Cultura Científica

11th Grade (1º Bachillerato)

Name and surname_____ Group: ___

Colegio de San Francisco de Paula, 2015.

Unit 1. OUR PLACE IN THE UNIVERSE

1.1 The Origin of Life

Science or belief?

Where do we come from? How did life on Earth start? What were our ancestors like millions of years ago? Questions about the origin of life have troubled mankind throughout time. There are different myths that try to answer those questions. "Each culture, each religion and each school of thought has its own answers, many of which are incompatible with each other". (1).

Science studies nature, its processes and the laws that govern our planet. On the other hand, Religion tries to give sense to life and the moral convictions that guide the behavior of humankind.

As scientists, we will try to answer those questions from a scientific point of view. As you know, to answer scientific questions hypotheses have been formulated based on research and observation. Some of the hypotheses concerning how life began on Earth and evolved into the forms we know today, have matured into widely accepted theories. However, as we are trying to answer questions about events that took place millions of years ago some aspects of those answers are far from unquestionable.

1.2 What Is Life?

The most widely accepted hypothesis about the origin of Life on Earth is that it came from inorganic molecules which combined together, in appropriate conditions, forming complex and ordered organic molecular aggregates. These organic molecules grew in complexity and were eventually able to self-replicate and carry out metabolism (the first primitive cell).

But how do we define life? There is no simple answer to that question. In order to better understand life we need to talk about a series of characteristics that all living beings share.

Characteristics of living beings:

- Living beings have a complex chemical and structural composition. (Inert matter, such as a rock is composed of few, very simple molecules, whereas living beings are much more complex).
- Living beings have the capacity to respond to stimuli (the environment which surrounds it).
- Metabolism: a series of complex biochemical reactions that are not present in inert matter.
- Reproduction: producing viable offspring for the continuity of the species.

1.3 A Perfect Place for Life

The Earth is the third planet in our Solar System, after Mercury and Venus, which are too close to the Sun to be able to hold life. Mars could, in theory, hold some form of life, as there is evidence that shows that liquid water once ran on its surface. However, there is very little water presents on Mars now and, it is found in the form of ice; Mars is a cold and dry place. At the end of the 20th century, a meteorite that had fallen from Mars (about 13 000 years ago), was found in the Antarctic. It seemed at first that the meteorite had some type of organic molecules (biomolecules).

However, after detailed studies of the meteorite the possibility was discarded by the majority of the scientific community.

Neither does the Moon hold any type of life; lacking an atmosphere and water it is a desert-like place.

So, what makes our planet so special? What are the necessary characteristics in order to hold life?

1.4 Our Primitive Planet

Our primitive Earth had a very different atmosphere, containing lost of hydrogen, methane, and ammonia. It is important to point out that the primitive atmosphere has no molecular oxygen, therefore being a reducing (electron-adding) atmosphere.

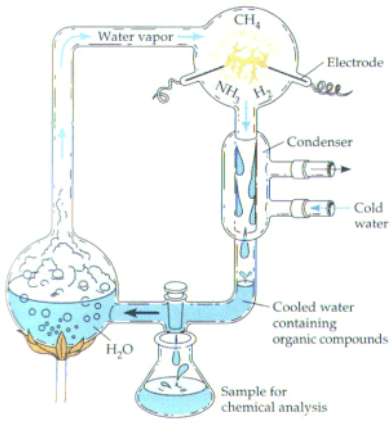
In the 1920s, A.I. Oparin (Russian) and J.B.S. Haldane (British) independently postulated that conditions on the primitive Earth favoured chemical reactions that synthesised organic compounds from simple inorganic compounds that were present in the early atmosphere and seas. They suggested that the energy needed for these reactions to occur came from the intense ultraviolet radiation that entered the primitive atmosphere, as there was no ozone at this point to screen them out. (There is also evidence that young suns emit more ultraviolet radiation than older suns). (2).

This synthesis of organic molecules from inorganic molecules cannot happen in the modern world, as the present atmosphere is rich in oxygen produced by photosynthetic organisms. The oxygen in today's atmosphere would attack chemical bonds extracting electrons, not allowing the spontaneous synthesis of complex molecules from simpler ones. On the other hand, the reducing (electron adding) atmosphere would have enhanced the joining together of simple molecules to form more complex ones.

These new organic compounds would accumulate in the primeval seas forming what is called the 'primordial soup', where these compounds were allowed to mix and become even longer polymers and more complex. It is in this primordial soup where the first forms of life would arise on our planet.

In 1953, Stanley Miller and Harold Urey tested the Oparin-Haldane hypothesis by creating in the laboratory conditions comparable to those of the primitive Earth. They were able to produce a variety of amino acids and other organic compounds found in living organisms today. Miller proved that it was indeed possible to make amino acids essential for life from inorganic matter.

- **Miller's experiment:** a warmed flask of water simulated the primeval sea. The atmosphere he created included water, hydrogen, methane and ammonia. Sparks were discharged to mimic lightning. After one week he analysed the contents of the solution and found a variety of organic compounds, including some amino acids that make up the proteins of organisms (2).



Similar experiments have since allowed other scientists to obtain other biomolecules. In 1960 a Spanish scientist Juan Oró synthesised adenine. And a few years later he also synthesised ribose and deoxyribose. However, there seems to be some doubts today about the actual composition of the primitive atmosphere, so we need to keep looking for the best scientific answer.

1.5 Chemical Keys for Evolution

Before we start talking about how the first cell arose, let's go back to Miller's experiment. We know that in the primitive Earth, organic molecules could have been synthesised from inorganic matter with energy obtained from lightning. And we also know that the primitive atmosphere was a reducing atmosphere lacking molecular oxygen. So, the absence of oxygen at that time prevented the oxidation and consequent decomposition of these organic compounds so they stayed and developed into more complex compounds. Some of these first compounds formed what are called **coacervates.** A coacervate is a protein molecule surrounded by a thin membrane, a microsphere. These microspheres would grow slowly and eventually would form buds that separated from them and followed the same growing pattern. Basically this is the formation of stable entities that can separate themselves from the surrounding environment and maintain their integrity. It is thought that these coacervates eventually then gave rise to the first cell.
The first cell was probably very simple, having a low metabolic capacity. It was most likely a heterotrophic organism, obtaining its energy by the fermentation of nutrients of the environment that surround it. (Fermentation is a type of anaerobic respiration). As these microorganisms proliferated, the nutrients diminished, and therefore, a selection process would start. These microorganisms probably underwent different mutations in the genetic material due to the constant impact of UV rays (no ozone at the time), giving rise to the cells with a different metabolism, capable of synthesising their own food: the first autotrophic cells. These autotrophs were now able to produce the organic compounds they needed to survive.

The appearance of these autotrophs brings along some significant changes, such as the capacity to synthesise carbohydrates from CO_2 and H_2S, using sunlight as their energy source and releasing sulphur in the process.
Soon enough new variations came about, other autotrophs appeared, that use H_2O, then a pollutant compared to the more ecological, H_2S, **releasing oxygen** in the process. This oxygen was lethal for the earliest microorganisms used to living in a non-oxidising atmosphere. Photosynthesis then became the first source of contamination on our planet and these autotrophs called cyanobacteria the first to use it.
The gradual change to a more oxidising atmosphere killed the very first heterotrophic microorganisms (Precambrian prokaryotes) as oxygen attacks the bonds of organic molecules. This caused the extinction of many bacteria unable to cope with the change, but disappearing without leaving a fossil record behind. Others survived in habitats that remained anaerobic, where we find their descendents living today. (obligate anaerobes, such as many fermenting bacteria).

Cyanobacteria continued releasing oxygen and their activity was such that eventually they were able to change the atmosphere, becoming an oxygen rich atmosphere, further protected by an ozone shield screen.
These changes allowed the appearance and propagation of new species that used oxygen to carry out respiration, including us, humans.

1.6 Some Alternative Views. The Possibility of an Alien Origin.

(Laboratory simulations cannot establish that the kind of chemical evolution that has been described before actually created life on the primitive Earth, but only that some of the key steps *could* have happened. The origin of life remains a matter of scientific speculation.)

It is possible that at least some organic compounds reached the early Earth from space.

First the scientist Jacob von Berzelius (in the first half of the 19th century) showed that a particular meteorite, *carbonaceous chondrites* contained organic matter. A few years later (1864), the Chemist Berthlot analysed the fragments of another meteorite of the same type that had fallen in Orgueil (France), and again confirmed the presence of organic compounds in it. Again in the last years of the 20th century, more meteorites and comets were analysed, and many organic compounds were found in them.

So the idea called **panspermia,** (first proposed by the Greek philosopher Anaxagoras more than 2 000 year ago), was proposed again by S. Arrhenius in 1903. This idea holds that meteorites and comets hitting the early Earth brought organic molecules from outer space, somehow seeding the early Earth with organic compounds. It could be that both panspermia and chemical evolution could have contributed to the pool of organic molecules that formed the earliest life.

1.7 Evolution of the Species

There are many ways to describe or define evolution, some more complete than others. But in simple terms, as Campbell says, "In biology, **evolution** refers to the processes that have transformed life on Earth from its earliest forms to the vast diversity that characterises it today" (pg 420 Campbell book)

1.7.1. A Revolutionary View

(Towards the end of the 18th century and the beginning of the 19th century, several naturalists suggested that life had evolved along with the evolution of Earth. However, the creationist point of view, (the doctrine of fixed species, where species were individually created by a superior entity) was firmly embedded in Western thought, well until the beginning of the 19th century. Additionally, scientists of the time, such as George Cuvier or Carolus Linnaeus argued and defended that the species were permanent creations (had always been the same). Even then however, more and more signs of evolution were being discovered and collected (paleontology-studies fossil records; anatomical studies, comparative embryology, etc.) all of which cast doubt on the doctrine of fixed species.

Jean Baptiste Lamarck was the first one to publish a theory of evolution (Inheritance of Acquired Characteristics) in 1809 (the year Darwin was born). But it was not until Darwin published his theory of evolution in 1859 (The Origin of Species by means of Natural Selection) that the scientific community really started to understand the mechanisms of evolution. They were still missing some important aspects of genetics, and population genetics that, later on helped us better understand the mechanisms of inheritance and evolution of populations. This important progress would lead us to the Modern Evolutionary Synthesis.

1.7.2. Evolutionary Theories

Lamarck: Inheritance of Acquired Characteristics (1809).
Darwin-Wallace: The origin of Species by means of Natural Selection (1859).
The Modern Evolutionary Synthesis or neo-Darwinism.

- **Lamarck's Theory of Evolution (1744- 1829)** What is his theory based on?

1. All organisms tend to change to higher and more complex ones and they do that unconsciously driven by a metaphysical force (**vital force**)

2. This innate tendency to perfection is influenced by environmental changes, therefore becoming better adapted to their environments. These environmental changes would create 'new needs' in organisms, having to use certain organs or characteristics more than others.

