

Evolution of Immunity & Immune System

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ABSTRACT

Around 4.6 billion years ago the solar system was discovered. Earth only had one continent known as the Pannotia Supercontinent. Before 600 million years ago, life started to take place on the earth's surface with the help of a single-celled organism, Amoeba. Amoeba gave rise to a more complex form called algae. Algae gave rise to marine life that was around 530 million years ago. This biodiversity was not here to stay permanently, so a volcanic eruption took place, which is referred to as the Cambrian explosion by researchers. After the explosion, only a few insects, reptiles, arthropods, and other species remained. It later gave rise to Carboniferous Period that was 460 million years ago.

Then comes the Mesozoic era, the era of dinosaurs, which began more than 180 million years ago. Global warming and forest fires were common during this period. They went extinct because of a meteoroid collision. It was just a positive coincidence for the birth of Homo sapiens. The Cenozoic era began 6 million years ago and is still continuing for Homo sapiens. Evolution took place and they diverged from their closest relatives, i.e. chimps and bonobos. It was not a fast process; it took years from stage 1 to the final stage, i.e., from Dryopethicus, Ramapithecus, Australopithecus, Homo erectus, Homo Sapiens Neanderthalensis, Homo Sapiens Sapiens.

Evolution is continuing now and it also a necessity. The evolution of human immune system starts back around four billion years ago with the first bacteria on earth. All living species require an immune system because it protects them from various pathogens. Illness is caused by pathogens such as viruses, fungi, bacteria, and others. The immune system is further split into two parts: the innate immune system (which everyone is born with) and the adaptive immune system (develops when body is exposed with). Innate immune cells include basophils, mast cells, NK cells, and eosinophils, whereas adaptive immune cells include macrophages, dendritic cells, and B cells. The innate immune system is the first to respond when an invader is identified. They defend against hazardous infections, parasites (such as worms), or cells (such as cancer). The innate immune system is passed down via generations. When this system senses an intruder, it takes rapid action. The invader is destroyed within the immune system cells (called phagocytes). To protect your body from a specific intruder, the acquired immune system produces specific proteins (called antibodies/immunoglobulins) with the help of the innate immune system. When the body is exposed to the invader, B lymphocytes create these antibodies. The antibodies are still present in your child's system. Antibodies might take many days to develop. Acquired immune system changes with time. Immunizations trains the immune system to develop antibodies that protect them from potentially fatal illnesses.

KEY WORDS - Evolution, Cambrian explosion, Homo sapiens, Immunity, Innate immune system and acquired immune system.

Date of Submission: 07-03-2023

Date of acceptance: 20-03-2023

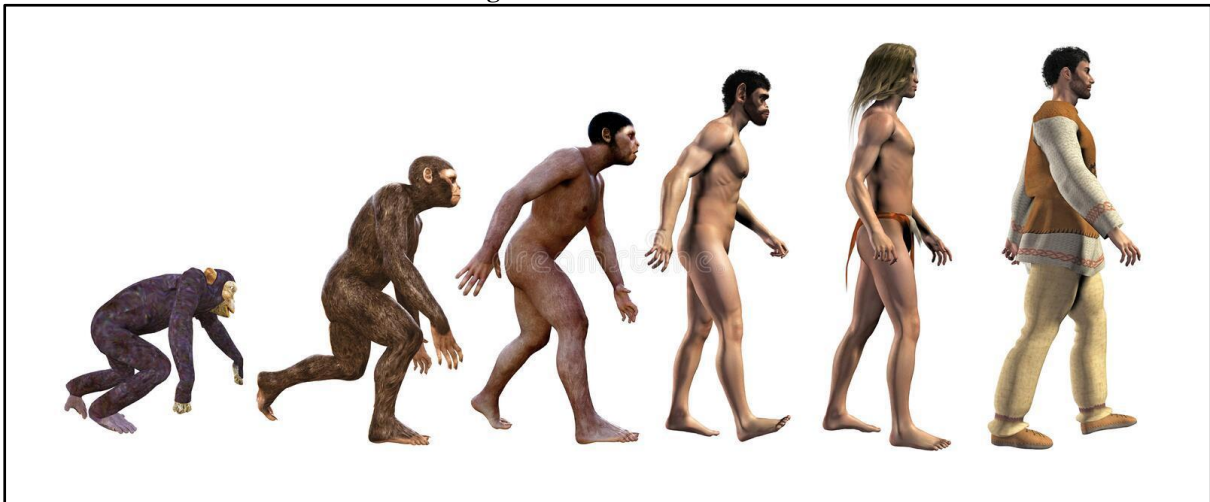
I. INTRODUCTION

EVOLUTION

Humans are thought to have evolved from simpler forms through incremental changes from simple to more complex ones. It is thought that billions of years ago, amid the oceans, evolution first took place.

The third significant era in the history of Earth is the Cenozoic. Homo sapiens, or humans, separated from their closest ancestors approximately 6 million years ago and have continued to do so up to the present. Chimpanzees and bonobos made way for the contemporary Human sapiens as a result of evolution. Fig.1 - Human evolution.

Fig.1 – Human evolution



Source - <https://www.dreamstime.com/illustration/human-evolution.html>

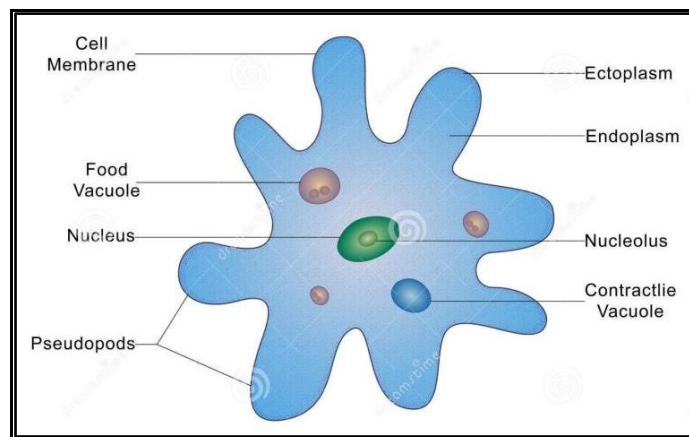
1.1 Background

Our solar system was created by a thick cloud of interstellar gas and dust around 4.6 billion years ago. Life began 600 million years ago with the aid of the Amoeba, a single-celled organism. Life existed before dinosaurs, as demonstrated by fossils. Before then, the Pannotia Supercontinent, the only continent on Earth, existed 600 million years ago. The ozone layer was absent during the Pannotia Supercontinent era. Because of this, the earth's surface is more permeable to direct UV rays, making nascent life forms more susceptible to damage. Life "always finds a way out to proliferate," as the saying goes. On land, life was impossible, but in water, it was feasible (aquatic life).

