

EDITORIAL

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Challenges and Hopes of the 21st Century

Wyzwania i nadzieje XXI wieku

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Streszczenie

Ziemię zamieszkuje około 600 milionów ludzi, którzy ukończyli 60 lat. W 2150 r. ludzi w tym wieku będzie prawdopodobnie 3 miliardy. Grupa ta stanowi obecnie 10% populacji, a w 2150 r. będzie to już 30%. Istotnie zmieni się procentowy udział ludności zamieszkującej poszczególne kontynenty. W 1995 r. ludność afrykańska stanowiła 12% ogólnej populacji świata, w 2150 r. będzie to prawdopodobnie 24%. Zmniejszy się liczba ludności zamieszkującej Europę (z 13% do 5%) i Chiny (z 22% do 14%). Przewiduje się, że w 2020 r. najczęstszą chorobą będzie choroba niedokrwienna serca, a następnie odpowiednio: depresja, urazy na skutek wypadków drogowych, choroby naczyniowo-mózgowe, rozedma płuc, infekcje układu oddechowego, gruźlica, okaleczenia wojenne, biegunki, AIDS, uszkodzenia płodu. Analizując dane, trzeba jednak podkreślić, że w grupie chorób niezakaźnych w ciągu tych 30 lat największy przyrost liczby chorych dotyczy: chorób nowotworowych, psychicznych, układu krążenia i przewlekłych układu oddechowego. Z pewnością mamy podstawy, aby twierdzić, że niezwykle szybki postęp – tak jak to się dzieje do tej pory – odnotują w XXI w. nauki biologiczne. „Będziemy musieli przywyknąć do tego, że niektórzy z naszych przyjaciół będą zaprojektowani genetycznie” – przewiduje Michio Kaku, znany amerykański fizyk, próbujący przewidzieć, co nas czeka w XXI w. Twierdzi, że „będziemy w stanie ożywiać to, co nieożywione i nadawać życiu formę zgodną z naszym wyobrażeniem”. Co jednak będzie, jeśli za pomocą genetyki zdołamy pokonać nowotwory, choroby układu krążenia i wiele innych? Natura nie znosi próżni. Z pewnością powstaną nowe choroby, o istnieniu których nawet jeszcze nie wiemy. Prognozy dotyczące długości ludzkiego życia mogą więc okazać się błędne. Opierają się bowiem na wynikach z ostatnich lat. Trudno przewidzieć, czy w ciągu kilkudziesięciu lat nie wybuchnie nieprzewidywana epidemia, czy nie zostaniemy zaatakowani przez nowe wirusy. Wyjątkowo dobrze obecną sytuację określają i wskazują przyczynę naszych lęków następujące słowa: „Świat, jaki obecnie powstaje, wzdycha jeszcze do resztek tego, co się teraz rozpada. A w czasie gwałtownego zamieszania nikt nie może powiedzieć, ile ze starych instytucji i obyczajów powstanie, ile zaś zginie bez śladu”. Tę diagnozę zapisał Alexis de Tocqueville w 1840 r. (*Adv Clin Exp Med* 2006, 14, 6, 1137–1143).

Słowa kluczowe: wyzwania, nadzieje, medycyna XXI wieku.

Charles Duell, the head of the Federal Office of the Patent USA, in 1899, expecting inventions of the 20th century explicitly said: “Everything what it is possible to find was already found”. Wilbur Wright, the pioneer of aviation, in 1901 declared: “The man won’t be flying still through 50 closest years”. Wilbur committed with the brother Orville of the first flight with the engine aeroplane of the own structure in 1903. Henry Hertz, the discoverer of radio waves forecast by J. C. Maxwell, congratulating him on scholars, in 1886 said: “Don’t mention it, this discovery doesn’t have littlest practical meaning”. However Albert Einstein when they already knew about huge energy being stuck in atoms, in 1930 stated:

“There is no smallest sign on the Earth which would show we will manage at any time to use the nuclear energy”. Einstein warned 10 years later than president of United States against the possibility of constructing the atom bomb by Nazi scholars, and in 1942 the first atomic reactor was already active in Chicago. Darryl F. Zanuck, the head of a film studio in Hollywood, in 1946, after watching the first TV programmes announced: “Television will stay on any market longer than half a year. People will be toing have had enough of fixing their eyes every evening into the tin of the plywood” [1].

