

Medicine in millenniums

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J. Fac. of Vet. Med., Tehran Univ. Vol. 55, No. 2, 107, 2000

Ever since man acquired knowledge of himself, he became aware of the certain diseases. This is the first step in medical history and medical research, it is as old as man's thinking. In this article we will express some aspects of a few medical discoveries specially in the last millennium. The most important medical basis was the theory of four humors or four natures established by Hippocrate, Galen and developed by Avicenna and Jorjani. Najib al Ddin Samarghandi one of the greatest Iranian physician (Killed in 1221 A.D.) was the first scientist who did not care about this theory. After medical discoveries of Louis Pasteur and other savants the four humors theory abolished totally. Ibn Nafis Gharshi in 1242 about 300 years before Micael Servetus expressed the theory of the pulmonary circulation. W. Harway (1578-1657) discovered the blood circulation which was a fundamental basis for physiology. Ibn Gof (d. 1336) expressed anastomosis of arterioles and venules via small valves 4 centuries before M. Malpighi. Rhazes (d. 925) for the first time expressed his fermentation theory 900 years before Louis Pasteur, he said that a ferment in the blood is causal agent of smallpox. Pasteur and Koch in 19th century definitely indicated microbial agents of some infectious diseases. Rhazes wrote the first article on the subject of allergy and Biruni (1048 A.D) mentioned an antibody like theory. The use of liver from a rabid dog on a bitten wound preconised by Avicenna (d. 1038) is a practical application of serotherapy and vaccination. Edward Jenner in 1798 found that inoculation of cowpox has immunizing character against smallpox, then the method of vaccination was applicable. Several diseases were controlled after development of microbiological knowledge but new disease like AIDS was appeared with it's terrible figure. The never ending struggle between patient and disease is still going on. We must prevent the recurrence of the deadly diseases in man and animals with the best trying and wisdom.

Key words : Medicine, Millenniums, History of Medicine.

The pioneer man during thousands centuries and successive millenniums had been incessantly opposing, deliberating and challenging against unfavorable condition of nature and pathogen factors but did not find any resorts however escape from disease

and surrender to destiny. Since millennium ago some curious and intelligent people, regarding time and place, started to think about natural occurrences and diseases and found some interesting points by experiment and conveyed it by word of mouth until invention of scription in skins and stones. Consequently they registered it on papers and offered it to the commings (14, 15, 16).

In this brief, we concern about some major medical inventions, particularly in the second millennium and expressing some expectations for the third millennium.

The most important medical theory in the second half of millennium before Christ up to the last quarter of the second melleinium is four humours or four natures. Hippocrate (460-375 B.C) saved medicine from philosophy and metaphysic and showed it off in this world and he believes that there is a reason for any disease and the basis of his work is upon exact observation and recording sign of the sickness. Hippocrate's medicine is based on four humours and believes fire, air, water and soil are essence of the all existence. Then Galen (131-201 AD.) according to this basis, enacted the theory of four natures. The great Iranian authors, specially, Avicenna and Seid Esmaeel Jorjani completed these theories. The basic of hipocrat's theory is in Bundahish that refers to Sasanian and Avestai's resources but is written in much older proves and it points to the similarities of Kehjahan (Small word) and great world (Mehjahan). According to four nature's theory: The natural outlook effects are as follow; fire : warm and dry; air: warm and wet; water: Cold and wet; soil: cold and dry. All the material are made up of this four elements.

According to different nature it would appears a medium quality from interaction which is called humor or temper. Blood has similarity with air, phlegm or lymph with water; black bile with soil; bile with fire. If merely one of the property dominates the other one following the contrast effects and mixing, these four individual humours or temperaments, hot, cold, wet, dry will appear. If this prevalence could not be so significant, the four humours will appear in compound form of hot and dry, hot and wet; cold and dry and cold and wet. If in some cases the four quality mixed with each other equilibrium would be replaced, so that the moderate temperament could be seen.