1.2 Amoeba

The advent of the amoeba was the catalyst for everything. Fig.2 - A simple illustration of an amoeba. Eukaryotic, single-celled amoebas are cell membrane encloses the contents of the cell, and the nucleus is the area in the centre of the cell where the DNA of the cell is stored. Also, it has specialised parts called organelles that carry out a variety of cellular tasks, such as protein transport, phagocytosis, and energy synthesis.

Fig.2 - A simple illustration of an amoeba.



Source -

https://www.google.com/search?q=amoeba&sxsrf=ALiCzsbKMdGau1OwkOeZtDhXpN4hSoCJcw:1663854910758&source=lnms&tbn=isch&sa=X&ved=2ahUKEwiWjafHxqj6AhVv9XMBHXHCA9kQ_AUoAXoECAIQAw&biw=1536&bih=722&dpr=1.25#imgrc=2ZsWZUnKeyv8HM&imgdii=c-8XarjZUiuPdM

1.3 Algae

Later, a more complex kind of algae was created (see Figs. 3 and 4 for examples of underwater and surface-level algae, respectively). An alga is a typical plant that generates energy through photosynthesis. In the course of photosynthesis, oxygen (O_2) is produced as a by-product.

Fig.3 – Algae under water



Source –

<https://www.worldatlas.com/articles/what-is-the-ecological-importance-of-algae.html>

The amount of oxygen in water bodies increased along with the pace of algae development. Since oxygen (O_2) gas is lighter than water (H_2O), it mixes with the atmosphere from the ocean's surface resulting in the evolution of life on land.

Fig.4 – Algae observed on the water surface.



Source - <https://www.times-standard.com/2022/08/13/humboldt-county-health-officials-warn-of-blue-green-algae-in-big-lagoon-area/>

At the same time, that is around 460 million years ago, the ozone layer was developed because of extra oxygen (O_2) from marine life. Also, there was an increase in the number of predators (which were bigger than white sharks) arthropods and reptiles that came onto the land surface for their survival. The arrival of the reptiles and arthropods on the land surface caused the following changes – algae were converted into fungus; fungus was converted into small plants (herbs and shrubs); and finally, small plants were converted into 100-ft plants and trees, i.e., forests. Due to its connection to carbon, researchers gave it the name Carboniferous Period (C). The amount of carbon in the air was so high that the trees on the property began to deteriorate. Because there were no bacteria or fungi that would cause decay at this time, the trees gradually became covered in dirt. The trees turned to coal as the temperature and pressure in the area increased.

Insects were considered equivalent to animals at the time and nearly ruled the world. The 15% more oxygen in the atmosphere was the cause of the insects' huge size. Meganueria, a species of enormous dragonflies Fig.5 –

Meganueria feed on various insects, animals, including amphibians. Now that the cards are turned, amphibians eat dragonflies and tiny insects. This is evolution and the idea of the strongest surviving the others.

Fig.5 – Meganueria



Source -

https://www.google.com/search?q=meganeura&sxsrf=ALiCzsbZaGXSOomWQ4KpQawyNmkuFWKYhA:1663876497360&source=lnms&tbn=isch&sa=X&ved=2ahUKEwiW3Mz8lqn6AhVSCbcAHdD2BqUQ_AUoAXoECAMQAw&biw=1536&bih=722&dpr=1.25#i mgrc=6Erk1NndDgHaQM

On the surface of the earth, there was a tectonic plate movement that triggered a volcanic eruption. The Permian Mass Extinction was the term used for it. That was 298.9–251.9 million years ago, during the Permian epoch. Sulfuric gas was produced during volcanic eruptions, and as this gas disintegrated in the atmosphere, it resulted in sulfuric acid rain. The amount of oxygen in the atmosphere has dropped while the amount of carbon has increased. 95% of all organisms went extinct, and the insects that survived became smaller.

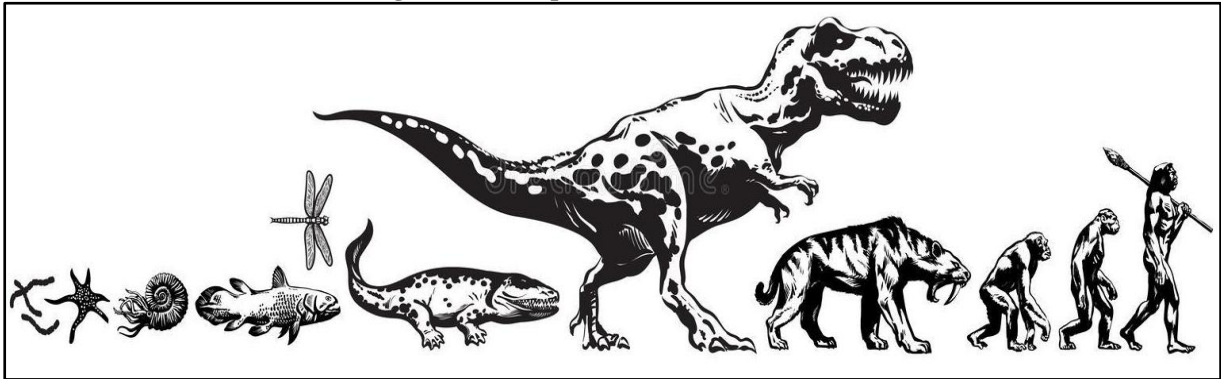
1.4 Dinosaurs and *Homo sapiens*

More than 180 million years ago, dinosaurs ruled the planet. The era was referred to as the Mesozoic. In addition to meteoroids, they also perished from exhaustion and low oxygen levels. Just a fortunate coincidence led to the emergence of *Homo sapiens*.

Approximately 250 million years ago, during the Permian historical era, global warming was at its worst. Then a new species or form of life known as the dinosaur, with a hard body and an internal life support system, landed on the surface of the world. Forest fires were frequent during the Cretaceous era due to climate change. A glacier melted. In comparison to the present average worldwide temperature of 13.9°C (57.0°F), the average temperature ranged from 21 to 32°C (70 to 90°F).

Humans relied on three essentials for survival: food, water, and shelter. They required food for energy, water for metabolism, and defence against other predators, particularly carnivorous dinosaurs like the T. rex, raptors, and other such creatures. Fig. 6 depicts a raptor dinosaur with a tyrannosaurus rex Fig. 7.

