built similar machines to allow open heart surgery. The result was to be an effective heart-lung machine that could take over the functions of the heart and lungs during operations so as to allow surgery on the human heart.

Analysis of the order of discovery in the history of medicine

The question of the origin of infectious disease was in dispute for thousands of years, the matter not being settled until the late 19th century. The earliest cultures and civilizations considered the cause of diseases to be supernatural and the appropriate remedies to be appeals to the Gods and magical incantations. Such beliefs were perfectly reasonable based upon the knowledge available to our pre-historic ancestors and to early civilizations. They had no awareness of bacteria, viruses or other microscopic organisms. Given that beliefs in Gods were used to explain other mysterious events, such as earthquakes, storms and volcanic eruptions, the Gods were an obvious explanation of disease. Given also that diseases can kill human beings, it would be reasonable to assume they are caused by powerful beings, like Gods or powerful demons and evil spirits. As the body automatically tends to repair itself, due to the immune system, it must have appeared to our pre-historic ancestors that on occasions the magical incantations and appeals to the Gods had worked. When the patient died the death could be put down to the capriciousness of the Gods or the great power of the evil spirit, rather than there being anything wrong with the treatment used.

In the west, from the time of Hippocrates, natural causes of diseases, such as the four humors theory, were the favoured explanation, although supernatural explanations continued to find acceptance. The same situation existed in China with natural causes of disease such as inadequate or imbalanced Qi and Yin and Yang being considered to be the causes of disease. A similar situation existed in India where a balance of the three elements, air, bile and phlegm was required for good health. The Greek, Chinese and Indian explanations of disease are quite similar all involving imbalances in bodily substances and all acquired a status that made them impervious to criticism and a block on innovation.

The presence of blood, urine, vomit and diarrhoea clearly shows the body has many internal fluids. Vomit and diarrhoea particularly seem to be present at times of sickness and recovery often occurs after vomiting and diarrhoea so that it would appear that getting rid of fluids from the body could cure sickness. Even bleeding was often followed by recovery from injury so that a limited loss of blood could be seen as promoting recovery. It is because the human body has these fluids and because getting rid of the fluids with vomiting, diarrhoea and bleeding seemed to cure sickness and injury, ideas such as an imbalance of fluids caused ill health arose in Western, Chinese and Indian cultures. This gave rise to theories such as Hippocrates and Galen's four humors theory and to remedies such as bleeding and

purging. The Chinese theory of an imbalance between Yin and Yang causing disease appears to be a more abstract version of the same idea. Given the knowledge of non-scientific societies these theories make good sense. A theory that micro-organisms, invisible to the naked eye, cause disease is hardly credible for societies that have no evidence of the existence of the micro-organisms. On the other hand bodily fluids plainly do exist and their removal from the human body seems to be associated with recovery from disease and injury.

The medicine of Hippocrates and Galen did not just relate to the four humors. It also dealt with qualities such as hot, cold, dry and wet. This is because many of the symptoms of disease relate to these qualities for example if a person has a temperature or fever, they are hot, if they are perspiring, they are wet. If they do not have a temperature, they are cold, if they are not perspiring, they are dry. Galen's theory was built up from the way the human body acts, both when it is sick and when it is healthy. If the human body functioned in a different way it would have led to a different type of medical theory. If for example the human body changed color when it was sick, rather than changing temperature, medical theory would likely involve explanations and treatments that involve colors with the aim of restoring the patient to his or her normal healthy color.

The traditional Chinese theory of medicine has considerable similarities to the classical theories of Galen. The western idea of *pneuma*, a vital spirit taken into the body by breathing, is similar to the Chinese concept of *Qi*. Galen's theory of the four humors considers much sickness is caused by an imbalance in the body fluids. The Chinese theory also deals with body fluids, known as *JinYe*. A healthy person will have the body fluids in balance, but if the body fluids are deficient, or if there is an accumulation of fluids, sickness can result. A further similarity between Galen's humoral theory and the Chinese theory is that the Chinese theory of Yin and Yang, like the humoral theory considers sickness is caused by imbalances within the body. The Chinese theory of blood also emphasizes that imbalances can cause sickness. Given that Yin and Yang, body fluids and blood should all be in balance to avoid sickness in Chinese medical theory, it has considerable similarities with Galen's humoral theory which considers sickness is caused by imbalances in the four humors. In both the humoral theory and traditional Chinese medicine the weather could cause imbalances in body fluids. A further similarity between Galen's theory and traditional Chinese medicine concerns the elements. Galen's theory uses the idea of the four Greek elements, air, fire, earth and water. Each element is associated with a particular organ, a particular humor and with the qualities of hot, cold, dry and wet. Water for example is associated with the organ, the brain, the humor phlegm and the qualities of cold and wet. Traditional Chinese medicine uses the Chinese elements of fire, earth, water, wood and metal. The elements are each associated with organs, one of which is a Yin organ and the other a Yang organ. Water for example is associated with the bladder and the kidney, while earth is associated with the stomach and the spleen. The elements are all interconnected so that if one of the organs and its element is in a state of imbalance, it will affect the other elements and their organs. This could affect the individual's facial color and emotional state as well as the functioning of the relevant organs. The Western and Chinese theories of medicine were so similar, because each was derived from the same source. The source was the human body and the environment that could affect the human body. If the human body and the environment were different the theories would be different.