3. This use and disuse of certain organs causes those organs that are used more often to cope better with the environment, making them become larger and stronger (hypertrophy), while those that are not used deteriorate (hypotrophy or even atrophy).(In other words: the function makes the organ). So, organisms could acquire certain characteristics throughout their lifetimes, and lose others.

4. Lamarck believed that the changes in organs by use and disuse during their lifetime were passed to the next generation (inheritance of acquired characteristics).

Flaws on his theory:

1- There is no kind of data or proof of that innate tendency to complexity (vital force).
2- **Acquired characteristics are not inherited**. Only characters regulated by genes can be inherited and only if those genes are present in reproductive cells.

- **Darwin's Theory of Evolution**

In 1859 Charles Darwin and Alfred Russell Wallace published together their theory of Evolution (it should be called the Darwin-Wallace theory), which replaced Lamarck's theory. Darwin explained his theory on his book *The Origin of Species*, where he presented his theory of natural selection as the mechanism of evolution.

Basically, his **theory of natural selection** is based on three observations and two conclusions from such observations:

1. Without environmental pressures, all species have such great potential fertility that their population size would increase at an exponential rate.

2. However, in normal conditions, the number of individual of a species tends to remain more or less constant, except for seasonal fluctuations.

3. Individuals within a species are different from each other (Think of your classmates, you each have your particular characteristics, which define you).

4. There is a "struggle for existence" caused by environmental pressures.

5. Each individual, being different from others, will be more or less fit for the particular environment where it lives (so facing the harsh environmental factors differently).

6. Some organisms are better adapted than others, and so they are selected by the environment- Natural Selection. Those better adapted individuals are likely to have more offspring than those less fit. (Many of their offspring will also be well suited to the environment). And over time and over generations their characteristics will be dominant within the population. (Sometimes called 'Survival of the fittest,' although neither Darwin nor Wallace used this).

7. What Darwin was not able to identify was the cause of individual variations among organisms of a population, and so he had to borrow Lamarck's acquired characteristics theory.

(Weissman did not carry out his experiments until 1880. Mendel enunciated the laws of heredity six years after Darwin published his book, however Mendel's work was not recognised or appreciated until 30 years later, which considerably slowed down the understanding of evolutionary mechanisms).

(Over vast spans of time, and always due to environmental factors, a group of individuals could accumulate a considerable amount of favourable characteristics giving rise to a new species from the original population).

- **The Modern Evolutionary Synthesis or neo-Darwinism. Today's Theory of Evolution**

(A comprehensive theory of evolution that became known as the **modern synthesis or neo-Darwinism** was forged in the early 1940s. This theory is not the work of one but many scientists. It is called synthesis because it integrated discoveries and ideas from many different fields, including population genetics, paleontology, taxonomy, etc)

We can define evolution as *the natural selection (via differential reproduction), which acts upon genetic variations (that are in turn the outcome of mutations and sexual recombination) that appear among the members of a population.*

Differential reproduction: individuals within a species compete with each other for mates, and those that are best equipped to succeed in this struggle will produce the most offspring. As a consequence, their genes will increase in the population.
Genetic variations among individuals can only happen in two ways: a mutation, which is a common process to individuals of both asexual and sexual reproduction; and genetic recombination, which takes place during meiosis, which can only happen in individuals with sexual reproduction.

1.7.3 Species and Speciation

We can define 'species' as a group of organisms capable of interbreeding and reproducing fertile offspring. A species is characterised by its gene pool. The formation of a new species, speciation, is caused by changes in the genes of an existing species that result in change in their characteristics. The process of speciation is very difficult to study in the laboratory as it is a very slow process, therefore not easily reproduced.

There are different mechanisms by which a species evolves into a new one. In some situations, populations of members of the same species can be isolated or separated by a geographical barrier (river, a mountain, etc), which will avoid a gene

interchange between them. With time their genetic makeup will be different and therefore they will not be able to interbreed. This is known as **allopatric speciation**.
However, at other times, a behavioral or temporal isolation could exist which would also lead to speciation. This is called **sympatric speciation**, the formation of two or more descendant species from a single ancestral species all occupying the same geographical location.

Thanks to these mechanisms new species are born and others disappear. At the moment there are believed to be around 2 million species and millions more are believed to be as yet undiscovered.

1.8. Evidence for Evolution

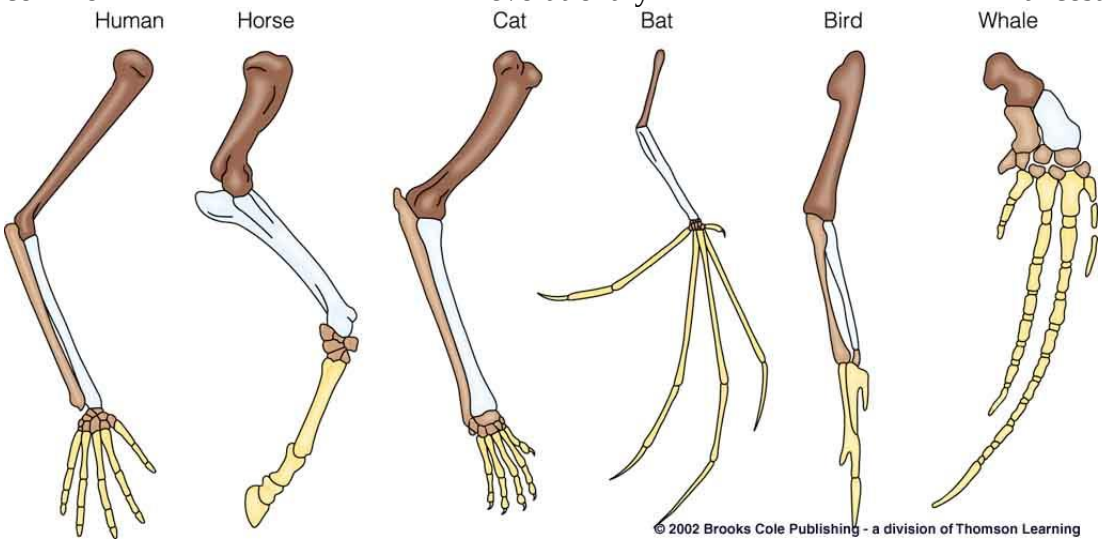
Evolution leaves observable signs.

- **Biological evidence**: when a species undergoes a change in some of its biological characteristics, such as the appearance of pigments in certain butterflies for camouflage.

E.g. the butterfly *Biston betularia* is a nocturnal animal that sleeps during the day on the trunk of trees covered by grayish lichen. The insect exists in two forms, one with clear wings and the other, rarer, with dark wings. Before the industrial revolution, the clear winged variety was more predominant, but after the industrial revolution the dark wings one started to be more abundant. The hypothesis to explain this is that at the advent of the industrial revolution much of the landscape became covered with soot and dark colours due to contamination. The dark coloured butterflies became better camouflaged and survived more against predators than the clear coloured variety.

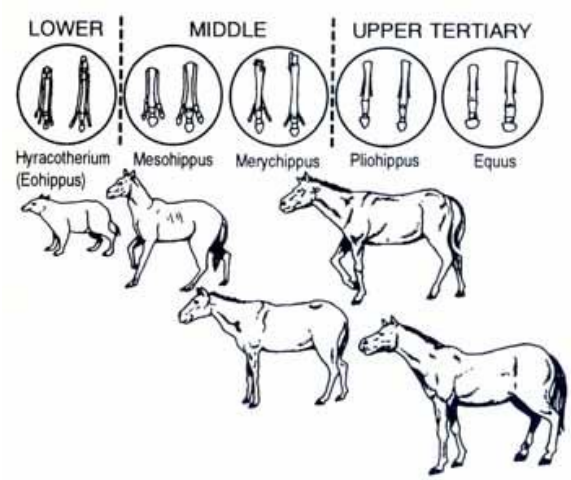
We can also talk about anatomical signs of evolution. An example would be homologous structures: The limbs of all mammals are constructed from the same skeletal elements, suggesting that a common ancestral for limb has been modified for many different functions.

Homologous structures or organs are anatomical resemblances that represent variations on a structural theme originally present in a common ancestor. Homologous organs have the same embryological origin, but different function, therefore indicating a common evolutionary ancestor.



On the other hand **analogous structures or organs** are those that have a different origin, but carry out the same function (e.g. the wings of bats and the wings of insects)

- **Paleontological evidence; the fossil record:** As you should recall, fossils are the remains of plants and animals that lived in the past. Thanks to the fossil record we can demonstrate an evolutionary transition of a species. A famous example can be found in the evolution of the horse. (Bones of horses were found in different strata of rocks that indicate the time at which these horses lived. It is clearly seen through the fossil record how the horse ancestor has gradually undergone many changes while evolving into our modern horse).



- **Comparative embryology:** The study of embryos has proven that closely related organisms go through similar stages in their embryotic development.

  (E.g. all vertebrate embryos go through stages in which they have gill pouches on the sides of their throats).

- **Molecular evidences:** All living organisms are made of and make use of the same molecules, and all of them use DNA for the storage of their genetic information (genes).

Additionally, biochemical processes are the same in living organisms. But most important, the more closely related two species are, the greater the percentage of DNA they have in common. Evolutionary relationships among species are reflected in their DNA and protein (that is to say, in their genes and gene products).

1.9 The Human Species

About 65 million years ago a group of mammals appeared that adapted to a nocturnal life in trees. This group of mammals is the ancestor of all primates. The includes, besides humans and our other close relatives such as gorillas, chimpanzees, and orangutans, also includes other families like monkeys and pro-simians (lemurs). Over time, a hominid group evolved into the modern day human, *Homo sapiens,* characterised by the following:

- Being taller in height than other hominids.
- Living in a more complex social system.
- The development of language.
- Eating meat on a regular basis. (high protein foods)
- Making and using tools.
- Development of the child and childhood stages of life.
- Intelligence (slower development of the brain than in other mammals which allows more and more complex neurological connections).
- Burial rituals (showing an understanding of death).
- Wearing clothes.

Unit 2. LIVING BETTER AND LONGER

In the year 2000 the United Nations in the Declaration of the Millennium developed goals to be achieved by 2015 in order to obtain a more peaceful and just world.

All nations should make a pledge to: reduce poverty and hunger; improve global health; achieve gender equality; ensure access for all people to education; have drinkable water and improve the well being of our environment.

The eight Millennium Development Goals (MDGs) of the United Nations.

1. Eradicate extreme hunger and poverty.
2. Achieve universal primary education.
3. Promote gender equality and empower women.
4. Reduce child mortality.
5. Improve maternal health.
6. Combat HIV/AIDS, malaria and other diseases.
7. Ensure environmental sustainability.
8. Develop a global partnership for development.

As you can see many of these goals are directly or indirectly related with health. But, what is health?