Fig. 8 – Basic representation of Evolution



Source -<https://www.dreamstime.com/illustration/human-evolution.html>

Due to high water temperatures and frequent forest fires that force fish and other aquatic life deeper into the water or into shallow waters, aquatic life appears to be disappearing.

1.5 Human Evolution

We have the theory of evolution thanks to Charles Darwin. The Origin of Species is a book he also wrote. Darwin postulated that natural selection processes led to evolution. The theory placed emphasis on the following ideas: Natural Selection, Variety, Fight for Existence, and Survival of the Fittest are all examples of evolution.

The interaction of the following mechanisms led to evolution-

- i. Mutation
- ii. Genetic Recombination
- iii. Chromosomal Abnormalities
- iv. Reproductive isolation
- v. Natural Selection

The process of change in which anatomically modern humans evolved from ape-like forebears is known as human evolution. Our forebears, the hominins, spent millions of years foraging before *Homo sapiens* emerged. The diet of hominins was based on foraging for plants, small animals, birds, and insects from the surrounding environment. They used archaic hunting techniques in addition to scavenging animals that other predators had already killed [1].

The key phase was deemed to be the control of the flames. Amazing changes were brought about by cooked meals. Cooked food also promoted brain growth since it increased nutrition, decreased chewing time, and restricted their intestines. Social living was facilitated by cooking and primitive agriculture.

Homo sapiens' earliest fossils date back about 300,000 years. It was discovered in Morocco at a location in Jebel Irhoud [2]. This fossil of a *Homo sapiens* is 100,000 years older than any that have previously been found. This is the first time that such fossils have been found in North Africa. The fossil was originally found in South or East Africa.

The fossils, which were made up of a lower jaw and a half skull, belonged to five separate people: three young adults, a teenager, and an 8-year-old child. The same layer also contained remains of fire, animal bones, and stone tools. Fig. 9 - An old fossil that shows the face of an early human ancestor.

Fig. 9 – Ancient fossil of reveals face of early human ancestor.



Source -

https://www.google.com/search?q=oldest+human+fossil&tbm=isch&chips=q:oldest+human+fossil,g_1:found:qUGQky1ccQk%3D&hl=en&sa=X&ved=2ahUKEwiU8-OX96n6AhW62HMBHYR8DyIQ4IYoBnoECAEQLw&biw=1519&bih=664#imgrc=RtUJ6y-8j3vu-M

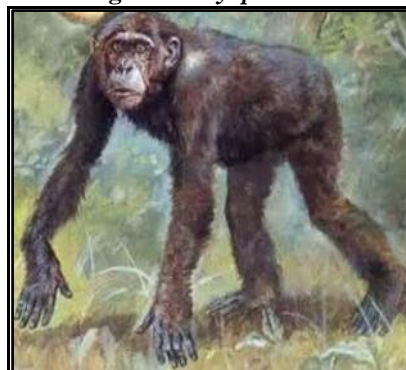
The development of modern humans from ancient apes took place over many generations. It has taken a very long time for humans to go from walking on all four limbs like other primates to walking on just two of our hind limbs today [3].

Homo sapiens is the modern name for the human species, which belongs to the genus *Homo*. Primates like the orangutan and humans are most closely linked to each other. Hominidae is the family to which humans belong. The initial stage of evolution was *Dryopethicus*, and some people think they are the ancestors of both humans and apes [3,4].

The following are the stages of evolution of *Homo sapiens* –

- I. ***Dryopethicus*** – They were the earliest known ancestors of both man and apes. At the same time as his existence, *Ramapethicus* existed, who was more human-like than *Dryopethicus*. *Dryopethicus* inhabited the European region and some parts of Asia and Africa (China, Africa, Europe, and India). The genus *Dryopethicus* refers to the oak wood apes. Fig. 10 – *Dryopethicus*. The members of the species were herbivores.

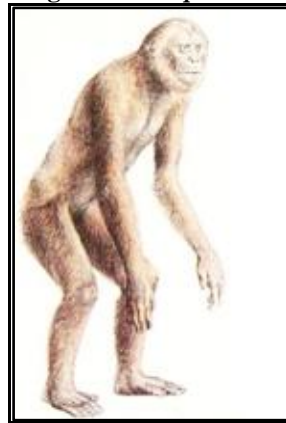
Fig. 10 – *Dryopethicus*



Source - <https://dinopedia.fandom.com/wiki/Dryopithecus?file=Dryopithecus.jpg>

Fossils of *Ramapethicus* have been found in Saudi Arabia, Africa, and the Punjabi Shivalik range. They had strong jaws, thickened tooth enamel, and shorter canines. They also began extending the use of an upright posture by using their hands for both feeding and defence. *Ramapethicus*, Fig. 11.

Fig.11 – Ramapethicus



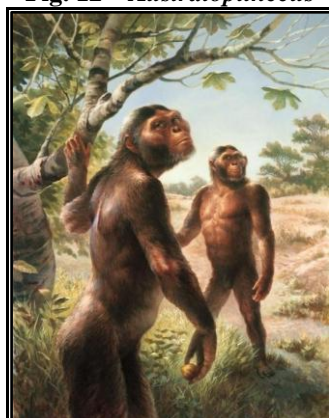
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II. Australopithecus — The fossil was found in South Africa in 1924. They walked upright, used stones as weapons, and lived on the earth. They ranged between 27 and 36 kilogrammes and stood 4 feet tall. *Australopithecus*, Fig. 12.

- *Australopithecus ramidus*: This species stood 1.2 metres tall, and its fossils display a wide foramen magnum, which suggests upright locomotion distinct from that of its earlier ape-like forebears. They have human-like teeth.
- *Australopithecus afarensis*: This species produced the well-known fossil known as "Lucy." They possessed a small cranium with flat noses and no chin, were shorter than *Australopithecus ramidus*, and were without a chin. They could stand on two legs, but they had slightly bowed legs. They were able to climb trees and dwell there thanks to their bowed fingers, toes, and legs. Their jaws and teeth were very huge.
- *Australopithecus africanus*: These bipedal creatures had little skulls and brains. In addition, they were herbivores with huge jaws and larger teeth than modern humans.
- *Australopithecus robustus*: Although they were taller, they retained ape characteristics.

Fig. 12 – Australopithecus



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III.Homo - The first fossil of *Homo erectus*, known as *Pithecanthropus Erectus*, was discovered in Java in 1891. These are the apes' and humans' final common ancestor. Tools composed of wood and bones were utilised by *Homo erectus*. Also, there is proof that fire was used. It is thought that *Homo erectus* lived in caves.

• *Homo habilis*—Based on the size of their skull and brain, it's possible that they may have spoken. Because *Homo habilis* was the first species to create and use tools, they are referred to as "handy men." He was upright and around five feet tall. Figure 13 shows a *homo habilis*.