The naturalistic and supernatural explanations of disease co-existed for thousands of years, sometimes with one dominant, and at other times, the other being the more powerful. Neither was more convincing than the other, in that both sometimes appeared to work and that both sometimes failed to work. When they failed to work, both the supernatural and naturalistic theories provided explanations for the failure. If the human body did not have an immune system, so that if a person got sick they inevitably

died and the incantations to the Gods and the treatment provided by doctors never worked, then the supernatural and naturalistic explanations of disease and the treatments they gave rise to would never have existed. It is only because the human body fights against disease, often successfully, that the incantations to the Gods and doctors treatments often appeared to be successful which suggested that the explanations of disease were true and the treatments provided were sometimes working. Both the supernatural and naturalistic explanations of disease could have been proved wrong with modern double blind testing, but such testing was not done in the past because it required knowledge of sophisticated statistical techniques that only became available in the last 400 years. Even in the 18th century the English and French were unable to agree as to whether smallpox inoculation was desirable, while in the first half of the 19th century Pierre Louis conducted trials which showed bleeding was a useful treatment. Even today, drug trials sometimes produce contradictory results. Even if testing had been done the theories would probably have survived due to the lack of serious alternatives.

It was not until the late 19th century with the development of the germ theory of disease that the question of the origin of infectious disease was settled in favour of a naturalistic theory, but a theory completely different from any of the naturalistic theories previously accepted. When Fracastorius in the 16th century suggested contagious disease was caused by tiny seeds invading the human body, the theory was quite reasonably not accepted, as there was no evidence of the existence of the tiny seeds, or that they caused disease. Fracastorius theory was almost identical to the germ theory of disease and the germ theory was only accepted in the late 19th century with the work of Pasteur and Koch. Leeuwenhoek had discovered micro-organisms in the late 17th century but that did not mean that they caused disease. In fact the vast majority of micro-organisms do not cause disease in humans. It was only with the more powerful 19th century microscopes that Pasteur and Koch were able to discover particular organisms which caused particular diseases in humans. They were able to show the organisms were the causes of the disease by isolating the organisms and by preparing a pure culture of the organism, which in the case of animals would then be injected into an animal causing the disease in the animal. This procedure known as Koch's postulate established the germ theory of disease and was able to show which particular germs caused which disease.

The explanations of infectious disease were based upon the knowledge available to a society at a particular time. When that knowledge changed (the discovery of micro-organisms and the discovery that some of them cause disease) the explanations of disease changed. Societies that considered the activities of supernatural beings as explaining otherwise inexplicable phenomena used supernatural explanations for the cause of infectious diseases. Supernatural explanations and naturalistic explanations of disease co-existed for thousands of years. Each was as convincing as the other until the germ theory of disease arose in the late 19th century. Naturalistic explanations of disease were based upon the natural world, and in particular, on the human body itself. Body fluids, organs and the elements of the natural world all had a prominent role in both Western and Chinese naturalistic explanations of disease. The Chinese and Western explanations of disease were similar because they had similar knowledge of the natural world and of the human body, so they developed similar theories to explain the origin of disease. If the natural world and the human body were different, then the theories explaining disease would have been different. When human knowledge of the natural world increased, with the discovery of micro-organisms in the 17th century and the discovery in the late 19th century that some of those micro-organisms caused disease in humans, the theories explaining the causes of disease changed. The germ theory of disease became the accepted explanation of infectious disease throughout the western world.