The World Health Organization (WHO) definition of health

Health is a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity

(Compare the lives of Natalia and Shani) pg.48 in the CCMC book.

According to research, there are seven personal conditions that can have a direct influence in the longevity and quality of our lives: smoking or not, moderate consumption of alcohol, having a stable relationship, performance of regular physical exercise, maintenance of correct weight, a good educational level, and a positive attitude towards problems.

http://www.infoplease.com/ipa/A0779147.html

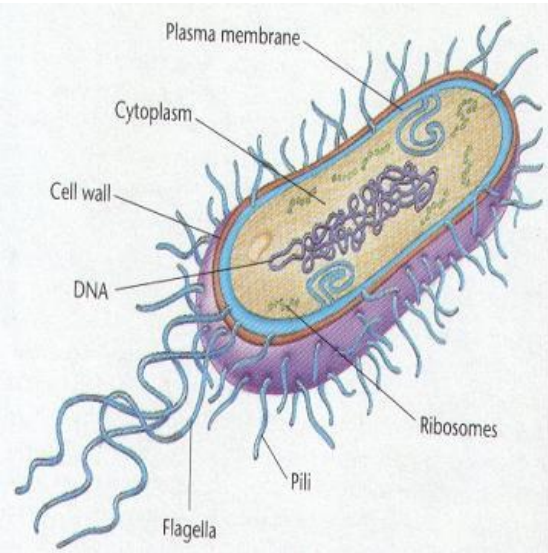
Top 20 Causes of Mortality throughout the World

		All countries	
Rank	**Cause**	**Total deaths (in thousands)**	**% of total**
1.	Ischaemic heart disease	7,208	12.6%
2.	Cerebrovascular disease	5,509	9.7
3.	Lower respiratory infections	3,884	6.8
4.	HIV/AIDS	2,777	4.9
5.	Chronic obstructive pulmonary disease	2,748	4.8
6.	Diarrhoeal diseases	1,798	3.2
7.	Tuberculosis	1,566	2.7
8.	Malaria	1,272	2.2
9.	Cancer of trachea/bronchus/lung	1,243	2.2
10.	Road traffic accidents	1,192	2.1%
11.	Childhood Diseases	1,124	2.0
12.	Other unintentional injuries	923	1.6
13.	Hypertensive heart disease	911	1.6
14.	Self-inflicted	873	1.5
15.	Stomach cancer	850	1.5
16.	Cirrhosis of the liver	786	1.4
17.	Nephritis/nephrosis	677	1.2
18.	Colon/rectum cancer	622	1.1
19.	Liver cancer	618	1.1
20.	Measles	611	1.1

Source: The World Health Report, 2003, The World Health Organization (WHO).

Read more: Top 20 Causes of Mortality Throughout the World — Infoplease.com http://www.infoplease.com/ipa/A0779147.html#ixzz12nGjkdb

2.1 BACTERIA AND VIRUSES



Bacteria are unicellular prokaryotic organisms. That is to say, they are made of just a single cell that lacks a nuclear envelope.

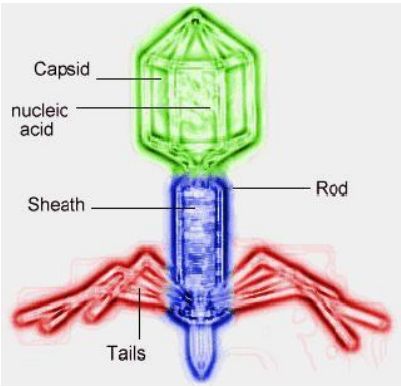
Bacteria can be found in all types of environments. That is due to their ablilty to adapt to any type of environment. They can be found as isolated bacteria or forming colonies.

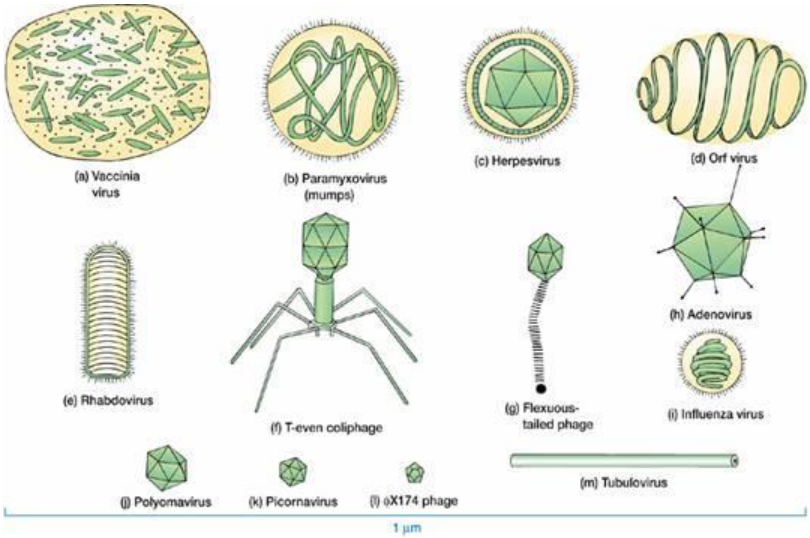
According to their shape, we can classify bacteria as: cocci, bacilli, spirilla and vibrios. Cocci are spherical or round;

bacilli are rod-shaped; spirilla and spirochetes look like a spiral, and vibrios look like a comma.

Viruses are strict pathogenic microorganisms. That is to say they can only survive if they take over the cells of another living organism.

They have a simple structure and present different shapes.

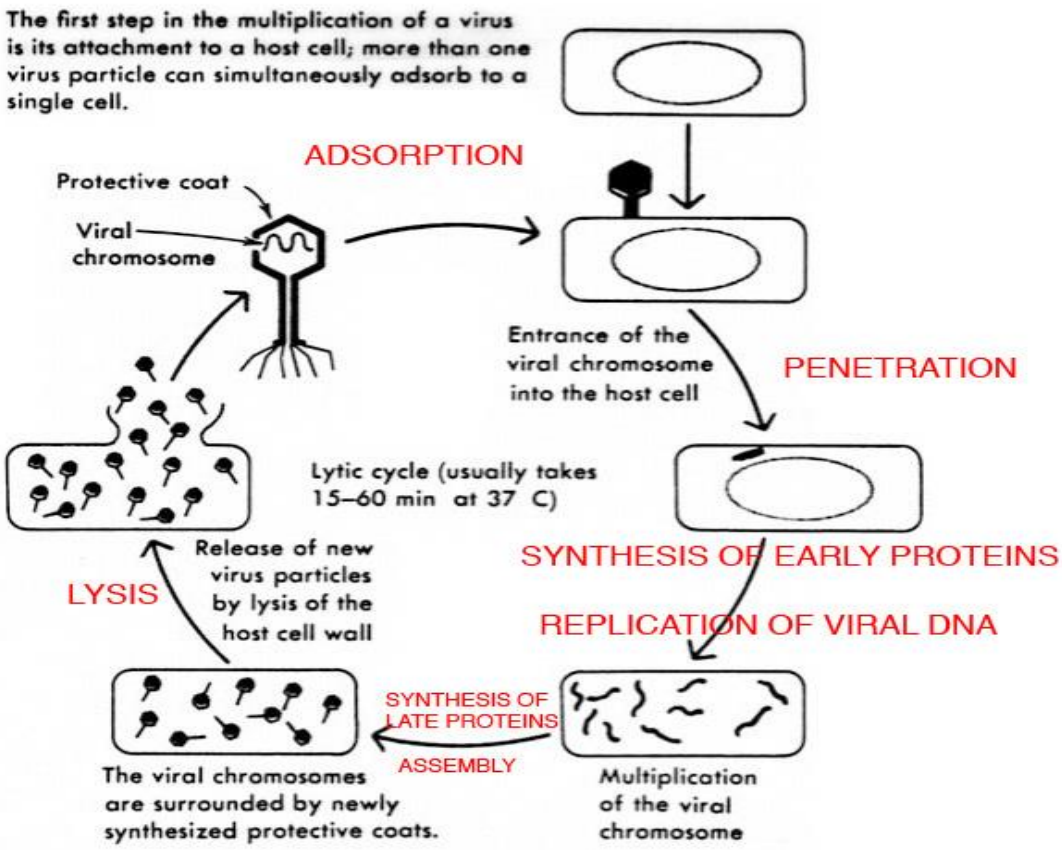




2.2 Life Cycle of a Bacterophage

A bacteriophage is any virus that infects bacteria. We can refer to them as phage for short. Bacteriophages may have a lytic or a lysogenic cycle and a few viruses are capable of carrying out both cycles. In the lytic cycle, bacterial cells are broken open (lysed) and destroyed after the replication of the virus.

Below are the steps followed in the lytic cycle of a bacteriophage:



1. **The viruses enter the host cell**. Viruses attach to the bacterial cell that is going to be infected. Then, the genetic material of the virus (DNA or RNA) is introduced inside the cell.
2. **Formation of the virion (a virus in infective form) components**. The virion components are obtained using the genetic material of the virus and enzymes of the bacterial cell which has been infected.
3. **Assembly**. The virion components come together, assembling new viruses.
4. **Release**. The new viruses leave the host cell to infect new cells.

2.3 Antibiotics

Alexander Fleming, a British bacteriological doctor, discovered penicillin on September 3rd, 1928. Alexander Fleming was working with colonies of the bacterium *Staphylococcus aureus*. By accident, he left one of the Petri dishes without the lid, and a white mould grew on it. The colonies of bacteria around the mould had disappeared; therefore the mould had to produce a substance capable of killing the bacteria. Fleming later on identified this mould as *Penicillium notatum.*

(In 1929 Fleming published his discoveries, however, it is not until 1940 when the antibiotic present in Fleming's cultures was actually efficiently isolated and tried in mice after three years of studies by a group of Scientists in Oxford. In 1941, the antibiotic was used in humans for the first time, saving the life of 5 out of six people with an infection provoked by the staphylococcus bacterium).

2.3.1. Main Groups of Antibiotics

The word antibiotic was first used in1941 to define substances that would kill or selectively inhibit the growing of microorganisms.

The majority of antibiotics are obtained from bacteria, but others are obtained from fungi or by chemical synthesis.

The main groups of antibiotics are the following:

- Penicillins: effective against staphylococci, streptococci, meningococci (meningitis) spirochaetes (syphilis) and infections caused by the aschomycete fungus.

- Aminoglycosides: (Isolated from *Streptomyces*, it is used to fight tuberculosis).

- Cephalosporins: effective against a variety of bacteria. (Produced by fungi - *Cephlosporium* sp.-).

- Chloramphenicol: these are often used in eye infections. (Formerly produced microbially by *Streptomyces venezuelae*. Nowadays it is chemically synthesised).

- Tetracyclines: often used in skin infections.

- Vancomycin: Nowadays, it is the last resource to fight against bacteria that have become resistant to other antibiotics.