Fig. 13 – Homo habilis



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• *Homo erectus* - They had a greater brain size, a shorter but longer face, no chin, and prominent speaking. They had the ability to create and manage fire. The first humans were carnivores. They started to spread from Africa to Asia and Europe once they were aware that groups existed. Figure 14 shows a *Homo erectus*.

Fig. 14 – Homo erectus



Source - https://www.google.com/search?q=homo+erectus&sxsrf=ALiCzsZ-5F6jOAFJas4_0XSMJ2qu8-iZtA:1663910999424&source=lnms&tbm=isch&sa=X&ved=2ahUKEwjPxbvAl6r6AhUkplYBHdAOAk0Q_AUoAXoECAIQAw&biw=1536&bih=722&dpr=1.25#imgrc=uIXXRAKSGMI0mM&imgdii=3dWeinrC1p_uAM

• *Homo sapiens* - These humans have evolved after *Homo erectus*. They were divided into two categories:

1) *Homo sapiens neanderthalensis* : They had a brain size larger than modern man. Also, they had a large head and jaw and were very powerful and muscular. They were carnivores and lived in caves. They lived in groups and hunted for food gathering. Fig. 15 – *Homo sapiens neanderthalensis*. The cranial capacity of Neanderthal grew from 1200 to 1600 cc. This species of hominids could hunt mammoths.

Fig. 15 – *Homo sapiens neanderthalensis*



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https://www.google.com/search?q=Homo+sapiens+neanderthalensis+&tbm=isch&ved=2ahUKEwjUofrB16r6AhVCSnwKHRmoBD8Q2-cCegQIABAA&oq=Homo+sapiens+neanderthalensis+&gs_lcp=CgNpbWcQAzoECCMQJzoECAAQQzoFCAAQgAQ6BwgjEOoCECdQ9wVYrBVgnSBoAXAAeASAAb0BiAHfCJIBAzAuN5gBAKABAAoBC2d3cy13aXotaW1nsAEKwAEB&scient=img&ei=WkQtY9SMIcKU8QOZ0JL4Aw&bih=722&biw=1536#imgrc=Po6YnQB6FQmyyM&imgdii=4IEr6Xum6oBbTM

2) *Homo sapiens sapiens* : They are the ‘modern-day man’. The brain size reduced to 1300cc and there was also a reduction in the size of the jaw, rounding of the skull and chin. Cro – Magnon was the earliest of the *Homo sapiens*. They spread wider from to Europe, Australia, and the Americas. They were omnivores, had skilful hands, and developed the power of thinking, producing art, more sophisticated tools and sentiments. Fig. 16 – *Homo sapiens sapiens*. Their cranial capacity was about 1350 cc. They gathered food through hunting and art first appeared during this time.

Fig. 16 – *Homo sapiens sapiens*



Source -

https://www.google.com/search?q=Homo+sapiens+sapiens+&tbm=isch&ved=2ahUKEwj20_ipmqr6AhVXj9gFHatkAF4Q2-cCegQIABAA&oq=Homo+sapiens+sapiens+&gs_lcp=CgNpbWcQAzIFCAAQgAQyBQgAEIAEMgUIABCA BDIFCAAQgAQyBQgAEIAEMgUIABCABDIFCAAQgAQyBQgAEIAEMgUIABCABDIFCAAQgAQ6BwgjEOoCECdQAFj1B2CzDWgBcAB4AIABpQG

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This was how evolution took place in humans.

2. EVOLUTION OF IMMUNITY – HUMAN SYSTEM

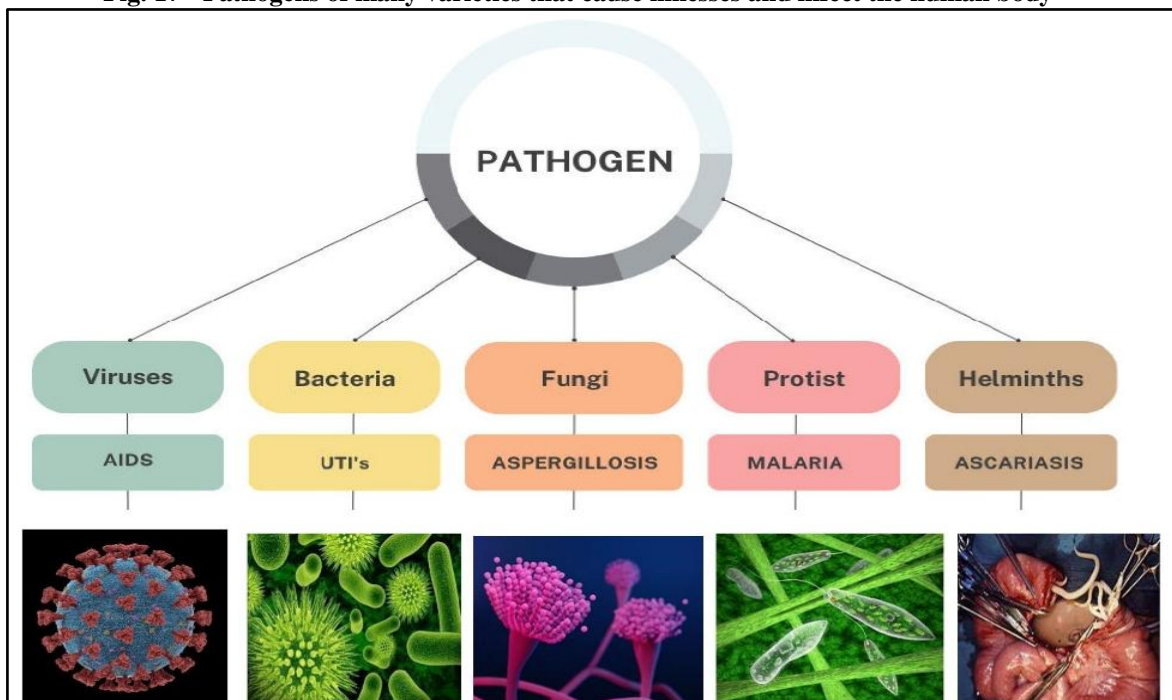
Humans have evolved mechanisms of innate immunity and immunological memory to survive recurrent infections. The evolution of the immune system within an individual possibly reflects the central role of the young adult in the survival of the species for its procreative potential. Higher organisms have highly developed immune systems because they have to defend themselves against a wide range of diseases. However, over the lifetime of an individual, these immune mechanisms change, first to adapt to the change from foetus to infant, and then to mature and expand during growth, subtly changing in pregnancy and finally decreasing in senescence[5].