The end of the 20th century showed how much they confused... Can we be equally brave to make

statements about what is about to happen in the 21st century?

In 1990 took the first place in the world unquestionably: infections of the respiratory system, diarrhoea, damage to the foetus, depression, ischemic heart disease, vascular-cerebral illness and further – tuberculosis, measles, grudges after road accidents, inborn defects, malaria, pulmonary emphysema. Health parameters also took turns in the world population during last two decades dramatically. Non-contagious illness is advancing to the first place in developing countries, so as depression, cardiovascular diseases which replaced traditional infections and the undernourishment and became the main cause of the disability and for the premature death. So developing countries soon will have to face with two problems: appearing epidemics and non-contagious illness. Infectious diseases still remain dangerous: AIDS,

malaria, tuberculosis and infections in children (Tab. 1)

About 600 million over 60-year-old people are inhabiting the Earth at the moment. In 2150 there will be probably 3 billions of them. This group is 10% of the population at the moment, and in 2150 it will be 30%. Percentage participation of the population inhabiting individual continents will change considerably. In 1995 the African population made 12% of the total population of world, in 2150 it will probably be 24%. Number of population inhabiting Europe will decrease – from 13% to 5% and China – from 22% to 14%.

In 2020 on the first place there will be ischaemic disease, on the second depression, and on the third grudges caused by road accidents and further – vasculo-cerebral illness, the pulmonary emphysema, infections of the respiratory system, tuberculosis, war bodily injuries, diarrhoea, AIDS,

Table 1. Diseases associated with the progress of civilization (“epidemics of the 21st century”)

Tabela 1. Choroby związane z rozwojem cywilizacji (epidemie XXI w.)

<p>Obesity In the last 10 years the number of obese persons rose from 200 to 300 million, 21% of cardiovascular diseases caused by the excess of kilogrammes, amongst 176 million of coincidences for diabetes in the world, positively 80% is a result of obesity [2]</p>
<p>Cardiovascular diseases Almost a million of persons are dying because of cardiovascular diseases annually in the USA, 150.000 of persons are dying of this reason in Poland annually [3]</p>
<p>Hypertension In 8.5 millions of adult Poles the condition is not treated, 12% is effective scarcely [4]</p>
<p>Diabetes In 2020 according to WHO there will be about 300 millions deaths for diabetes in the world [5]</p>
<p>Cancers Malignant tumours were the cause of 12% of around 56 millions of deaths in the world in 2000. There were noted 10 millions of new cases. They are predicting that there will be 15 millions of new cases of malignant tumours in 2020 [6]</p>
<p>Bioterrorism Global risk from 11th of September 2001 was confirmed by attempts on 11th of March 2002 in Madrid and 7th of July 2005 in London</p>
<p>Demyelination diseases of CNS Among others: Alzheimer’s disease – in Poland 200 000 ill, in the world 15 millions, and will develop in every fifth person in the retirement age in 2020 [7]</p>
<p>Infectious diseases We are still almost helpless towards the epidemic of viral illness. 40 millions people disappeared since the beginning of the 20th century due to flu virus [8]. 4.6 bln of dollars are spent in the USA on influenza and its complications treating every year. 42 million of people are living and breathe HIV in the world with the virus, including 3.2 millions of children up to 15 years of age. By 2020 according to UNAIDS specialists, there will be at least 68 million deaths due to AIDS. 3.1 millions died last year [9]. SARS, the new illness of the 21st century, is dangerous. It spreads worldwide attacking over 3500 persons every months. The effective method of treating the disease is still missing [10]</p>
<p>Influenza Drugs blocking the activity of neuraminidase were worked out – zanamivir and oseltamivir. Similar research are carried out today, with the purpose of finding the similar permanent fragment in different types of fast mutating viruses, including HIV and SARS [8–10]</p>
<p>Cancers Hopes are put in so-called “intelligent drugs” (attacking only cancerous cells), cancer therapy using certain amounts (of quantum dots), microchips, and diagnostics using pills early detecting cancers [11]</p>

damage to the foetus. Basing on global data, however, it must be underlined that in the group of non-contagious illness in the next 30 years the biggest growth in the number will be noted in: cancers, psychological illness, cardiovascular diseases and chronic illnesses of the respiratory system.