2.3.2. Antibiotic Resistance in Bacteria

(It may seem ironic the fact that *Staphyloccocus aureus*, the bacterium grown by Fleming and the reason why antibiotics were accidentally discovered, was the first bacterium showing resistance to antibiotics. Nowadays, 90% of the strains of *Staphyloccocus* are resistant to penicillin).

Antibiotic-resistant bacteria develop since, as in any other living organism, they can show slight modifications from one another. Since bacteria reproduce asexually, they generally do not change very often. However, there are two sources of possible changes in their genetic makeup. One would be mutations, and the other is known as plasmid transfer. A plasmid transfer is when a bacterium transfers genetic information to another bacterium in a ring of nucleotides, called a plasmid.

Taking antibiotics without needing them is the main and most important source that produces these antibiotic-resistant bacteria. The most frequent misuse of antibiotics is when they are uselessly taken when an illness is provoked by a virus, such as the flu. **Antibiotics do not kill viruses**. If a doctor prescribes an antibiotic it is because there is a direct or associated bacterial infection in the patient. It is important to understand that antibiotics should only be taken when prescribed by a doctor, as they are not always the best solution to a health problem.

2.4 The HIV Virus

As you will recall, the genetic material of a virus can be either DNA or RNA - **never both-.**

The human immunodeficiency virus (HIV virus) is the infectious agent that causes acquired immunodeficiency syndrome (AIDS). It is a retrovirus, that is, a virus containing RNA instead of DNA.

The HIV virus first appeared in humans in 1930, in Central Africa.

The HIV virus is lethal, as it slowly destroys the immune system of the organisms, whose role is to protect the organism against the virus.

The HIV virus attacks a type of lymphocytes known as T-helper cells. These lymphocytes play an important role in immunity as one of their functions is to activate other cells in charge of making antibodies and other immune responses. These T-helper cells have a surface protein CD4. The HIV virus has a receptor called gp120 which binds to the CD4 of a T-helper cell, this allowing the virus to enter and infect the host cell (T-helper cell).

Several weeks after a person has been infected with the HIV virus they present flu like symptoms; the immune system of the infected person tries to attack the virus and the virus hides in the person’s lymphatic tissues. The infected person can stay healthy between 5 and 15 years, but the virus continues to replicate, hidden. This process continues until one day, the patient’s immune system can’t defend itself any longer and the patient gets sick with an opportunistic infection such as pneumonia, tuberculosis, cancer, etc.

Transmission of HIV requires the transfer of body fluids, containing infected cells, such as blood, semen, vaginal fluids and breast milk. The virus can be transmitted via unprotected sex (without a condom), or sharing unsterilised needles between intravenous drug users or sharing shaving razors. The HIV virus can also be transferred from an infected mother to her child during birth, or from mothers nursing infants.

At this time, AIDS is incurable; however, there are some antiviral drugs, such as AZT, which may extend the lives of patients. However, they do not completely eliminate the viruses, becoming a chronic disease that the infected person will have throughout their lifetime. There are also some medicines used nowadays which inhibit protease (Protease is an essential enzyme for the new virion particles to be activated, without protease the HIV virus cannot make copies of itself). Thanks to all the new medications used to fight this disease, the numbers of infected people has decreased in developed countries. However, because these medications are very expensive, they are not accessible to all the needed people around the world.

HIV went directly from Africa to Haiti, and then spread to the United States and much of the rest of the world around 1969. HIV/AIDS is currently a pandemic, where infection rates are higher in less developed countries.

2.4.1. What is a Pandemic?

When an infectious disease has crossed all geographical boundaries and it extends throughout the world, becoming a worldwide infection, we can say that an epidemic has turned into a pandemic.

(AIDS is the worst pandemic in the history of humankind. It is estimated that 20 million people have already died and more than double are nowadays infected with the virus).

According to the WHO in order for an infectious disease to become a pandemic the following is necessary: a new microorganism must appear one that has not been around before; that this microorganism is able to cause acute symptoms in the diseased, and that the pathogen is easily and effectively spread through human populations.

2.5 Cancer

(Under normal conditions, our cells will replace themselves when needed. New cells are produced in adequate amounts, and cell reproduction is controlled by very specific mechanisms).

Sometimes cells start to multiply without control, and at the same time they are not able to specialise into the type of cell than they should be, according to the tissue or organ where they are found. This uncontrolled growth gives rise to a tumour; some of which grow relatively slow and don’t have negative consequences, a benign tumour. However, if the tumour expands quickly invading and killing the neighbouring healthy cells, we have a malignant tumour. Malignant tumours can also metastasise (spread to other locations in the body via lymph or blood).

(Note: benign tumours are self-contained, do not invade other tissues and do not metastasise).

Cancer is often considered the 20th century disease. However, it is not the first cause mortality in developed countries, as it is often thought, but comes after cardiovascular diseases.

Characteristics of cancer cells: 1. Unlimited cell proliferation. 2. No apoptosis (non-programmed cell death). 3. Not sensitive to factors inhibiting growth in normal cells. 4. Creating own growth factors. 5. Ability to metastasise: invasion of other tissues and organs 6. Capacity of angiogenesis: growth of new blood vessels.

Neoplasm: a new and abnormal mass of tissue in the body (as a result of a neoplasia), especially a malignant tumour.

Carcinoma: a cancer arising in the tissues of epithelial cells

2.5.1. Cancer treatment

Surgery: to surgically remove the tumour.

Radiotherapy or radiation therapy: the patient is given concentrated doses of radiation to kill and control malignant cells.

Chemotherapy: the use of medicines (chemicals) that kill cancer cells. Most commonly, chemotherapy acts by killing cells that divide rapidly, one of the main properties of most cancer cells. (This means that it also harms cells that divide rapidly under normal circumstances: such as cells in the bone marrow (decreasing the production of blood cells), the digestive tract (causing inflammation of lining of the digestive tract), and hair follicles (causing hair loss)).

2.6 Cardiovascular Diseases and Other Medical Terminology

Ischemia: an inadequate blood supply to a part of the body, especially the heart muscles. *(decreasing the amount of oxygen received).*

Stenosis: a pathological narrowing or constriction in the diameter of a bodily duct or passage.

Infarct: the ischemic necrosis of an organ or tissue. Could be caused by obstruction of local blood supply, pressure exerted by a tumour, etc.

(Ischemic necrosis: death of tissue due to an inadequate blood supply)

Cerebral stroke: Sudden interruption of blood to the brain.

Angina: Angina is pain, "discomfort," or pressure localised in the chest that is caused by an insufficient supply of blood (ischemia) to the heart muscle. It is also sometimes characterised by a feeling of choking, suffocation, or crushing heaviness. This condition is also called angina pectoris. It could precede a heart attack.

Ventricular fibrillation is a very rapid, unco-ordinated, ineffective series of contractions throughout the lower chambers of the heart (ventricles). Unless stopped, these chaotic impulses are fatal, causing failure of the heart.

Thrombosis: damaged provoked in an organ or tissue by a clot forming within the blood vessels that irrigate it.

Embolism: damage provoked in an organ or tissue by a clot forming somewhere else that travels via blood vessels to the particular organ/tissue

Anamnesis: the medical information a patient gives to the doctor, which includes the patient's medical history such as: past illnesses, surgeries, allergies, bone fractures, any genetic disorders in the family, etc.

Semiology: the identification of signs or symptoms of the illness in order to determine a diagnosis. This includes manual procedures (e.g. inspection, palpation, auscultation), physical (e.g. electrocardiogram), biochemical (e.g. blood tests) and histological (e.g. biopsies).

Nosology: The branch of medicine that deals with the classification of diseases. It describes, differentiates and classifies them.

Symptom: Subjective evidence that a patient gives as he perceives a change in his normal health condition. Such change is understood to be abnormal and caused by a particular illness.

Sign (**an indication of the existence of something):** A sign is any objective and measurable evidence of an illness. Therefore, it can be observed by the doctor.

There are symptoms that may be signs, because the doctor can observe: fever (patient may feel feverish). There are signs that may not be symptoms since the patient can not perceive them, such as hypertension.

An **infection** is caused by a microorganism (e.g. a bacterium), and an **infestation** is caused by a macroorganism (e.g. a worm).

2.7 HEALTH AND DIET

Nowadays diet raises a series of controversial issues mainly due to serious disorders, such as anorexia, bulimia and obesity.

The advances in nutritional and dietary fields in recent years reveal the importance of an adequate, healthy diet in order to promote good health, physical wellbeing and mental health.

It is important to know what we eat therefore you should know how to read food labels as they are the main source of information about the ingredients and properties of food. Food labels should include: expiration date, nutritional information (including energy value in Kcal, amount of protein, carbohydrate and fat per 100g of food. They may also include the amount of vitamins and minerals etc), the origin of the product and the list of ingredients (which are always in decreasing order by weight).

Unit 3. MEDICAL ADVANCES

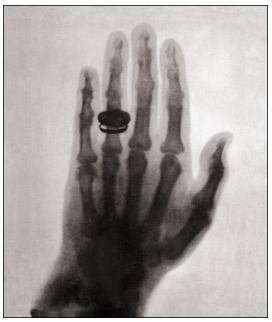
1. Diagnostics and Treatments

Physicians now have leading technology for diagnosis, ranging from laboratory analysis to computer-controlled machines, and technology that allows the viewing of almost all parts inside the human body. There are techniques to count the number of cells, to determine hormone levels, to monitor toxicity in blood and measure the level of key chemical components in the body. Electronic sensors have also been developed to monitor heart and brain activity. Looking inside the body now goes beyond the use of x-rays. Sound waves and particle beams are also used. We can see live images of the human body and its internal functions.

1.1 The Inner Eye

If the initial review of a patient is inconclusive, the doctor may use other more advanced diagnostic tools. The most popular technique used to peer inside the human body is the x-ray. **X-rays** are in the electromagnetic spectrum and travel as waves, like sunlight, but x-rays are much more energetic.

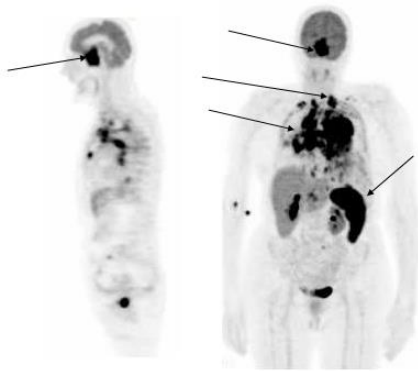
X-rays can pass through low density tissues of the body such as skin, fat or muscle. Wilhelm Roentgen, the German doctor, discovered x-rays by chance in 1895. The first x-ray image he showed the world was the bones of the hand of his wife and you could see her wedding ring 'floating' around the bones on her finger. To do this, Roentgen placed a photographic plate under the hand of his wife and shone an x-ray beam through her hand onto the plate. This image revolutionised medicine, as the doctors immediately recognised the potential of the technique to identify fractures, kidney stones, cysts and tumours.