2.1 Life on earth

About 1.5 billion years ago, eukaryotic life first appeared. Like other eukaryotic life forms, humans originated from a combination of two or more microorganisms. For instance, the genes that allow for the production of neurotransmitters, which make up 65% of human genes, appear to have come from bacteria, archaea, and eukaryotic organisms [5].

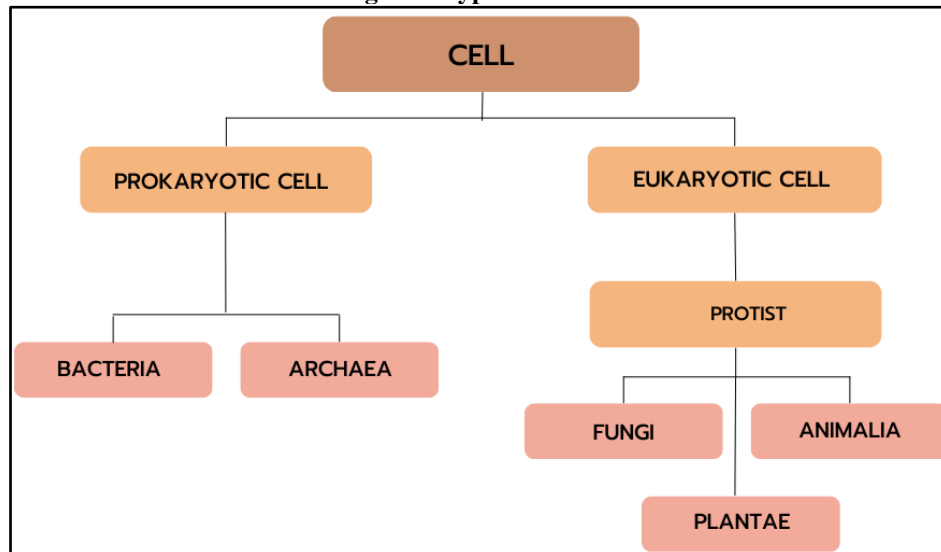
Immunity describes an organism's defence system. It offers defence against pathogens such as bacteria, fungus, viruses, helminths, and protists. These pathogens affect the human body and produce diseases such aspergillosis, UTIs, Covid-19, etc. Fig 17.

Fig. 17 - Pathogens of many varieties that cause illnesses and infect the human body



The prokaryotes, which were membrane-bound organelles, were the earliest organisms to emerge on Earth. Bacteria and archaea were the two main domains into which these prokaryotes were divided. But archaea gave rise to eukaryotes. Prokaryotes are members of the kingdom Eubacteria, while Archaea are members of the archaeobacteria. Protist creatures, which are members of the kingdom Protista, developed later from archaeobacteria. The Protista kingdom includes both multicellular and eukaryotic, often unicellular organisms. Animalia, plantae, and fungi all descended from protist. They comprise the various fungi, plants, and animals that populate the planet. Fig. 18 depicts types of cells.

Fig. 18 - Types of Cells.



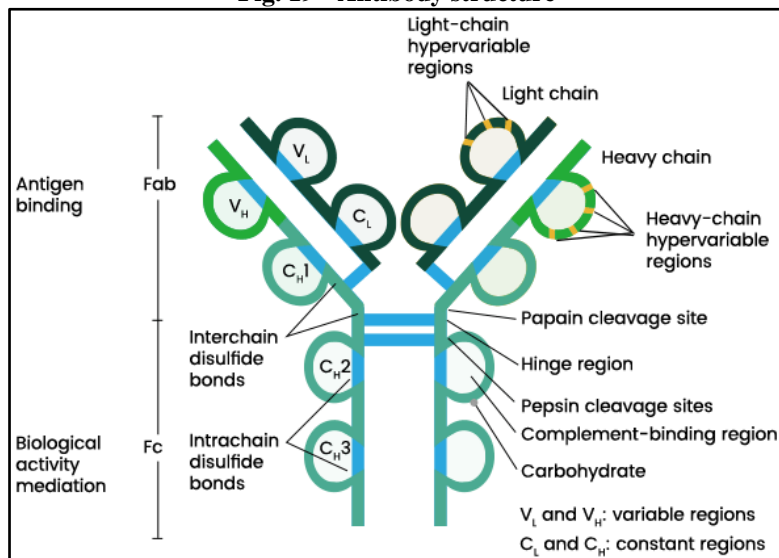
2.2 Immunity

The ability of an organism to fend off hazardous pathogens is known as immunity. It is a sophisticated biological system and is capable of identifying and tolerating both self and non-self substances. The Latin term “immunis” is where the modern word immunity comes from. Élie Metchnikoff, Russian zoologist was the first scientist to formulate a comprehensive theory of immunity. During 19th century, infectious diseases have been understood to be brought on by germs or bacteria, and vaccination programs have been implemented to increase immunity.

Immune cells make up the immune system. With the aid of immune cells and their proteins, as well as cell signalling processes, chemical messengers, etc., they fight against foreign infections that infiltrate the human body. Natural killer (NK) cells, basophils, and many other types of cells are always at work. They struggle to prevent any extraneous material from entering the body. When a pathogen enters the body, cells like macrophages tell T-cells (lymphocytes) and B-cells (memory cells) to kill it and make an antibody.

A protein called an antibody is produced by plasma cells (WBCs). An antigen triggers the action of an antibody (a substance that causes the body to make a specific immune response). An antigen-specific antibody binds to that antigen. The antigen is eliminated by the binding. The terms immunoglobulin and antibody are interchangeable (Ig). It is a Y-shaped structure consisting of two heavy polypeptide chains and two light polypeptide chains. Its structure enables the dual functions of facilitating biological activity and antigen binding Fig. 19. The two regions that make up the function of an antigen are the fragment antigen-binding (Fab fragment) and the fragment crystallizable region (Fc region). Antigens are bound by the Fab fragment region. The heavy chain and the light chain each have a constant and a variable domain in this region. The Fc region comprises the final region that interacts with certain complement system proteins and cell surface molecules known as Fc receptors. As a result, the immune system can be stimulated by the antibodies. Immunoglobulin (Ig) Fc regions have a highly conserved N-glycosylation site [7].