Certainly we have some reasons to claim that unusually fast progress – as it is happening so far – will take place in life sciences in the 21st century. “We will have to become accustomed to the fact that some of our friends will be designed genetically” – Michio Kaku, the renown American physicist, tried to predict what we are facing in the 21st century. He claimed that “we will be able to revive it, every inanimate and to grant the form in accordance with our idea of living” [1].

As everybody knows, already in 1999 American biologist Craig Venter declared that “we are able to build the living organism from dead organic elements, we know how to breathe into not living”, and in 2002 managed to make the year syntheses of the virus of deceased elements [1].

Laboratories enabling parents will come into existence “designing” healthy and beautiful children. We know that controlling genes is possible today and the scope of this inspectorate is increasing constantly. One cannot deny that it is very desirable from a point of view of medicine: in the fight against illness and aging. So, from the perspective of ill people and the elderly, it is road which cannot be allowed to leave and both progress in manipulating genes is inevitable and it will be coming faster and faster [50]. Correcting the appearance, designing looks and features craved in reliable professions will become also possible (e.g. athletes, soldiers) [1].

It is possible as a consolation to state that serious numerous illness will stop very shortly being, until now fatal, and in any case incurable. For example illness of Alzheimer, Parkinson, multiple sclerosis, diseases of the cardiovascular system, AIDS and the majority of cancers. Also numerous infectious diseases will disappear. But probably new, today unknown, diseases will arise. Luckily, effective methods of preventing and treating will develop unusually, among others, tissue culture of organs of own stem cells, as well as drugs produced by genetically changed animals and plants [1].

Of course there is hope in genetics as the magic key to many illness. Genetic therapy will let the impossibility of medicine defeat the border. Establishing risk groups and early diagnosing cancer will let treat the disease even before the first symptoms appear (e.g. in cystic fibrosis, Hodgkin’s disease, lymphoma, colon cancer, breast cancer, osteoporosis or rheumatoid diseases). It is one of the most realistic aspects of

genetic therapy. It has also application in the control of the graft rejection and also in process of blood vessels restenosis [12–14].

A lot of hopes are put in the research on drugs that will be able to treat infections of bacterial, viral and fungal origin. These defensins consist of several dozen of amino acids appropriately localized in space. Worldwide research on using them in bacterial and viral infections including HIV has been carried out for a few years. Defensins naturally support the immune system in most of organisms. Their action is to adhere to a microorganism what inhibits multiplying of bacteria or viruses and the organism has a chance to induce phagocytosis by the reticulo-epithelial system. The defensins also dissolve outer envelope of the microorganism they has adhered to and destroy it this way. The research on these drugs is intensive and some of them are tested in treatment of AIDS patients. The trials are carried out on drugs from this group to treat infection caused by herpes viruses [17].

A lot of hopes in preventing cancer are put in vaccines whose target is to prevent the emerging and progress of a tumor. The research in this area is advanced and probably in a few years’ time the vaccine that protects women from cervical carcinoma will be worked out. The most common cause of the tumor is human papilloma virus (HPV). Cervical carcinoma is one of the most frequent causes of death among women, and thus introducing the vaccine to the compulsory schedule of vaccination might protect women against this tumor. Cervical carcinoma is the second most frequent cause of death among women worldwide and the most frequent in the developing countries.

Research on this sort of vaccines against other viruses that are thought to be the cause of infections leading to tumor development is being carried out. For example, HTLV-1 virus induces some types of leukemia and lymphoma, Epstein Barr virus favors nasal and pharyngeal tumors, Burkitt’s lymphoma and some kinds of non-Hodgkin lymphomas. HHV-8 causes Kaposi’s sarcoma [18].

A lot of hopes are put in vaccines whose target is to control tobacco addiction. The vaccine stimulates producing antibodies which bind nicotine in blood serum before it has got to the brain. The second phase of the clinical trials has finished and the results are very promising. Over 33% of patients stopped smoking or smoked 2–4 cigarettes a day. Widespread use of the vaccine may help control epidemic of pulmonary carcinoma [19–20].

We are waiting for the day when it would be possible to give the appropriate dose of drug at the right time, into any place of the body, in the way

assuring selectivity and effectiveness of the therapy. They will be “drugs to the measure” well adapted for real needs and characteristics of the organism. 37 out of about 45 genes participating in the metabolism of drugs differs at individual nations and ethnic groups [11].