Today, x-rays are also used to detect lung and breast cancer.

X-ray technology combined with the ability to process using a computer allowed **Computerised Axial Tomography (CAT or CT scan)** to be developed. With a CAT scan, general images of body sections can be seen and many anatomical abnormalities can be detected without the need to physically penetrate the tissues.

Another testing technique was also created in the physics laboratories. This is **Nuclear Magnetic Resonance (NMR),** which is able to obtain highly detailed images of any part of the human body. In NMR apparatus, the patient is subjected to a powerful magnetic field - a thousand times more intense than Earth's gravitational pull - that interacts with nuclear hydrogen atoms present in all tissues. Analysing the response of the atoms, sequences of images can be obtained which look like "slices" of the body about 1 mm thick. The resolution and sharpness is far better than an x-ray.



These images are extremely useful for detecting small tumours, to observe the brain, to locate clots in blood vessels and explore damaged intervertebral discs.

Positron Emission Tomography or PET is another innovative approach. The patient has a mildly radioactive glucose injected into them which emits positrons, the antiparticles of the electron. Within minutes, the blood carries the glucose to cells throughout the body. The patient is then placed in an enclosed scanner surrounded by detectors that record the positrons, creating an image where each color represents different levels of activity (see left).
Today, only selected hospitals have this technique because of its high cost. However, the PET scanner has revolutionised the diagnosis of brain disorders, discovering anomalies impossible to detect with other methods: minuscule blocks in blood vessels; tiny tumors and it can also detect chemicals released as early warnings of schizophrenia, epilepsy or Alzheimer's.

Thermal imaging is another exploration system used to see inside the human body and is especially useful for detecting tumours. This technology can recognise differences in body temperature. Tumours are areas where there is an abnormal growth of tissue, so they emit more heat. The imager sees these areas and creates images that differ according to their temperature regions.

Bone densitometry is medical technology that, through small doses of x-rays, is used to determine the density of bones: the lower the density, the greater the risk of fracture.

In the past, patients were sent to the operating table for diagnosis. With all of these non-invasive techniques, operations can generally be avoided unless necessary.

1.2 Drugs

A drug is a chemical substance used in the treatment, cure, prevention, or diagnosis of disease or used to otherwise enhance physical or mental well-being. However, the majority of medicines are given once the disease has begun and has presented his symptoms. A drug must have sound scientific evidence of its quality, effectiveness and safety before being allowed to be put on sale.

Vaccines are also a type of medicine, because they are used to prevent disease. A vaccine is used to prepare the immune system so it is ready to fight a specific parasite.

1.2 Read the instructions on the medication

The risks involved in the proper use of a medicine are known and are considered generally acceptable. But in the event that a patient misuses the drug, risks become unpredictable and can be dangerous. Two examples of misuse of a drug are the self-medication and not following doctor's instructions. Self-medication is to consume drugs without a doctor's prescription or taking more than the prescribed dose.

2. Transplants

To avoid rejection of the transplanted organ, patients are given drugs called immunosuppressants, which reduce their defense response. Although these substances have made transplants possible, they have many side effects. For this reason it is best to administer the lowest possible dose; the greater the compatibility between donor and recipient, the lower the amount of immunosuppressants that are needed.

- **Xenotransplantation** (xenos- from the Greek meaning "foreign") is the transplantation of living cells, tissues or organs from one species to another, (such as from pigs to humans). Pigs are the most suitable animal for transplantation into humans.
- **Autotransplantation** is the transplantation of organs, tissues or even proteins from one part of the body to another in the same individual. Potentially, a human could reproduce whole organs. This would remove the problems of availability of organs and rejection by the receiver/use of immunosuppressants.
- **Allotransplantaion** is the transplantation of organs, tissues or even proteins from one individual to another of the same species excluding monozygotic twins.
- **Isotransplantations** is the transplantation of organs, tissues or even proteins between monozygotic twins (identical twins)

2.1 The Immunological Barrier

Each person's immune system is unique and, like your body, has a specific physical appearance. The membrane of each cell in the human body has, in chemical language, a code indicating their individuality. The key part of the cells code will be characteristic to the species it belongs to, for example - humans. Another part is the organ or tissue to which that cell belongs, and a third part is typical of the individual. These differences are noticeable when a cell meets a ´foreign body´, and gives rise to rejection reactions during and after transplantation.
Between the 1950´s and 1960´s, specific substances were found in the cell membrane, such as **human leukocyte antigens (HLA)**, which are recognised by the recipient's immune system as foreign and therefore the graft is rejected.

Rejected face transplant

The HLA indicate the similarity between the tissues of two relatives or two individuals in general.

2.2 The Social Barrier

Since 1964, laws on determining death have been implemented in all countries with active organ transplantation programs. Traditionally, both the legal and medical communities determined death through the end of certain bodily functions, especially respiration and heartbeat. The "Harvard Criteria" was a report completed in 1968 which defined death as an ´irreversible brain failure´ (Unreceptivity and unresponsiveness, no movement or breathing, no reflexes, flat electroencephalogram, EEG, (confirmatory), body temperature ≥ to 32º C, absence of CNS depressants). An EEG is the recording of electrical activity along the scalp produced by the firing of neurons within the brain. If

there is no activity (flat-line) the brain has stopped working in an irreversible manner and that is the end of the life.

3. Pharmaceutical Research

3.1 Clinical Trials

For a drug to be approved to sell on the market, it must go through many tests, beginning at the simplest level with tests on bacteria and increasing in complexity (until clinical trials on humans).

Tests on **bacteria** show whether medicinal compounds induce mutations. If so, these potential medicines are not developed further.

In **animals**, the initial studies are performed on mice, and later must include at least one non-rodent animal, since the results may be different between species. Initially, they are given large doses of the compound. The goal is to find what dose is toxic to half of the animals and what organs have been damaged.

The **human** trials of most drugs go through three phases. In the **first stage**, the drug is delivered to healthy patients who volunteer to participate in the trials and are paid for their time. They are warned that there might be side effects of taking the medicine and they then have to sign a consent form to say they take full responsibility should they become ill during the trials. The doctors study how the drug distributes itself throughout the body, how it is metabolised and how the body eliminates the compound, in order to determine the dosage and to detect possible toxic effects. There are about twenty people involved in these tests, which last about a month.

The **second phase** of clinical trials involves a hundred volunteers, without economic incentives who are suffering from the disease, being treated. Over several months half of the patients receive the medicine, while the other half receive a 'placebo' (an imitation drug which has no medical attributes). This is what is called a double-blind because neither the doctors nor the patients know who is taking the drug or the placebo.

The **third phase** of clinical trials establishes an optimum dose, how the drug should be administered and its safety in the long run. These trials may need many years and require thousands of volunteers.

As an average, clinical trials last five years, and then government agencies need at least another two years to study the results.

What is a generic medicine? A **generic medicine** is a drug that is identical in its composition and dosage to an already patented drug that exists on the market.

4. Insulin

Insulin, a low molecular weight protein, consists of 51 amino acids linked into two chains. It is an internal secretion of beta cells in the area of the pancreas called the Islets of Langerhans. Insulin is the main hormone that regulates the metabolism of carbohydrates. Insulin acts on all tissues allowing the body to absorb, store and use glucose, but also influences the metabolism of fats and proteins.
Until recently, the insulin that was produced to treat human diabetes was extracted from the pancreas of animals, particularly horses and pigs. It is now possible to produce human insulin on a commercial scale by genetic engineering techniques.

5. Alternative Medicines

Much of the scientific community define alternative medicine as any treatment whose efficacy and safety have not been tested and proven by controlled studies. This form of definition is not based on political views or protection, but solely on questions of efficacy and safety.

Among the so-called alternative medicines are acupuncture, aromatherapy, osteopathy, and naturopathy. But, undoubtedly the most well known of all of the alternative medicines is homeopathy. It is estimated that between 18% and 20% of the Spanish population have tried this treatment.

Unit 4. THE GENETIC REVOLUTION

1. Chromosomes

All cells have chromosomes; the number of these chromosomes is specific to every animal and vegetable species. Human cells have 46 chromosomes that come in 23 homologous pairs. The amount of chromosomes of a species remains constant because during the formation of sex cells homologous pairs undo and the number is reduced to half. Instead of taking two copies of each chromosome, they take only one. Both the human sperm and egg have 23 chromosomes, but the zygote formed at fertilisation will have 23 pairs, as will all the future cells which it will multiply into.

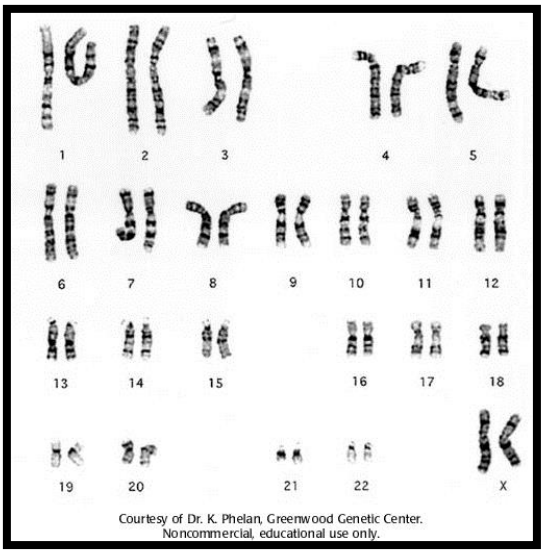


Fig.1 Karyotypes

An ordered set of chromosomes is called a karyotype. Human beings have, in every cell, a number of pairs of chromosome that are the same or homologous. The chromosomes can be very different in size and can contain different quantities of genes. (The biggest of chromosomes has 3951 genes, whereas the smallest only has 225). The 23 pairs of our human chromosomes are sorted according to their length, the longest to the shortest, and they are numbered, with chromosome 1 being the longest.

The reason there are 2 homologous chromosomes for each of the 23 is because at the time of fertilisation you receive a copy from your mother and a copy from your father.

Half of our chromosomes (and therefore our genes) are maternal and the other half are paternal. But the rule of the 2 chromosomes being the same has an exception, and these are called the sexual chromosomes, which determine the sex of the individual.

On occasions, nature can produce cells with a number of anomalous chromosomes. In these cases, when fertilisation happens the embryos often die, but, at times, they can develop, leading to illnesses or deformations.

The Environment and Its Effect on Genes

Let's revise what a gene is.

Gene: a sequence of nucleotides associated to a particular function (this is usually a DNA fragment, but in some viruses it can be an RNA fragment). The rest of the genetic material was called 'junk' DNA. However, scientists have already found functions to some of that DNA, so it should no longer be considered 'junk' DNA. Among the functions of a gene we can point out the following:

1. A gene controls a particular hereditary character.
2. A gene transcribes into mRNA and it is then translated into a particular protein (or polypeptide chain).
3. A gene is also transcribed into tRNA and rRNA, and
4. A gene regulates the expression of other genes.