Then nine kind of temperaments are assumed. People usually are sanguine (hot and happy), phlegmatic kind (poikilo thermal and slow), melancholic (sad and miserable) and bilious (hot and expeditious).

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There is not equable temperament or real health in living world, however approaching to that manner or a moderate level can be happened. Each organ member has special temperate level. The health will disappear and illness will be divulged while imbalance establish or one temperament inverts or inclines to other ones. Physicians have to know individual and corporal temperament of the patients and during illness should make effort to set the balance or return it back again by using drugs, cauterizing, bleeding and surgeries, etc. Any of the drugs also have one of these eight individual or combined temperaments. For instance they have been challenging against diseases with cold and wet nature with drug with dry and warm nature and vice versa. This was the principle of the ancient world medicine (2, 4, 7, 14, 15, 16, 18).

Najib al Ddin Samarghandi one of the greatest Iranian physician in kharazmshahian's reign who was killed in 1221 AD in public massacre by order of Tuli the son of Gengiz Mongol, did not care about four natures and humours theory and did not put his practice on that. After medical discoveries in 18th century, specially with worthy probes of Pasteur and determining the interaction of disease and microbe, the temperamental theory was abolished, however it can be partly justified with basic nature or creature's genetic. Or in the other word quality and quantity of major histocompatibility complex (M.H.C) genes and human leukocyte antigens (H.L.A), also with basic immunity and interaction of neuroendocrine (3, 5, 12).

The Belgium, Andreas Vesalius, was the structurer of new anatomy. He dissected as many as human and animal bodies and apparently engaged to many problems of Galen's opinion in 1539 and indicated that Galen's explanations conform with monkey's body rather than human body. In 1543 he published a worthy book about human body structure with pictures of beautiful dissect of different parts of the human body. This was one of the greatest scientific books in the world and provided the fundamental revolution in anatomy, surgery and new medical thought and related branches (12).

Ibn Nafis Gharshi (1210-1288) was from Gharshi (Nakhshab the Iranian Transoxania city). He was born in Damascus and was one of the notable physician in the world. Ibn Nafis is the main discoverer of pulmonary blood circulation. He has expressed his theory in the description part of anatomy of canon of Avicenna's. He expressed this discovery about 1242 A.D., that means approximately 3 centuries before Micael Servetus. Ibn Nafis words are exactly like what Servetus has said in *Cristianismi Restitio*. In fact Ibn Nafis's opinion has been diffused in Europe about 1520 AD and 30 years later in 1553 this theory has been expressed by Servetus and that caused to burn Servetus in fire by charter of Church.

Kolombo (dead in 1559) also has stated the theory of the pulmonary blood circulation. W. Harway (1578-1657) discovered the main blood circulation according to reasoning and observation. Thus body physiology got a strong basis. However he did not know how the end of arteries attaches the end of veins while he was

publishing his findings (12, 20).

Ibn al Gof Karki (died in 1336 AD) was one of the Jordan Christian physicians, who has written a description on Canon and expressed throughly the capillaries with his exact observation before the invention of microscope. He also believed the anastomosis of artery and venus with small valves which was discovered in Europe after four centuries. M. Malpighi (1628-1694), did the same discovery of Ibn al Gof with microscope and this mater was divulged with his name in the world (10, 16).

Mohammad Ibn Zakaria Razi (Rhazes: 865-925 AD) expressed a theory about the cause of infectious diseases for and this declares fermentation theory that approximately 1000 years later was explained by Louis Pasteur and lead him to reveal the cause of microbial diseases (1, 6).

Antony Van Leeuwenhoek (1632-1723) the Dutch savant merchant with his simple microscope which was invented in the early 17th discovered the microorganisms, spermatozoid, red blood cells. He was the man who studied the muscle fibers and also the structure of animal histology. All kinds of microorganisms that nowadays we know them such as protozoers, alges, funguses and bacteria were carefully described by Leeuwenhoek.