In the “tailor-made” drug administration, a patient’s genotype test will play an important role in the near future. It must be tested whether the patient should take chosen drug or not. Results of research showed that genetic differences in people population influence risk of some diseases and a patient’s reaction to the drug. Metabolism in hepatic cells depends on enzymes produced by P-450 cytochrome. Their role is metabolism of various substances including drugs. Reaction to the drug can be estimated if one knows composition of these enzymes. Hyperactivity of some of them is responsible for lack of therapeutic effect of antidepressants used by many Africans as they are metabolized quickly. For example, codeine is rapidly metabolized into analgesic morphine in patients from Africa. Hyperactive genes, which are found in inhabitants of some regions of the world where food toxins occur abundantly, are the cause of the increasing of drug doses or changing in the treatment as the organism metabolizes it too quickly in comparison with an average dose and one cannot achieve therapeutic effect [11].

Medicine will handle many illnesses with new drugs, also better and better standards of the medical conduct will cause that people would live longer in many areas of the world. According to forecasts, the medium longevity of the woman will increase from 79 to 88 years in 2150 and longevity of the man to 83 years. It is not distant perspective.

Ancient structure of societies will be changed practically worldwide (except for India and a few countries of third world). Number of elderly people will increase. It is a brand new challenge for medicine. This period of life of the man generates the biggest costs of treatment after all. According to forecasts, we will be fit and functional then, i.e. not-requiring full-time medical care.

A number of patients who saved their life thanks to transplants of the liver, kidneys, the heart, lungs is growing and therefore our hope is “husbandry” of organs for transplants, with xenogenic transplantation (thanks to the genetic engineering a domesticated pig is supposed to be the animal that will be in near future a bank of organs which will be used as transplants in the man) [24]. Prostheses as excellent as healthy limbs in the future and organs are being tested at present: Dextra (the first electronic prosthesis of the hand), C-LEG (intelligent prosthesis of the leg) and

Abiocor (the first entirely internal artificial heart) [25, 26].

Stimulators of brain were used as part of clinical tests worldwide within the last decade in 15 000 patients with Parkinson’s disease and different neurological diseases (in Poland 20 for patients). It will be possible to use stimulators of deep structures of the brain in treating epilepsy disease, dystonia, advanced neuroses [27].

Over 40 000 children and adults use colcheca implants worldwide. New technology will provide greater comfort while using them. Implants will enable the inner ear to hear in 80% of deaf patients. Retina implants and the system of the retina projection (VRD) – these are future methods of treating the blindness disease [28].

We are approaching practical applications of tissue stem cells faster and faster but research on embryonic stem cells are very slowly progressing due to serious ethical controversies. It has huge advantages: transplants of own cells are not rejected by the immunological system, whereas the indirect stage of “husbandry” enables to multiply them outside the system as well as to take genetic modifications, if it was necessary [1].

Soon a special technique of harvesting organs from a small piece of tissue provided by needle biopsy in laboratory conditions will be elaborated. The biopsy specimen cells can multiply in laboratory conditions (every cell includes information of the organ it originates in) and this way replicate the organ grown in the incubator and transplant it to the patient. The therapy will be exceptionally important for children as the transplanted organ, while growing along with the recipient, would be recognized as their own by their immune system. Today, in laboratory shelters smooth, skeletal muscles and cardiac muscle tissue are harvested [29–34].

There are reports today that leukocytes can be transformed into stem cells. However, it is a preliminary report by scientific workers from the English company TriStem but if one could provide stem cells this way it would be possible to regenerate damaged organs and cure cardiopathy and diseases of the nervous system more effectively. Although the research is in the phase of advanced experiments on animals, the hopes are put in the elaborated technique of providing stem cells [35].

Transforming the synaptic microchip will still take a few years into the surrogate for the retina certainly. The present microchip contains only four exits, while microchip of the artificial retina needs thousands of them so that it could imitate its function [36].