Environmental factors also determine the way in which a gene is expressed. Environmental circumstances can make individuals belonging to the same species taller, bigger, with brown hair or more intelligent although their genetic makeup doesn't change.

This is somewhat similar to what happens with cells of an organism, they all have the same genes, but according to where they are and how these genes are used, these cells may become heart, liver or muscle cells. And the same occurs when a plant changes because it is cultivated in different conditions of light, water and soil.

No individual circumstances like these are hereditary.

DNA

DNA is a whitish substance. The molecule consists of 2 large parallel chains twisted together into a double helix.
Every chain of DNA is formed by groups of phosphates, sugars and nitrogenous bases. There are 4 types of these bases: Adenine (A), guanine (G), cytosine (C) and thymine (T). The bases of one strand bind to each other as follows: adenine with thymine and cytosine with guanine.

DNA can be easily replicated, as the two chains separate and each chain can then retrieve the same bases that the other chain had (we know that every A joins with a T, and every C joins with a G).
A gene is a fragment of DNA which contains the information necessary to synthesise a protein. The information stored in the DNA determines the type and the order of the amino acids in the proteins that are formed by following its instructions, using RNA, a versatile substance that is capable of translating and transferring these core instructions and using them to make proteins.

Human beings share genes with all other living beings. The genetic difference is a measure of how far apart two species are from an evolution point of view. The human race shares 98.4% of its genes with a chimpanzee, 90% with a cow and 75% with a mouse.We can be compared to anything we can think of, but we appear to look very different.

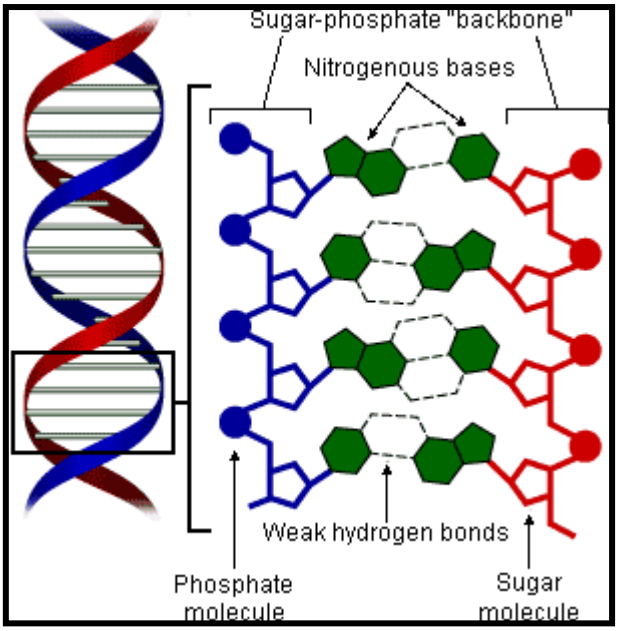


Fig.2 DNA structure

Some Concepts to Remember:

Transcription: The formation of a messenger RNA strand (mRNA) from a DNA strand that serves as a template, (changing T-Thymine for U-Uracil)
Translation: (or protein synthesis), takes place in the ribosomes. The nucleotides in a strand of mRNA serve as a template to make a protein. The relation between the nucleotide sequences of the mRNA and the amino acids of the protein being synthesised is determined by the genetic code.
Codon: A set of 3 bases in an mRNA molecule that determines the identity of an amino acid.

2. The Genetic Code

The genetic code relates the nitrogen bases to the amino acids. That is to say, it relates the nucleotide sequence of a particular gene to the amino acid sequence of the protein that it codifies. It is universal for all living things, and is not to be confused with genetic material that is unique for each living being.

This idea leads us to believe in the unity of life on Earth. Mutations can occur by altering the order of the nitrogen bases in the DNA. Many chemical substances and other physical agents have the capacity to provoke these changes. Mutations can go unnoticed, producing a cancer or even death. On occasions, they can also create new biological characteristics that improve the survival of the organisms. Genetic mutations are a key factor in the evolution of species.

3. Genetic Engineering

3.1 A Brief Introduction

Genetic Engineering is a group of techniques which allow the manipulation of the genome of a living organism. Genetic Engineering is the set of techniques aimed at transplanting genes between living species, a little bit like ‘cut and paste’ when you are working with text on a computer.

In 1968 it was discovered that bacteria synthesised substances called restriction enzymes to defend themselves against viral infections. They break the DNA of the infection into pieces; in particular they recognise particular sequences of nitrogen bases and always cut the DNA strand in the same place. Scientists have now isolated more than 400 types of restriction enzymes, and they are used to cut the DNA in different places.

With the help of these restriction enzymes we can isolate a particular gene.

The practical applications were so obvious that by 1972 the first recombinant DNA had already been replicated, and in 1973 the first living thing was genetically manipulated: a gene of an amphibian was introduced to bacteria. The name ‘genetic engineering’ was born. And soon after, the first company started to exploit it for economical gain. The future was so extraordinary that it was necessary to take a breath before continuing – could we control this?

We could create bacteria capable of feeding off oil, for example, which would be very useful in the case of an oil spill, but could this bacterium escape and become able

to live in the tanks of cars and feed on the petrol in the cars, in the service stations or in the refineries? So, it was declared that investigation into these activities was to be delayed for security reasons until they risks could be controlled.

Living beings began to be viewed with the same eyes as a mechanical engineer, who wants to make improvements to a car or a radio.

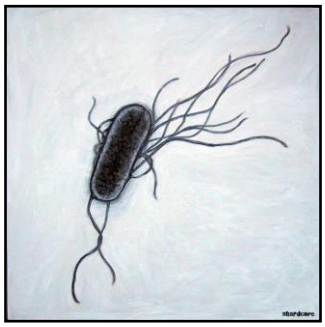


Fig 3. E.Coli bacteria

Nowadays we can create bacteria that break down oil, plants that can produce insecticides or glow like fireflies, rabbits that are twice the size of a normal rabbit and silkworms that can produce different coloured silks.
One of the first applications of genetic engineering took place in the health field.

Human genes were introduced the *Escherichia coli (E.Coli)* (bacterium that lives in the human intestine) to produce substances necessary in medical treatments. In the late eighties of the last century scientists began to use human growth hormone that was obtained from bacteria, as it was safer and cheaper than extracting it from the brains of corpses. Nowadays, other hormones such as insulin or interferon (used to treat viral diseases and cancer), hepatitis controlling vaccines, blood clotting agents and many other substances are obtained by these techniques.

Today, the work in genetic engineering is aimed at creating a bacterium whose genetic material is wholly synthetic, meaning that their DNA is manufactured completely in the laboratory. These are the first steps to creating artificial life.

3.2 THE PROCESS OF GENETIC ENGINEERING IN DETAIL

Genetic Engineering (GE) is a branch of Molecular Biology that allows us to manipulate the genome of a living being. In general, there are three purposes of GE:

1. To eliminate harmful genes.
2. To introduce healthy genes.
3. Modifying genes.

One of the most usual practices of this GE is the technology of Recombinant DNA (rDNA), this allows us, for example, to clone a specific gene.

Many people are diabetic because they have a faulty gene that encodes for the protein insulin. In the past, patients were injected with insulin originating from human corpses or other animals, which led to associated problems. At present, the gene of the human insulin can be cloned in bacteria, which means that insulin can be produced in large quantities at a much lower cost. Before explaining the steps, you should understand some prior concepts.

- Restriction enzymes, endonuclease (from now on, EnRes), are enzymes that are found in bacteria. They destroy the DNA of the virus that try to parasitise them by cutting the DNA. They cut the double helix of DNA at particular base sequences called palindromic sequences. Each EnRes cuts a specific palindromic sequence.

- A sequence of double helix DNA is said to be a palindrome if it is equal to its complementary sequence read backwards. A palindrome is usually some 6 to 12 pairs of bases. (Palindromes are frequently found in proteins).

  Example: 5´ A G G T C G A C C T 3´
  3´ T C C A G C T G G A 5´

This is a palindrome of 10 pairs of bases. If an EnRes is specifically designed to cut the DNA at this palindrome, it will cut the double helix each time it detects this sequence in the genome. AN EnRes will cut a particular base sequences forming (for our purposes) **sticky ends** to the cut fragments. (This will be explained in class).

- Plasmid. This is a piece of circular, double stranded DNA which is independent of the genome. They occur naturally in bacteria. They are extracted easily and are therefore useful in genetics.

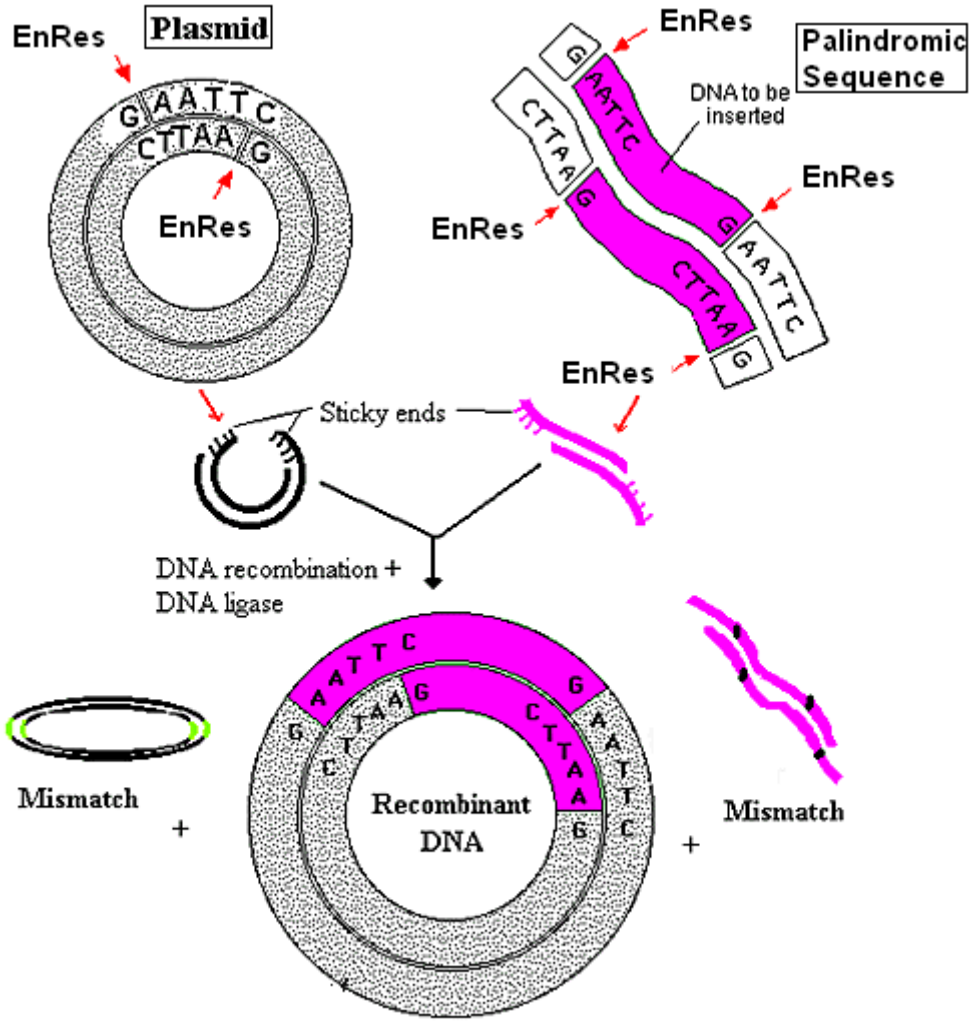
There are four main steps through which genetic engineering is accomplished.