After Leeuwenhoek's discoveries the scientists were surprised about the origin of such microorganisms. In this matters there were two believes, some thought that microorganisms were yielded by spontaneous generation or abiogenesis from lifeless material. This idea was accepted since ancient time. Leeuwenhoek and some other scientists believed that these germs were originated from seeds or progeny that usually exist in the air. Lazzaro Spillanzani Italian naturalist and specially Louis Pasteur banished the spontaneous generation with their valuable experiments and believed that the germes have been born or generated from their ancestors.

In this situation, the possibility of challenging with germs was imagined. Louis Pasteur (1822-1895) one of the everlasting scientists of medicine, following his probes on effect of tartarat and para tartarat solutions on polarized rays could determine the border between live and dead world. He inclined to consider the ferment phenomenon which is a view of life spectacular. He mentioned fermentation is the result of a small and live microorganism function. So that, it is the function of life not death. He observed the production of vinegar from wine or "maladie des vins". In 1862, he demonstrated that wine is converted to vinegar by infecting with special kind of ferment which is different from alcoholic ferment. For preventing the infection he recommended to boil the wine up to 55° (Pasteurization). Surprisingly he found that contagious diseases should be related to microorganisms. During his life he discovered the causes of many microbial diseases such as anthrax, infectious gangrene, puerperal fever, Hog cholera and pneumonia. Robert Koch (1843-1910) started, his searchings about cause of anthrax and discovered the rule and method of demonstrating the condition of pathogenesis. He made a revolution in tuberculosis treatment by discovering *Mycobacterium tuberculosis* (1882). Following year he discovered



Comma Bacillus, the causal agent of human type cholera in India and finally used tuberculin that means extract of Mycobacterium tuberculosis for tuberculosis diagnosis.

Pasteur and Koch's researches formed a revolution in medical world that saved millions of the human's lives (3, 6).

Mohammad Ibn Zakaria Razi (Rhazes) is the one who discovered allergy and also wrote the first article in allergy and immunology. In this short article, he expressed rhinitis caused by smelling rose in spring. Baha-al-Ddola Razi (dead in 1507 AD) the latest great Iran and Islamic world's physician gave a definite description about hypersensitivity or allergic rhinitis, food and drug allergy in Kholasat al Tajareb beyond his observations. Bottalo spoke about sensitivity caused by plants in 1565 and Bostock comments the indications of hay fever in 1819 (9, 11, 16, 18, 19).

Avicenna (980-1037) says in his book "Canon" about rabies " If they put dogs liver on the wound of person bitten, it would be very helpful ". Also he mentions " rabid dog's blood is antitoxin for bite of rabid dog ". We know in rabid dog's blood there is rabid antibody so that, its application on wound's region specially at the early time of bite, can be exceedingly cause to reduce and naturalize the virus and give the body an opportunity to oppose with it. Nowadays it is used to inject the anti rabic serum in the wound's region and also by systemic application. This is an interesting Avicenna discovery in the way of producing vaccine and treating serum (2, 5, 8).

Abu Reihan Birouni (973-1048) indicated something about Hyssop in " pharmacology or seidaneh " that should be considered in the antibody like theory. During explaining this substance which is the sweat secretion of deer forehead, he comments that: Dear accustomed to eat viper and also opposing with poison by their instinctly power and currently viper antitoxin appeared in his secretion and was secreted out from its forehead. Some how a kind of antibody and special kind of serotherapy is expressed (8, 13).

Edward Jenner in 1798 found out that milkers whom are infected by cowpox following contact with cow's teat are immunized against smallpox. Then he inoculated, the cowpox to human and understood that it causes immunity against poxvirus attack.

Louis Pasteur discovered that attenuated culture of Pasteurella multocida will induce resistance in birds against this pathogenic factor. In 1881 A.D. for the first time he used the term of " Vaccine " which was enacted in memory of that cow which pox juice was extracted and in honor of Edward Jenner. It is important to know that since centuries ago in China, Iran and some other middle East countries vaccination was common by using dried smallpox crusts (5, 8).