Fig. 19 - Antibody structure



Source - <https://www.sinobiological.com/resource/antibody-technical/antibody-structure-function>

Immunity involves specific and nonspecific components. The nonspecific components act as barriers or eliminators of a wide range of pathogens irrespective of their antigenic make-up. Other components of the immune system adapt themselves to each new disease encountered and can generate pathogen-specific immunity. The immune system has been primarily moulded by evolution to respond efficiently to acute infections in young people, to adapt to pregnancy and to transmit protection to infants, and is adapted to cope with many chronic infections lasting for decades. Apart from fighting viruses, bacteria, fungi and parasites, the immune system also assumes other roles such as tissue repair, wound healing, elimination of dead and cancer cells, and formation of the healthy gut microbiota.

There hasn't been a drug developed to increase immunity. Medicines simply kill alien objects; it's a natural process. Only natural food consumed as part of a healthy lifestyle can increase immunity.

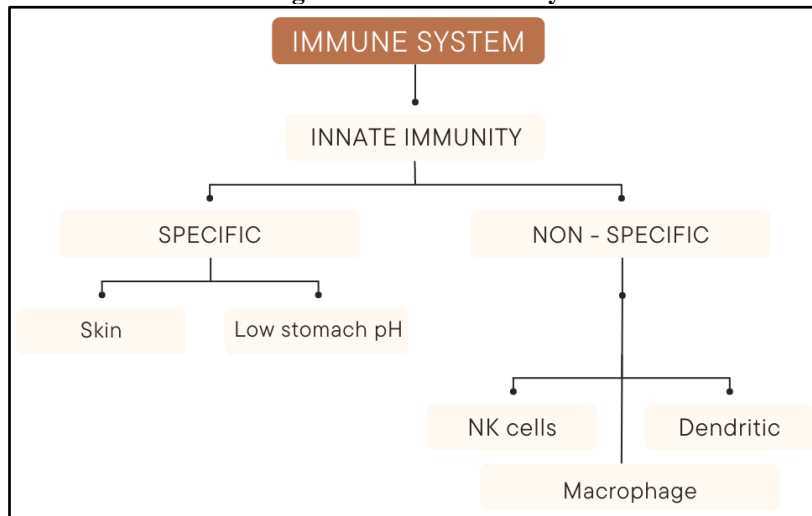
3. IMMUNE SYSTEM

Two categories of the human immune system can be distinguished: innate immunity and adaptive immunity, or immunological response. We have approximately 1600 genes that are involved in innate and adaptive immune responses, according to studies. The immune system is immature at birth, develops into adulthood, and then begins to diminish as we age[8].

3.1 Evolution of Immune system in early life

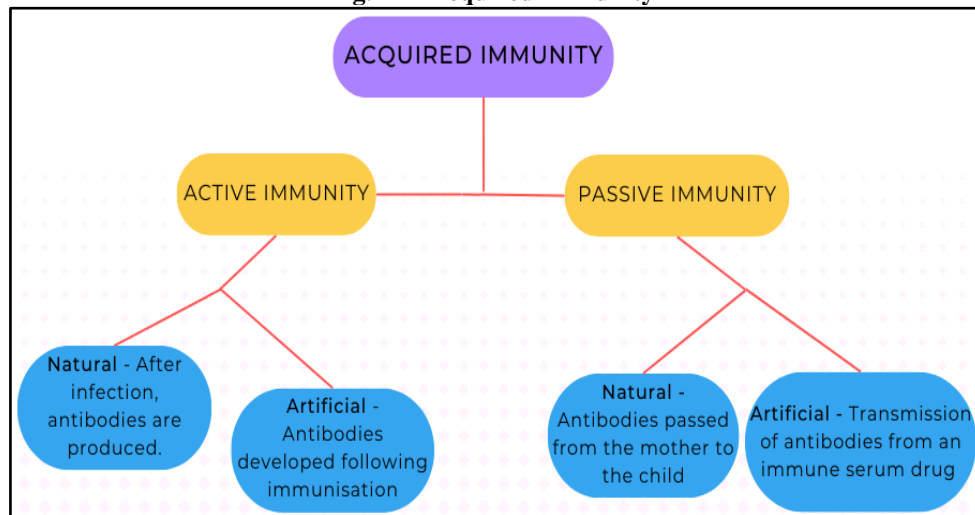
The defense mechanism that is natural or that humans are born with is known as innate or non-specific immunity. First Line of Defense is another name for innate immunity, which serves as a barrier for hazardous chemicals trying to enter the human body. Moreover, it is separated into two categories: Specific and Non-Specific Innate Immunity. Fig. 20.

Fig. 20 - Innate Immunity



The acquired immune system is another name for the adaptive immune system. It evolves as we grow older. Its functions are to get rid of infections or stop their growth. Active Immunity and Passive Immunity are the two categories. A further division is made into Natural Immunity and Artificial Immunity. Fig. 21 shows acquired immunity.

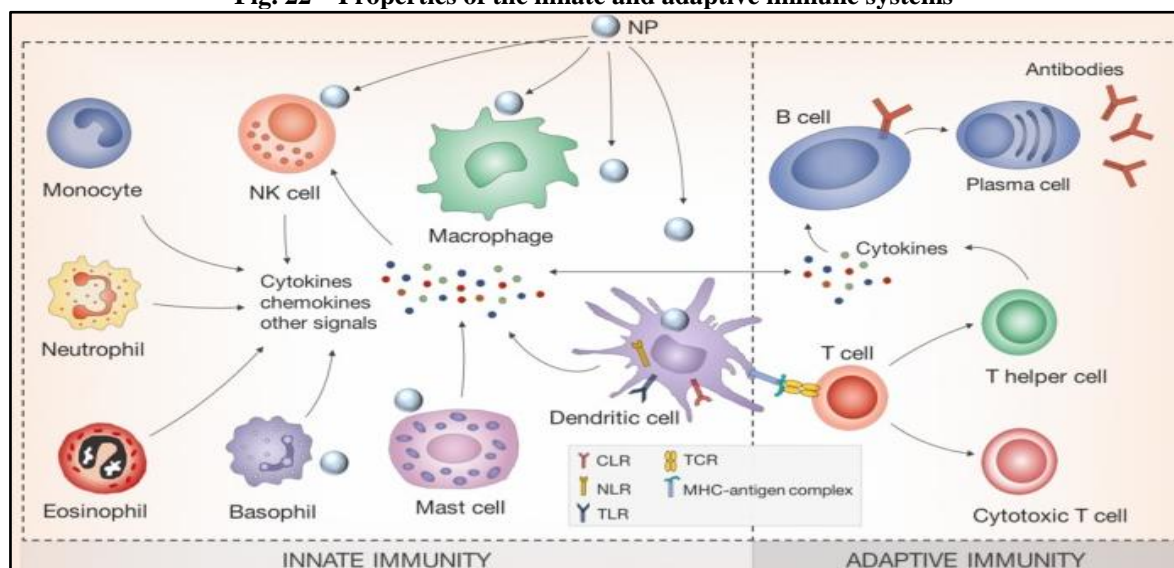
Fig. 21 - Acquired Immunity



3.2 Innate Immune System

Neutrophils, monocytes, macrophages, and dendritic cells are components of the innate immune system.