1. **Location and Isolation of the genes of interest**. Obtaining the portion of DNA which contains the gene that we want to transfer is accomplished by the use of gene-splicing techniques. Gene-splicing cuts the DNA into small fragments, easy to work with, by using restriction enzymes. By looking more closely at the example of human insulin, as you know, the human genome is formed by 46 very long filaments of DNA (the 46 chromosomes), to make them more manageable and controllable we have to cut them into smaller pieces. To do this we use a suitable EnRes. Each time that the EnRes detects its palindrome, it will cut the DNA, so that we obtain multiple small pieces of human genome. In one of these will be the gene of the insulin, the gene we want to clone.

2. **Insertion** of the genes into a **cloning vector**, a vehicle for transferring genetic material into a cell. The cloning vector is a bacteria plasmid. First we collect many similar plasmids and we use the same EnRes that we used to cut the human genome. The EnRes cuts the plasmid 'opening' the circle. Subsequently, we put the plasmid in contact with the pieces of our genome. A circle of recombinant DNA is formed, with the human genome filling in the space created where the plasmid bacteria ring was opened. In one of them will be the insulin gene. Now we put these recombinant plasmids in contact with bacteria, so that they can enter them. We sow the bacteria on Petri dishes, so that each one will grow a colony. In one of those colonies will be the bacteria that have received the plasmid containing the insulin gene. **Gene cloning**. This is the production of multiple copies of the genes of interest. The host cell with the cloning vector, is made to reproduce

3. **Localising** the descendants of the host cell that contain the genes of interest, and detection of the colony that contains the gene of interest. We can locate the correct colony containing the insulin by using a biochemical test that detects the presence of insulin and its corresponding bacteria. Another form, a lot more complicated but more efficient, is the hybridisation of nucleic acids. This involves manufacturing a complementary radioactive nucleic acid to the gene of the insulin (for example, the mRNA of said protein), so that upon putting it into contact with the colony that interests us, it will hybridise with the gene locating the bacteria.

4. **Cloning**. Finally, we collect these bacteria and grow them in a culture medium. In 24 hours we will have thousands of millions of bacteria that produce human insulin that, after being purified and bottled, will alleviate the lives of millions of diabetics.



Inserting a DNA Sample into a Plasmid

4. Transgenics

Living things which have genes from another species are called transgenics or genetically modified organisms (GMO).

The speed with which they developed the first transgenic plants was due to a discovery that had little to do with genetic engineering: a bacterium that causes tumours in plants, *Agrobacterium tumefaciens*, whose plasmids (circular DNA chains) are integrated into the chromosome of the host it infects. The ability of *Agrobacterium* to transfer genes to plants and fungi is used in genetic engineering for plant improvement. (in the soil *Agrobacterium tumefaciens* can infect wounded plant tissue transferring a large plasmid to the plant cell. Part of the plasmid randomly integrates into the chromosome of the plant. Genes from the plasmid that are integrated in the plant chromosome are expressed at high levels in the plant. These plasmids can be genetically

modified ("disarmed") by deleting the genes of the bacterium and inserting those of interest. These plasmids are used as vectors of the desired genes).

It is harder to develop cereals and other species that are resistant to infection with *Agrobacterium*; in this case, a vector made of microscopic gold pellets with the genes attached are fired onto the recipient plant. Using this method, we can produce tomatoes which take longer to rot, as well as cotton and potatoes resistant to certain species of beetles.

The cultivation of transgenic plants outside the laboratory, and their use in human food, causes a broad social controversy about how healthy and how environmentally safe they are. In favour of their production, no food is subjected daily to as much quality control as transgenics, and there is no evidence to discourage consumption. Other, usually larger, companies argue in favour of transgenics in order to promote their own crops. Small farms in poor countries are unable to compete as they cannot afford to use transgenics.
It is an issue involving science but it involves economic, political and social aspects also, so these decisions must be taken by society as a whole.

One of the findings (1988) which has increased the amount of transgenics in animals, is the ability of embryos that only need three days to integrate the gene into the transplant location. There are already sheep, cows, pigs and chickens that are transgenic.

Dolly, the first transgenic sheep, 1991

The main interest of transgenics is producing useful substances for medical treatments, but they are also developing other things that have a commercial interest. For example, the gene of the silk spider has been inserted into goats with the intention of isolating this marvellous fibre from their milk. Other companies are confident that they can manipulate chicken so that their eggs can be the source of many products of interest.

5. Gene Therapy

Now that we know how to transplant genes, can we do so between people and repair defective genes? It can be used not only to cure thousands of inherited diseases, but also to address the many others that have genetic components, such as cancer, Parkinson's or the many autoimmune diseases.

Genetic engineering in humans will need to use retroviruses, because they have the unique ability to make the cells they infect make copies of the viral genes which are then integrated into their chromosomes.
The investigation began by creating nonpathogenic retroviruses that were carriers of a human gene. (Once that vector was ready, scientists must have asked themselves if those viruses would do what was expected of them or would they do something different).

The next achievement was to cure a serious and deadly disease, severe combined immunodeficiency (SCID), which is due to the existence of defective white blood cells.

Children who suffer the disease can only live in a completely sterile environment (the so-called 'bubble children').

This disease was chosen because it is caused by the malfunction of a single gene. In September 1990, genetically engineered white blood cells were prepared with a healthy gene and therapy was performed. Thanks to the intervention, a three year old girl came out of the bubble that isolated her from the outside and could, for the first time in her life, go to the park and touch things and people around her. (However, the girl was not cured, and her survival depended upon more similar injections).

David, a 'bubble child'

Addressing diseases that are caused by the failure of a set of genes, such as cancer, is far more complex, even though science has taken the first steps. For example, healthy copies of the p53 gene, whose function is to remove tumours, have been used to treat lung cancer.

6. The Human Genome Project

(The Human Genome Project is perhaps the most ambitious biological research project worldwide up until today. This effort to map the entire human genome is not only very expensive, but it will also take many years to be accomplished. The goal of this project is to locate each and every gene of the 23 pairs of chromosomes that make up the entire human genome, and to study its mechanisms of expression. It has been estimated that human DNA contains about 20 000 – 25 000 genes, though this number is constantly been modified. The sequencing of all the nucleotides that make up the human genome has already been accomplished (2003). However, the most difficult task is still under progress: determining all coding genes, localise each and every gene, study how they are expressed, etc. In many years, once the project is completely finished, among many others we will be able to determine: what parents could have children with particular genetic disorders; there will be some significant advances in gene therapy, we will have a better understanding of some diseases such as cancer and their possible treatments, etc…….But it will also raise significant ethical questions).

The public laboratories had 1100 workers who took human blood cells and sperm cells and split their individual chromosomes into fragments. They could identify the sequence of the bases for each chromosome. Each fragment of bases was localised along the chromosome.

Firstly they mapped DNA sequences in the small fragments, then in the genes then in whole chromosome and finally the whole genome.

The genome is the group of all of the genes that living things are made up of.

The process of mapping the human genome is similar to tearing off all of the pages of an encyclopedia, page by page, and then trying to recombine them page by page.

In the 90s of the last century scientists from the USA had a vision. They understood the commercial potential of such a process and started to do research on their own to try and make a profit from the project.

Craig Venter, who was a professional surfer and Vietnam War veteran, abandoned the public consortium and founded Celera Genomics. He confronted the research with a different method of working which was faster. He split the genes simultaneously – splitting the encyclopedia all at once (not page by page), and the way they carried out the sequencing was to trust the power of computers to reorganise the genes into the correct sequence of the complete genome. They didn't believe that this method would be successful, but it actually worked!

6.1 A Box Of Surprises

Today we know the sequence of the 3000 million pairs of nitrogen bases that form the human genome. We inherit a version of this from each of our parents.

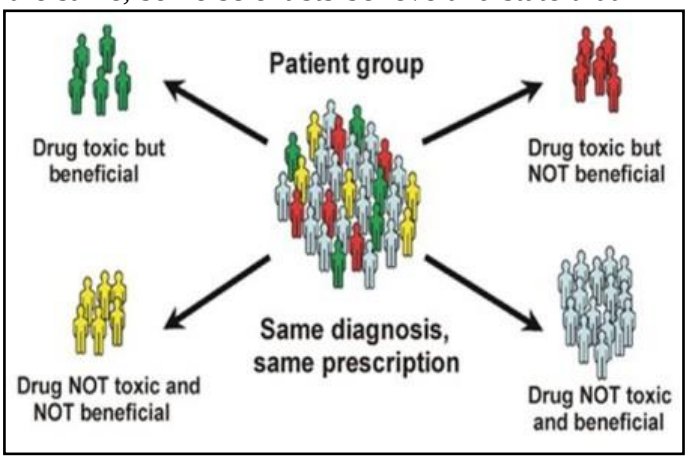
One of the first surprises is that our species has only about 25 000 genes, when it had been assumed that would be about 100 000, a number quite close to the amount of different proteins that our cells can synthesise. So, with only a few genes more than a mouse, a fly or a worm a human being can be formed and maintained.
This fact might suggest that our genome is simpler. However, the opposite is true. Then, equally surprisingly, the classic genetic principle of 'one gene contains the instructions for making one protein' was broken.

The same gene can synthesise different proteins by regulating the expression of its sequence.

It is the eternal paradox of science that whenever it finds an answer more questions arise. Also, 95% of the human genome contains no genes, but only sequences that until now seemed useless, with no function, and were called 'junk' DNA. The latest DNA news is that this junk DNA is much more important than previously thought, since it plays an important role in the regulation and efficiency of gene expression.

Although the Human Genome Project works with DNA from several donors of different ethnicity and gender, studies have been oriented more towards the similarities rather than the differences. 99.99% of the genes of all people are equal, but it is the remaining 0.01% that makes us different, unique.

Although many of our genes are the same, some scientists believe and state that there is no human genome because each gene can have many versions. In addition, our genome, like that of other species, is subjected over time to evolutionary changes by mutations.