Consequently in 18th century, this procedure was divulged and advocated in England and other European countries by Lady Worthey Montague and that made a reduction in mortality of people in these countries and helped their scientific and industrial developments. Vaccination like Jenner procedure was very common in Baluchestan of Iran several centuries ago before him. Any how, vaccine was invented and immunology science was

developed that saved millions and millions of human's life each year (5, 8, 17).

Richet and Portier discovered anaphylaxis in 1902. Von Piquet justified allergy term with a philosophical state in 1906. Landsteiner discovered human blood group (A.B.O) in 1900 and gradually transfusion was performed in 1940. Landsteiner and Winer discovered Rh factor in human blood system. According to that, the transfusion side effect reduced and a procedure was found for preventing fetal erythroblastosis.

Erlish mentioned side chain theory and before description of antibody nature, he has anticipated the condition of its producing and effect. Kabat and Tiselius approximately 900 years after Abu Reihan Birouni presented this fundamental discovery that the antibodies are Gamma globulin (The author is honored for acquiring science in presence of Kabat for a short time).

Bruton presented the first report of agammaglobulinemia. Porter and Edlman exactly determined the structure and formation of Gamma globulin in 1960. Jerne and Burnet presented clonal selection theory on antibody biosynthesis. Miler and Good determined the role of thymus in immunity.

Milstein and Kohler in 1970s formed a new interesting procedure by discovering the method of monoclonal antibodies in fundamental immunology field which has many uses in researches and treatments. So in the third millennium, the result will possibly become more effective. Milstein and his colleague were awarded the medicine Nobel prize for their universal researches in 1984.

In 1888 Bouchard indicated that Pseudomonas aeruginosa prevents the growth of many bacteria. Dubos in 1939 indicated that a kind of substance is generated by mean of Bacillus brevis that can prevent the growth of Streptococcus and Pneumococcus. Then A. Fleming reported that penicillium prevents growth of Staphilococcus and finally he discovered penicillin. Since then many antibiotics were sequently known and produced at a commercial level. However beyond this subject, bacterial resistance manifested and increased (15, 16).

Several diseases were controlled after development of microbiological science and man overcame them. Thus newborn mortality considerably were reduced with immunology and other medical progress so the average age of man was increased. However increasing of population particularly in undeveloped and developing countries became a problem and caused destroying of environment which is obvious all over the world including in our country. In the third millennium it is necessary to find solution for this problem otherwise the existence will be exposed to annihilation.

In second half of 20th century new industries such as fermentation and its branches, antibiotic production, vitamins with microbial origin, biological material and chemical drugs have been developed. The souvenirs of this period was accompanied with more progress in immunology and bacterial physiology. That has been the base of new genetic and molecular biology.

The general aspect of biology has changed and developed human's thought about environments. The condition of many



phenomenons were falsely explained up to the middle of 19th century and different infectious diseases could not be distinguished. In the 20th century, all of these subjects such as biology, cellular organization and its role in microbial multiplication, heritage mechanism and plant and animal evolution were illustrated.

The other biological improvements in early 20th century were related to basis of genetic which was yielded from Mendelian analysis and cytological studies. Avery and his colleague defined DNA as genetic basis with their amazement consideration on pathogenic and non-pathogenic lineage of *Streptococcus pneumoniae* and discovered transformation phenomenon. Watson and Crick in 1953 presented the molecular structure of DNA and have been awarded Nobel prize and soon after the genetic codes or "Life mystery language" was discovered. Jacob and Monod discovered the regulation of genetic expression and A. Lwoff discovered lysogenic state of bacteria, these three scientists received Nobel prize of medicine in 1965 (Author has honor of being student of these scientists in Paris Pasteur Institute for two years). Regulation of gene expression made a new world in life, but more researches is needed in future to distinguish the mechanism of cellular regulation in human's life.

In the last quarter of 20th century, the progresses that has been obtained in knowledge of gene and plasmids and some other bacterial genetic caused creation of the science of molecular biology and its applicable methods.