Fig. 22 – Properties of the innate and adaptive immune systems



Source - <https://ars.els-cdn.com/content/image/1-s2.0-S1044532317300404-gr1.jpg>

At birth, the innate immune system is deactivated. Mature neutrophils multiply rapidly before birth thanks to granulocyte-colony-stimulating factor. Fig. 22 basic representation of cells of immune system. Nevertheless, it quickly diminishes and exhibits weakened immunological responses, which may result in bacterial infection in babies. TLR9 and TLR7 levels in newborns are the same as in adults [8].

IgG, IgM, IgA, IgD, and IgE are the several types of immunoglobulins. The type of heavy chain distinguishes them. IgG molecules contain heavy chains known as gamma-chains, IgM molecules have mu-chains, IgA molecules have alpha-chains, IgE molecules have epsilon-chains, and IgD molecules have delta-chains.

3.3 Adaptive Immune System

T cells develop in the thymus, which is largest at birth and during the first years of life. Mature single CD4⁺ and CD8⁺ positive T cells are first detected in the thymus at week 15 and abundant in the periphery well before birth. Thymus aids T-cell growth, which is greatest during the early years of life. In week 15, CD4⁺ and CD8⁺ cells may be easily seen in the thymus. The function of T cells during the neonatal stage differs from that of adult T cells. T cells exhibit theroeneic activity during development and have weak responses to foreign antigens. CXCL-8 aids T cells in the production of antibacterial neutrophils and T cells. $\gamma\delta$ T cells can generate substantial levels of IFN- γ .

B cells are present in secondary lymphoid organs and bone marrow, and they play a role in all humoral reactions. There are two categories of B cells present; B1 cells release IgM in small amounts but serve as the first line of defence. It is derived from the multi-lineage CD34⁺ and accounts for 40% of blood cells at birth. It also secretes IL-10 and TGF- β , which aid in the promotion of the Th2 response.

T cells are in charge of antibody reactions. TCR aids in the interaction of Th2 or helper T cells with co receptors such as CD28 and CD40, and it also interacts with HLA peptide, CD80/86 and CD40 with antigen specific B cells. Meanwhile, neonatal B cells express less of these, limiting their ability to react.

They lead to decreased humoral immune responses due to inadequate immunoglobulin switching. Memory B cells are generated at the same time. Because newborns have fewer B cells than adults, affinity maturation of antibodies is limited.

3.4 From infancy to maturity

IgG antibody is passed down from mother to child. The danger is lowered with the use of immunisations, which also aid in immune system maturation. The memory lasts till old age. The first time a person is exposed to germs or any other parasite infection occurs during childbirth. As soon as the infant is born, he or she is exposed to germs, viruses, and other pathogens in the environment. Fig. 23 - Graph depicting the evolution of the immune system.

In the stomach, 20% of lymphocytes are present. Gut bacteria produce Th17 cells, T_{reg} cells and memory T cells. Throughout development, all T lymphocytes have the CD45RA glycoprotein and have never encountered a foreign antigen. T_{reg} cells numbers decrease early on, whereas Th1, Th17, and Th2 cell numbers grow. The cross-reactivity is caused by discrete short (8-15 amino acid) peptides (epitopes) that fit into peptide-binding grooves on the cell surface of HLA class I or II molecules and are subsequently recognised by T cells.

Clostridium spp. promote colonic Treg cells and bacteria in the gut aid in the formation of Th17 cells. ABO blood types cross-react with microorganisms in the stomach, resulting in IgM antibody reactions. B cells produce antibodies against HIV-1 gp41 proteins. IgG immunoglobulin preserves memory B cell half-life. Plasma cells that produce antibodies travel to the bone marrow, where they dwell for a long time. Memory B cells and T helper cells reproduce indefinitely. Cross-reactivity and antigen persistence keep B cells alive, multiplying on occasion, and cells secrete antibodies.

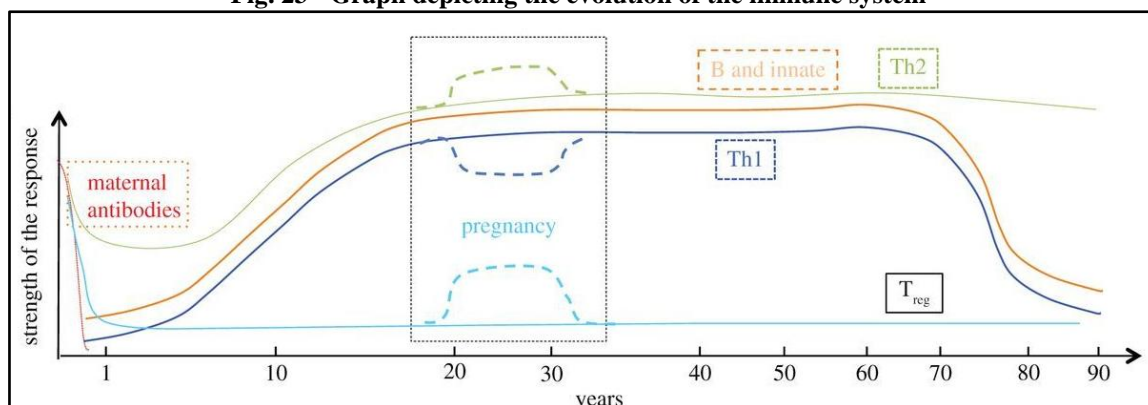
T cells aid in the activation of immunosuppressive medication; they control the virus and its depletion, which can have disastrous repercussions. HLA class II molecules are found on the surface of T helper cell receptors, which react and convey signals such as IL-21 to B cells. T cells, on the other hand, have low affinity and co-receptor-ligand combinations that are not antigen specific, which also transmits signals to divide and function.

T and B cells are rapidly depleted as a result of activation-induced cell death and retention over time.

3.5 Gestation Period

The trophoblast present at the maternal interface at the site of first implantation is responsible for the immunological response to graft rejection. Non-polymorphic non-classical HLA antigens are expressed on the trophoblast, local immune suppression is mediated by invading NK cells, monocytes, and T regulatory cells, and T-cell activation is inhibited by tryptophan catabolism. During pregnancy, the mother's immune system can shift the balance of T cell responses from Th1 to Th2. As a result, pregnant women have remissions from autoimmune illnesses, which can be hazardous to the mother.