In fact, it is these small individual genetic differences that are of most interest to pharmaceutical companies, as it is the cause of many drugs not having the same effect on the entire population. This is the reason why a drug that is used to treat

a type of diabetes has already caused over 60 deaths around the world from hepatic toxicity (toxic liver disease).

So, the pharmaceutical companies are working on what is called 'pharmacogenetics', i.e., developing drugs 'to fit' the genetic profile of the client. There have already been hundreds of tests sold that detect the presence of genes and diseases and to some extent, whether our genes are capable of suffering from a disease in the future.

7. Genetic Fingerprints or Genetic Profiling.

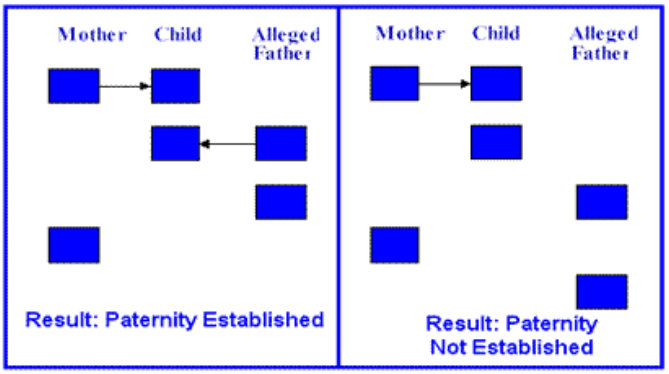
The DNA of an individual is a very precise way of identification, as it is a large sequence of 3 000 million letters that only coincides exactly with an identical twin…or with a clone. But since 99.9% of the sequence of the genome is the same as the entire human race, it is difficult to find the differences in the long chain of the remaining 0.1%.

In 1985, an English geneticist, Jeffreys, discovered a method to obtain a genetic fingerprint (or DNA fingerprinting), which distinguished with ease some individuals from others. The key was that there are certain regions of DNA where some small fragments (minisatellites) are repeated again and again, and it turns out that the number of times each minisatellite is repeated changes from individual to individual.
That geneticist, today known as Sir Alec Jeffreys, devised an experimental technique that analyses the recurrence of such sequences and results in a kind of bar code that identifies any living being.

These are a couple of the applications:

7.1 Paternity Tests

In this case, you compare the genetic fingerprints of the mother, the child and the possible fathers. The child will have a series of bands that correspond to the mother and the rest will correspond to the father. The genetic fingerprint does not ensure 100% paternity, but the probability of it being incorrect is so low that if it went to court the father would have to accept the evidence.



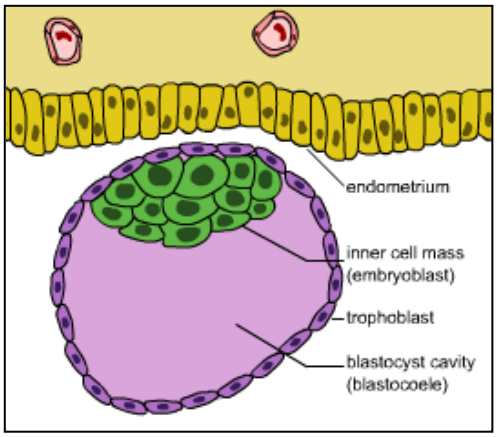
Paternity test results

7.2 Criminal Investigations

In these types of investigations you compare the genetic fingerprint obtained in the samples found at the crime scene with the genetic fingerprints of the suspects.

8. A Likely Meeting

The fertilisation or result of the union of a female reproductive cell (ovum) with a male reproductive cell (sperm) is a new cell called a zygote. It begins to multiply and after a development of four or five days results in a blastocyst, a set of about 150 cells that form a hollow sphere, the outer layer is formed by cells and the interior is filled with a fluid where we find other types of cells, so-called embryonic stem cells.



(The blastocyst possesses an inner cell mass (ICM), or **embryoblast**, which then forms the **embryo**, and an outer layer of cells, or **trophoblast**, which later forms the **placenta**. The trophoblast surrounds the inner cell mass and a fluid-filled blastocyst cavity known as the blastocoele or the blastocystic cavity).

8.1 Stem Cells

Stem cells are the cells of an organism that are not specialised for any function. They can multiply actively maintaining that state, and are able to transform into any of the 200 cell types that an adult has (heart, nerve, kidney, etc).

Stem cells are crucial in the processes of growth and repair of damaged tissues.

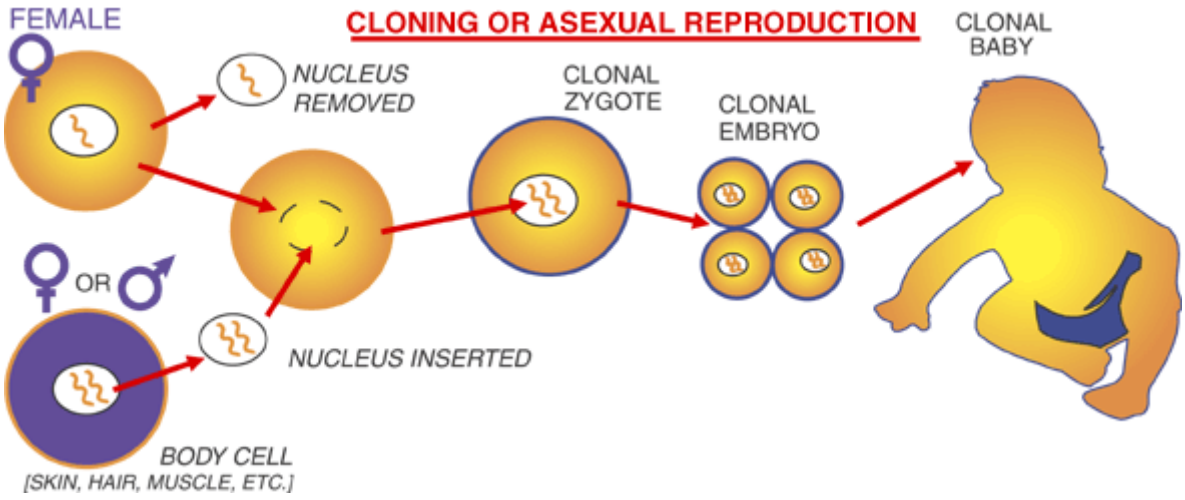
All animals and vegetables possess stem cells in maturity (they can be obtained from tissues such as bone marrow, the umbilical cord or the liver), but they are abundant in embryos and fetuses. Stem cells were first isolated in 1998.

There are 3 types of stem cells:

Type	Characteristics
Totipotency	a single cell that divides and produces all the differentiated cells in an organism
Pluripotency	stem cells that can give rise to any fetal or adult cell type
Multipotency	are those stem cells that only create cells of a given tissue

As it grows, the development potential of the stem cells decreases. During the first two days after fertilisation the cells are still totipotent, after four or five days, pluripotent, and after that they are mulitpotent. The first two types are called embryonic stem cells.

It has been possible to obtain clones, which have been created using a technique called **nuclear transfer**, shown on the next page:



8.2 A Fiction That is Becoming a Reality

We are constantly investigating cloning for the development of new medical treatments and also to aid human reproduction.

Specifically, the aim is to achieve therapeutic cloned stem cells that could be used to regenerate diseased or damaged tissues without rejection problems.

The generalisation of this treatment would allow reconstruction of myocardial injury, burns, fractures, severe fractures or infected tisues. Also, we could treat many diseases, such as diabetes, Alzheimer's, Parkinson's, leukemia and rheumatoid arthritis. The fact is that so far, we have achieved regenerated heart, epithelial and pancreatic tissues.

The goal of reproductive cloning of human embryos is to obtain the same DNA as another person; to create a newborn identical to it, genetically speaking.

This use raises important questions, but scientists acknowledge they are carrying out investigative research, athough at present, it is still without success.

Scientists have also used cloning to try to recover plant and animal species that are missing or endangered.

Ethical Challenges

Reproductive cloning is not yet sufficiently developed to achieve healthy humans.

The few cloned animals that have been born have presented a wide variety of anomalies: premature aging, heart and lung problems, weak kidneys, blocked intestines, weakened immune systems and physical malformations.

Another ethical issue of major concern is the possibility that reproductive cloning could be used to manipulate human embryos and create people with specific genes.

9. Assisted Reproduction, Selection and Retention of Embryos

The newspapers began to publish headlines like these: '*Semen taken of a dead Spaniard on his honeymoon at the request of his widow*' , '*A surrogate mother carries twins for a gay couple*', and '*They want to have a grandson with their dead son's sperm and a surrogate mother*'.

Children on Demand

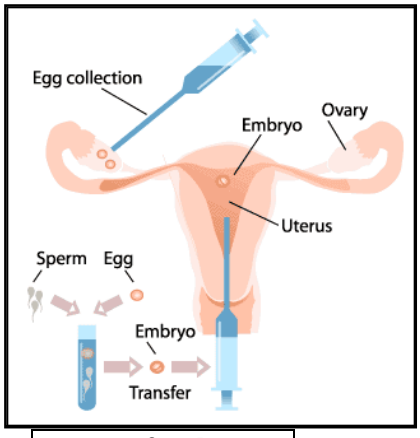
Preimplantation diagnosis is another of the current objectives of assisted reproduction.

Couples at risk of transmitting hereditary diseases are keen to ensure the health of the unborn child before implanting the blastocyst into the uterus. The selection of future embryos, which some years ago caused social disapproval, has begun to be practiced. Thus, for example, many sex-linked diseases can be avoided by selecting a healthy embryo.

Specimen Children

The difficulties that many women have in becoming pregnant are related to an obstruction in the fallopian tubes (tubes where the eggs travel from the ovaries to the uterus).

Steptoe, a gynecologist, believed that the problem could be solved if you could collect an egg at the time it was matured, join it with a sperm in a laboratory petri dish until fertilisation occurs, and then deposit the blastocyst in the uterus of the female. (This is called 'in vitro fertilisation' and the children were called 'test tube babies').

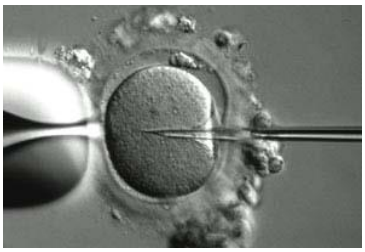


In vitro fertilization

Human fertilisation began to dissociate from sexual relationships and from body to body contact.

The Chance to Decide

The development of techniques to preserve human blastocysts and sexual cells at very low temperatures, without losing their fertilisation potential, is a route that more and more couples are taking.


sperm being injected into an egg

The objective of assisted reproduction is to ensure that both men and women with a reduced capacity to produce sex cells can develop, and even facilitate, reproduction when they would be unable to do so on their own.

It was not such a long time ago that an egg first became fertilised with a sperm cell precursor (spermatagonia).

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