Genetic engineering or recombinant DNA technology is related to procedures that provide a possibility to select different and desirable parts of DNA. This means selection of genes from any types of cells, separation, manipulation and their mass production. Then put them within bacteria or ferments and extract their products to use them for treatment and correction of defects of some vital functions. By this way many of complex and unknown life mechanisms were discovered and these procedures could be useful for fighting against genetic disorders and incurable diseases. In the other hand there is a risk of abusing of genetic manipulation. Thus there should be strict regulation to prevent the dangerous consequences of this matter.

Acquired immunodeficiency syndrome (AIDS) gradually showed itself since 1970 and was recognized in 1981 and Barré-Sinoussi and Montagnier isolated its viral agent in 1983. This is an incurable disease for present time and millions of people are infected and many thousands of them are dying each year (5, 6, 20).

Nobody but God knows the world destiny in third millennium. Whether man will continue war, quarrelsomeness, destroying environment, annihilating plants, jungle's and animal, etc ...

We are looking forward to reduce these problems that were specially dominant in the previous century. Certainly the human average life expectancy will increase and world's population particularly in underdeveloped countries will get an accelerating trend. I wish the people of these countries come to themselves and blend their tradition and previous ideality with modern science to control the population with reasonable limits and not destroy the

nature savagely and preserve the environments for future generation.

The third world will be depended on biological and industrial fields day after day regarding the accelerated rhythm of new technology, thus if we do not make an effort honestly, we will fail to gain.

The people of third world should be more cautious in using their limited natural resources. They should acquire knowledge and experiences of new science and technology. Thus they will be able to decrease their dependency to the other countries and obtain more scientific and industrial freedom according to their natural resources.

Acknowledgements

The autor would like to thank Dr. I. Nowrouzian, Dr. H. Keyvanfar, Dr. A. Ali Akbarzada, Mrs. M. Massah and Miss M. Mohaqeq Rad for their assistance.