Fig. 23 - Graph depicting the evolution of the immune system



Source - <https://royalsocietypublishing.org/doi/10.1098/rspb.2014.3085#RSPB20143085C22>

3.6 Immune function deteriorates with ageing

The immune system undergoes remodelling as humans age, which has a significant influence on human health and survival. Vaccine effectiveness is reduced due to a weak immune response. Since the immune system fails to tolerate self-antigens, the human body becomes polluted with various autoimmune illnesses as it ages. There is also a decline in T cell activity and macrophage clearance of apoptotic cells. The number of T cells in the thymus decreases, resulting in thymic output.

T cells multiply and expand the virtual memory system while decreasing the ability to build immunological memory in response to de novo antigens. The generation of cytokines by CD4 and CD8 T cells is hindered, and the main surface markers are changed and reversed from CD4⁺ to CD8⁺ T cells. T cell responses that keep EBV and CMV under control while decreasing CD8⁺ T cells. Although the number of B cells does not drop with age, just their makeup does. Memory cells replace naive B lymphocytes, resulting in lower affinity maturation and isotype switching. The alterations in the T- and B-cell compartments hinder the proper immune response to future acute and latent viral infections and vaccines.

The immune system deteriorates with ageing as well. The amount of innate immune cells also alters with skewing of haematopoiesis towards the myeloid lineages. Senescent neutrophils have diminished phagocytic capacity and superoxide generation, which is owing in part to decreased Fc receptor expression. Similarly, the respiratory burst of ageing macrophages is reduced. They exhibit impaired phagocytic activity and HLA II expression when combined with DCs. The immune system's 'silent' clearance of apoptotic and senescent cells is therefore impaired, which may contribute to the pro-inflammatory phenotype.

The most remarkable modification in innate immunity as humans age is an increase in the immune system's pro-inflammatory cytokines IL-1, IL-6, IL-18, and TNF α .

Immune senescence's cellular and molecular foundation is largely unknown. Three phenotypes characterise senescent cells: telomere attrition accompanying each cycle of proliferation, leading to stopped cell division or 'replicative senescence'; increased mitochondrial load/dysfunction and reactive oxygen species; and

senescence-associated secretory phenotype (SASP), defined as the release of pro-inflammatory cytokines, chemokines and proteases by senescent cells. These characteristics have an effect on mitotically active cells through depletion or stopped division (e.g., HSCs or T cells), as well as post-mitotic immune cells through cellular dysfunction.

Memory T cells and HSCs divide infrequently to avoid telomere attrition, yet consistently in response to infection (memory lymphocytes) or tissue renewal (stem cells) throughout the lifespan. End-stage senescent CD27, CD28 T cells have the shortest telomeres and display reduced proliferation following activation, but they still retain robust effector capabilities. These cells increase in the elderly, as well as in people suffering from autoimmune disorders and persistent viral infections. The second distinguishing feature of aged cells is increasing mitochondrial dysfunction, which results in oxidative damage to proteins and DNA. The first two mechanisms of ageing are linked by oxidative stress, which induces DNA breaks and may be the source of telomere attrition. The build-up of oxidative damage might be caused by a reduction in lysosomal and autophagy activity. Autophagy, the process by which bulk cytoplasmic material is degraded by transferring it to lysosomes, declines with age, especially in human CD8+ T cells. Failed memory T cells' responses to flu vaccination reported in the elderly can be restored by an autophagy-inducing chemical. A third more recent addition to these basic alterations of aged cells is the adoption of the SASP, contributing to increased pro-inflammatory cytokine release and low-grade inflammation.

4. CONCLUSION

Life on the earth's surface started around 600 million years ago with a tiny organism referred to as Amoeba. Amoeba gave rise to a more complex structure called algae. Photosynthesis is the phenomenon used by algae to produce energy, with its by-product being oxygen (O₂). This gave rise to marine life. Later, marine life organisms got into the food chain. Shrimps eat small crabs -trilobites. The race between prey and predators had begun, and now comes Charles Darwin's theory of survival of the fittest. Arthropods and reptiles came onto the land surface because of their survival. Due to volcanic eruptions, they became extinct with only a few left and the size became small because of the low oxygen present in the environment.

Then came the era of dinosaurs, and they ruled this planet more than 180 million years ago. They became extinct not only as a result of meteorite collisions, but also due to low oxygen levels. The oldest fossils of *Homo sapiens* were discovered over 300,000 years ago in Morocco. Evolution made development in shape and size of the brain, skull, body structure etc. The stages of evolution of humans in ascending order are – *Dryopithecus*, *Ramapithecus*, *Australopithecus*, *Homo Erectus*, *Homo Sapiens Neanderthalensis*, *Homo Sapiens Sapiens*.

Evolution is not a past. It is continuing now. Humans' evolution is by "natural selection" for many different traits based on their life and environment. Evolution is a necessity. It is believed that the jaw size is reducing and the wisdom teeth are soon going to become extinct. Vestigial muscles in the forearm are also absent, and 10–15% of the population are missing in one or both of the forearms. To withstand recurring infections, humans have evolved systems of innate immunity and immunological memory. The evolution of an individual's immune system may reflect the importance of the young adult in the survival of the species for its procreative capacity.

The immune system is required by all living organisms because it protects them from numerous infections. Pathogens such as viruses, fungi, bacteria, and others cause illness. The immune system is further subdivided into innate immune system (born with) and adaptive immune system (develops when body is exposed with), which is further subdivided into cellular, protein-mediated, and humoral immunity. Basophils, mast cells, NK cells, and eosinophils are examples of innate immune cells, whereas macrophages, dendritic cells, and B cells are examples of adaptive immunity cells.

When an intruder is detected, the innate immune system is the first to respond. It is composed of the skin, the cornea of the eye, and the mucous membrane lining the respiratory, gastrointestinal, and genitourinary systems. All of these things serve to develop physical barriers that safeguard your child's body. They guard against dangerous pathogens, parasites (such as worms), or cells (such as cancer). The innate immune system is passed down from generation to generation. When this system detects an intruder, it immediately goes into action. The intruder is eliminated within the immune system cells (called phagocytes). The acquired immune system creates particular proteins (called antibodies/immunoglobulins) with the support of the innate immune system to protect your body from a specific intruder. When the body has been exposed to the invader, cells called B lymphocytes produce these antibodies. The antibodies remain in your child's system. Antibodies might take many days to develop. Your child's acquired immune system evolves throughout time. Immunizations teach your child's immune system to produce antibodies that will protect them from dangerous infections.

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