The practice of immunization (the modern name for vaccination, also known as inoculation) has been one of the most successful medical practices in history. It has been responsible for an enormous reduction in human suffering and has saved an enormous number of human lives. The injection of dead bacteria or their toxins, or dead or weakened viruses into the human body to create immunity against disease, has eliminated or controlled a considerable range of diseases. Immunization has been used successfully against anthrax, bubonic plague, chicken pox, cholera, diphtheria, Haemophilus influenza type B, mumps, paratyphoid fever, pneumococcal pneumonia, poliomyelitis, rabies, rubella (German measles), Rocky Mountain spotted fever, smallpox, tetanus, typhoid, typhus, whooping cough and yellow fever.

Immunization works because the body's natural defences against infection are able to remember dangerous bacteria and viruses they have already had contact with and are able to react more quickly and more strongly to later infections from the same organism. When an infection occurs certain cells in the body respond by moving to destroy the invading bacteria or viruses. In order to destroy the invading bacteria or viruses the body's immune system, a collection of free moving cells, has to recognise which materials in the body are foreign invaders and what is part of the body. It does this by matching the shape of receptors on the surface of defending cells to the shape of the surface of the invading organism and if they fit together the defending cells recognise an invading organism. Once recognition of an invader has taken place other defending cells will attack and destroy the invading organisms. The defending cells can also produce memory cells which, in the event of a future invasion by the same organisms, are able to immediately clone large numbers of the appropriate defending cells to attack the invading organism, without having to go through the process of recognising the invading organism. This makes the immune systems response to invading organisms, which it has recognised before, much stronger, faster and more effective. This process known as the amplification of the response, is the basis for immunization. A dead or greatly weakened infectious organism is injected into the human body so that the defending cells will remember the organism, so that in a future attack the immune system does not have to go through the recognition process and can immediately attack the invading organisms with large numbers of cloned defending cells.

If the body did not work in this manner, for example if it did not produce memory cells which instantly recognise invading organisms, the process of immunization would not work. This would mean that the wide range of diseases immunization is effective against would still be killing vast numbers of people.

Smallpox was the first infectious disease to be treated with immunization, partly because it was one of the worst and most persistent diseases in history and partly because nature provided a ready-made immunizing material, in the form of cowpox, which saved people from having to identify, isolate and produce a safe vaccine. The high mortality rate from smallpox and the observation that survivors were protected from future attacks, which could only be observed with a disease which was continually or often present made smallpox the obvious disease to immunize against. A disease which came and then disappeared often for centuries is a less urgent case to immunize against as it may well not come back for centuries making immunization unnecessary. Given that smallpox was often or continually around it made sense to immunize against it. It also made it more easily observable that survivors were protected against future attacks. This was not so easily observable with diseases which involved major epidemics and then disappeared for long periods of time, so there were no future attacks from which the victims of earlier attacks could be shown to be immune. However early attempts at variolation were so dangerous, that it is not surprising that it never really caught on.

The reason why smallpox was the first disease effectively treated with immunization was because nature provided, in cowpox, a ready-made vaccination material which was not dangerous to human beings. To produce effective vaccines for other diseases it was necessary to discover the bacteria or virus involved, to isolate it and to reproduce it. This process enunciated in Koch's postulates could only be done with better microscopes than was available in the 18th century. It also needed the understanding that germs cause infectious disease which was not established until late in the 19th century by Pasteur and Koch. This understanding was not needed for smallpox, where it could be empirically observed, even by milkmaids, that the natural vaccine, cowpox, prevented smallpox. With the other diseases it was necessary to understand the germ theory of disease and then to artificially produce a vaccine before it was possible to immunize against those diseases. The process of immunizing against smallpox was a lot simpler than the process of immunizing against other diseases, so immunization against smallpox occurred before immunization against the other diseases.

The taboo on human dissection applied in most human societies, except India, Ancient Egypt and Europe since the Renaissance. The result was substantially erroneous beliefs concerning human anatomy and physiology. Beliefs that the heart was the centre of thought, sense perception and controlled bodily movements, while the brain cooled the heart and blood held by Aristotle resulted from the taboo on human dissection. When the taboo was not present, such as in Alexandria during the Ptolemaic era, it was discovered, that the brain dealt with sense perception and bodily movements. Further progress in anatomy and physiology was delayed until the Renaissance when some dissections of the corpses of executed criminals was allowed. This eventually resulted in the anatomical discoveries of Vesalius and the circulation of the blood by Harvey. Many future developments in medicine, especially in surgery, were dependent upon the new knowledge of anatomy and physiology obtained from the lifting of the taboo on human dissection.