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پزشکی در هزاره‌ها

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انسان از وقتی که اندیشه را پشتیبان خود قرار داد و به خرد ناب روی آورد به چاره‌جویی بیماریها در خویشتن و حیوانات اهلی‌شده پرداخت. این آغاز پزشکی است که همراه با آغاز تفکر بشر است. در این مقاله به ذکر چند کشف بزرگ پزشکی بویژه در هزاره دوم میلادی پرداخته و آرزوهایی را برای هزاره سوم بیان می‌کنیم. مهمترین بنیان پزشکی کهن جهان در نیمه دوم هزاره پیش از میلاد تا ابتدای ربع آخر هزاره دوم میلادی، نظریات چهار مایه (اخلاط) و چهار سرشت که به‌وسیله بقراط (۴۶۰-۳۷۵ پیش از میلاد) و بعدها جالینوس (۲۰۱-۱۳۱ م) بیان شد و بعدها توسط ابن‌سینا به خوبی تشریح شد و پزشکی جهان را زیر سلطه خود گرفت. نجیب‌الدین سمرقندی، پزشک بندگی ایرانی (فوت ۶۱۸ هـ/ق ۱۲۲۱ م) اولین کسی که به این گونه نظریات توجه نداشت. از قرن هجدهم به بعد خصوصاً با پژوهشهای ارزنده لوئی پاستور (ف ۱۸۹۵) و تعیین رابطه علت و معلولی بین بیماریها و میکروبه‌ها نظریات ارکانی و مزاجی، منسوخ شد. ابن‌نفیس قرشی (۶۸۷ هـ/ق ۱۲۸۸ م) پزشک بزرگ ایرانی‌الاصول کاشف اصلی گردش کوچک خون است و همین کشف بزرگ را میخائیل سروتوس در ۱۵۲۰ م عیناً در ارش بیان نمود. ابن‌الف کترکی (۱۳۳۶/۶۸۵ م) جراح بزرگ مسیحی اردنی مویرگهای خونی را کشف کرد و مالپیگی (۱۶۹۴) با استفاده از میکروسکوپ همان کار را بیان کرد. محمدبن زکریای رازی (۳۱۲ هـ/ق ۹۲۵ م) برای اولین بار در جهان در زمینه بیماریهای عفونی نظریه تخمیری را بیان کرد و هزار سال بعد پاستور نظریه اصلی میکروبی را به خوبی بیان کرد. البته قبلاً لیدن هوک (۱۷۲۳ م) با میکروسکوپ ساده خود میکروبه‌ها و یاخته‌های خونی را کشف کرده بود. اسپالاتزانی و پاستور تولیدمثل خودبخودی را مطرود شناختند و این سد راه علم را شکستند. تحقیقات پاستور و ربرت کخ (۱۹۱۰) بسیاری از باکتریهای بیماریزا را شناختند و علم میکروبی‌شناسی و ویروس‌شناسی پایه‌گذاری شد. محمدبن زکریای رازی کاشف آزری است و ابوعلی سینا (۴۲۸ هـ/ق ۱۰۳۷ م) در کتاب قانون نظریه‌ای را درباره درمان هارگزیدگان بیان کرد که به نوعی نظریه واکسیناسیون است. ابوریحان بیرونی (۴۴۰ هـ/ق ۱۰۴۸ م) به نوعی فرضیه تولید پادتن را بیان کرد. ادوارد جنر در ۱۷۸۹ م/۱۲۱۳ هـ ق به‌وسیله تلقیح آبله کاری، انسان را در برابر آبله ایمن کرد و پاستور پس از کشف تأثیر باکتریهای تخفیف‌حده‌یافته در ایجاد ایمنی، این شیوه را واکسیناسیون نامید. کابات و تیزلیوس حدود ۹۰۰ سال پس از مرگ بیرونی، پادتنها را به‌طور بنیانی کشف کردند دانش ایمنی پایه‌ای محکم از بیولوژی مولکولی گرفت و همه ساله جان عزیز دهها میلیون نفر را نجات می‌دهد. سرانجام، فلمینگ در اواخر نیمه اول قرن بیستم پنی‌سیلین را کشف کرد و در پی آن آنتی‌بیوتیکها یکی پس از دیگری شناخته شدند و آرزوی هزاران ساله بشر برای سرکوب بیماریهای واگیر به آستانه تحقق رسید ولی مقاومت‌های میکروبی در این کار، خلل ایجاد کرد. در قرن بیستم بنیانهای ژنتیک در باکتریها و سایر موجودات شناخته شد و DNA به‌عنوان محل خاص سرشتی (ژنتیک) مشخص شد. مهندسی ژنتیک شیوه نوینی است که جهان دانش را دگرگون کرد و نتایج شگرفتر آن در هزاره سوم در انتظار بشر است. AIDS در اواخر قرن بیستم شناخته شد و روز بروز قربانیهای بیشتری می‌گیرد تا در هزاره سوم چه کند. بیماریهای حیوانی نیز در سده‌های نوزدهم و بیستم بهتر شناخته شد و در بسیاری از نقاط جهان برخی از آنها را تحت کنترل در آوردند و برخی را ریشه‌کن کردند، اما هنوز در جهان سوم از گزند آنها در امان نیستیم. هیچکس نمی‌داند سرنوشت جهان در این هزاره جدید چه خواهد شد. اما اتکاء به دانش و وارستگی نویدهای خوبی برای بشر می‌دهد. با آهنگ سریع فن‌آوریهای جدید، در زمینه‌های زیستی و صنعتی، جهان سوم روزبه‌روز وابسته‌تر می‌شود. باید به خود اطمینان و با کسب دانشهای جدید به‌طور بنیانی، کوشش فراوان و کم‌کردن اتکاء به منابع زیرزمینی هویت جهانی، ملی و علمی خویش را زنده نگه داریم.

واژه‌های کلیدی : طب، هزاره‌ها، تاریخ پزشکی.