Progress in surgery was also dependent on the discovery of anaesthesia and anti-septic and a-septic practices. There were two main consequences from the discovery of anaesthesia. The first was that surgery became far more common as patients no longer tried to avoid it. The second was that surgical operations became a lot longer with emphasis being on precision and accuracy rather than on speed. With increasing time being spent on operations more intricate and complex operations could be performed which greatly widened the range of operations available. With much longer operations and the need for anaesthetics and anaesthetists the cost of operations went up as did the status of surgeons who were now able to do so much more for their patients. Surgery became a practical solution to many medical problems.

The idea that cleanliness was important to stop infections in surgery and obstetrics was only accepted after Pasteur had established the germ theory of disease which showed that bacteria in the air caused infections. Prior to the germ theory of disease being accepted suggestions that cleanliness was important, were ignored as there seemed to be no reason why cleanliness could stop infection or lack of cleanliness could cause infection. The discovery that infection was caused by bacteria in the air, led to the anti-septic idea of killing the bacteria to stop infection and then to the a-septic idea of sterilising everything that came in contact with the patient.

The ending of the taboo on human dissection resulted in vastly improved knowledge of anatomy and physiology, this, and the discovery of anaesthesia and the realisation of the importance of a-septics, formed the basis of modern surgery. Only when these developments came together, was it possible for modern surgery, with its sophisticated and intricate operations, to become a reality.

This led to new types of surgery which had never before been developed such as abdominal and brain surgery. Plastic surgery, which had been practiced crudely in the past, improved enormously and later led to cosmetic surgery. Hip replacement operations were developed after the invention of a practical artificial hip. Organ transplants began when surgical techniques were developed for joining small blood vessels and when the problem of rejection of donated organs was solved by the development of appropriate drugs. Kidney transplants developed rapidly after the invention of the kidney dialysis machine as it is a relatively simple operation and because there is a better supply of donated kidneys as human beings have two kidneys and only need one so as to allow transplants from living donors. Open heart surgery and heart transplants were developed after the invention of the heart-lung machine to keep the patient alive during surgery.

The use of anti-biotics in medicine is only possible because nature provides such organisms that inhibit the growth of bacteria and allows the production of synthetic compounds that achieve the same result. If nature did not provide these organisms, or allow such compounds, there would have been no anti-biotics used in medicine. Without anti-biotics, medicine since the 1940's would have been much less effective and hundreds of millions, who were cured of infections, would have died. The discovery and use of anti-biotics was impossible before the development of microscopes capable of observing bacteria. Only when such microscopes existed was it possible to observe that certain organisms were capable of killing or inhibiting bacteria. A number of such observations were made in the late 19th and early 20th century and eventually it was realised that penicillin, a substance taken from one of those bacteria killing organisms, could be used against infectious disease. When penicillin was proved to be effective, a systematic search was made for other anti-biotics which resulted in the discovery of a number of other anti-biotics. However, it was only because nature has provided the anti-biotics, that we have them, and we have only had them, since we acquired the knowledge of their existence and of how to use them.

The use of statistics in medicine has been of enormous use in showing the causes of disease and in assessing the effectiveness of treatments. Yet statistics are never able to provide a perfect answer to questions of drug effectiveness and the causation of disease. They may show a co-relation between two variables, for example people living close to the sea have higher rates of cholera, than people further from the sea. This does not however mean that proximity to the sea causes cholera. Co-relation does not prove causation as the correlated variable may be caused by a third factor, such as polluted river water which is more common closer to the sea. The third factor, often called a lurking variable, may well not be considered in the data so no effort is made to compare cholera rates among people drinking polluted water close to the sea with those drinking clean water close to the sea. If the comparison was made it would show that it was the quality of drinking water rather than proximity to the sea that was the important variable concerning cholera rates. When trying to discover the cause of increasing lung cancer after World War II, air pollution and asphaltting of roads were considered likely causes as both were increasing at the time lung cancer rates were increasing. Working out, which variable to study, when trying to discover the causes of disease, can be very difficult.

A further problem concerns trying to ensure the chosen sample is representative of the population which is being studied. Pierre Louis concluded bleeding was a useful treatment, but one of the groups he studied was substantially younger than another group. The sample must also be of sufficient size or simple co-incidence and high margins of error may provide misleading results. Pierre Louis' study of bleeding was criticised for having insufficient numbers in his sample.

Given the difficulties of doing good statistical studies it is not surprising that the causes of diseases and the effectiveness of treatments were never accurately assessed until recently. Modern

statistical methods were only developed in the 17th, 18th and 19th centuries and arose from probability theory. It was only with the development of modern statistical methods that it has been possible to identify the causes of many diseases and to evaluate the effectiveness of treatments. Even with modern statistical methods the causes of some diseases, for example some cancers, are still difficult to pinpoint. Often different studies of the same phenomena will produce different results. In these circumstances it was impossible for people in the past to discover the effectiveness of treatments and the real causes of disease until the discovery of modern statistical analysis.

Modern diagnostic technology began with the discovery of X-rays. X-rays however could not be discovered until certain earlier discoveries had been made. X-rays were discovered through the use of a Crookes tube which required prior discoveries of an efficient air pump to create a near vacuum in the tube and the ability to send an electric current through the tube. Only when these discoveries had been made was it possible to discover X-rays. The use of X-rays was eventually improved and extended by the use of contrasting media and eventually by CT scanners after the invention of computers.

X-rays are a form of electro-magnetic energy and are useful due to their property of being able to pass through matter of low density but not matter of high density. This allows X-rays to be used to produce photographs of the interior of the human body, which is why X-rays are so useful in medicine. It is only because nature has provided such a form of electro-magnetic energy that we have X-rays available to be used for medical diagnosis. If nature had not provided electro-magnetic radiation with that property we could not have the ability to see inside the human body for medical purposes by means of X-rays.

Endoscopy only became practical when Hopkins and Hirschowitz discovered a practical method to make light travel around corners. It was only because such a method exists that we are able to have modern endoscopy, and modern endoscopy could not exist until the discovery of how to make light travel around corners. Endoscopy was further enhanced when Hopkins discovered that thin lenses of air gave much greater light transmission than thin lenses of glass, so as to allow much better endoscope photography. If such lenses did not provide improved light transmission, then endoscope photography might still not be practical.

Our brief examination of the history of medicine has shown how the environment relevant to medicine has affected the history of medicine. The relevant environment includes the human body, how the human body works, the diseases that attack the human body, how the materials in the environment affect the human body and how the body reacts to disease and injury. If the human body was different then the history of medicine would have been different. If, for example, there was no immune system, then a lot of the confusion concerning the effectiveness of treatments used in the past would not have existed. When patients treated with prayers, incantations, herbs, medicines, moxabustion and bleeding recovered, it looked as though the treatment had worked. If patients died all the time, as they would have if there was no immune system, it would have been clear all these treatments were failing and they would have been abandoned. If there was no immune system then modern treatments such as immunization would not work and would not be available. If the human body was different, the theories as to what went wrong with it when people got sick would have been different. Galen's humoral theory and traditional Chinese theories were based on the human body and how it behaved in sickness and in health. If the body was different then those theories would have been different.

Anaesthesia was only possible as materials in the human environment had the property of making people so unconscious that they could not feel pain. X-rays were only possible as electro-magnetic energy of a certain wave length will pass through matter of low density but not matter of high density. Modern

endoscopy is only possible because light can be made to travel around corners and thin lenses of air provide excellent light transmission. The use of anti-biotics is only possible due to bacteria killing organisms existing in the human environment and the ability to create compounds that will kill bacteria. The properties of materials and matter and forms of energy in the environment determine what is possible in medicine.

When knowledge of the environment relevant to medicine changed, this resulted in new theories, such as the brain being the centre of thought and emotions rather than the heart, the circulation of the blood and the germ theory of disease. These ideas were the logical explanations of the new knowledge that human beings had acquired, just as the previous theories were the logical explanations of the knowledge humans possessed at those times. Increasing knowledge of the environment, relevant to medicine, also led to the development of new treatments such as anaesthetics and new drugs. The new theories and treatments inevitably had significant social and cultural consequences, such as greater life expectancy, reduced suffering and different attitudes concerning religious beliefs, all of which would themselves result in further social and cultural consequences.

Where taboos existed against the acquisition of new knowledge, such as the taboo on human dissection, then the acquisition of new knowledge will be delayed until the taboo is removed. This, in the case of medicine, meant erroneous ideas of human anatomy and physiology continued for as long as the taboo remained in place. Only after the taboo was lifted was it possible to make the anatomical discoveries of Vesalius and for Harvey to discover the circulation of the blood.

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