In future medicine, appropriately designed clothes will play an important role. Owing to nanotechnology they will help to keep stable body

temperature. Nanomolecules will accumulate thermal energy from the body in case of too high temperature and store it in order to release it and warm the body in case of too low temperature. In pieces of the garment there will be special devices for measuring multiple parameters of the body, e.g. blood pressure, pulse, body temperature, metabolism, glucose level in blood serum, ECG, natremia, kalemia and oxemia. The information will be sent on via Internet to specialists for permanent, twenty-for-hour analysis [37–39]

Swiss criminologists and court doctors managed to work out comprehensive method of noninvasive examining bodies of victims of accidents and crimes using newest achievements in radiology. As many as over 100 virtual post-mortem examinations were carried in Bern in the Institute of the Forensic Medicine of the University. Court doctor supervising the virtopsy plan Michael Thali presented the idea and results of this multidisciplinary cooperation on an annual convention of American Association of Radiologists at the beginning of December 2003. “Virtopsy” determines the size and character of changes examining with the technique of magnetic nuclear resonance, concerning the chosen fragment of the tissue, muscles or the organ combination. The computer reconstructs digitally the image of given area basing on these two examinations. Measuring the level of metabolites in tissues after death with the use of MRI spectroscopy enables to establish the time of the death and the three-dimensional scan of the surface of the body records all changes (e.g. gunshot wounds) and simulates the course of the injury. The virtual post-mortem examination permits to respect customs of some cultures, besides, some people do not accept the post-mortem examination and the family often disagrees. Data is stored in agreement with the PACS protocol (Picture Archiving and Telecommunication System) and they can be sent on. Thali realizes that such an examination is expensive and it cannot replace classical posthumous examination entirely [40].

The most will happen in the technique especially these carrying the prefix “tele”, meaning “working on the distance”. Electronic networks will be more and more useful in everyday life. In the sphere “tele” people will deal with machines, and there will be close integration of virtual and real world [1]. The network soon will become global in any case – as equal if not dominating, irreplaceable, helpful, intelligent, fast partner of people [1].

In the future, diagnostics, therapy and the monitoring will be provided for the patient online. Surgeon’s robots will be used universally. Telemedicine, i.e. exchange of medical information in

the distance, including voice, the image, medical data, and the telesurgery, i.e. the operation to the distance, consisting in instructing the surgeon’s robot, are developing [41].

We will learn about new peculiarities of bioengineering: genetic, embryonic. Finally there will be laser treatment in neuroengineering therapy, far more widely, and in diagnostics DNA depicting. Studying memory, studying dreams, emotion, speech will bring new data. Perhaps new possibilities of manipulating these processes, supporting them will appear. A new sphere of examinations will unfold – proteomy (from proteom – team of proteins of the given organism). Proteins as the material of our bodies, the carrier of the life, they were undervalued until now and their biological role is far more important than it was supposed to be in court until now. Proteomy will open the new chapter in biology – a view of life and the human organism will change again.

Nanotechnology, i.e. miniaturization, will bring brand new possibilities to many devices, including intelligent robots of molecular sizes. Medicine will benefit from it probably the most: nanomachine, cleaning our arteries and repairing injured organs, nanoprocessors, supporting different positions of the organism including senses and functions of the brain [1].

Certain elements of nanomedicine are already applicable today. The miniature device is already produced and applied in the human body. They created microcamera which sends the image of the inside over after swallowing down the digestive tract.

Nanomedicine would enable to treat cancer disease by destroying cancerous cells without damage to surrounding tissues. The injection of covered with antibodies, acting nanomolecules will let uncover the presence of viruses in tissues of the patient, like tiny magnets, while examining with the MRI method. The pill will free the army of nanorobots whose task is to detect, diagnose and heal every illness even before the patient feels any signs of it. The process of treatment will take place on the level of isolated cells.

Conceptions behind creating nanodevices already exist: quantum dots – very small crystals about the diameter c 5 nm which can be lead easily into the interior of organism; dendromers – sizes of the molecule of the protein; devices consisting of isolated atoms [42–45].

Nanomedicine will find application in destroying neoplastic cells and metastasis without damaging surrounding tissues. It will then make a selective and guided therapy. “Quantum dots” are very small crystals of 5 nm in diameter which are introduced into the organism and bond with proper flu-

orescent chemical markers. When they bind with a neoplastic cell they start to emit light and mark precisely damaged cells or fragments of tissue.

In the near future one hopes that the “quantum dots”, owing to the light energy, will not only emit the light, marking the damaged cells and tissues, but heating up, they will destroy damaged cells selectively, leaving healthy cells and tissues intact. Using dendromers, whose diameter is similar to “quantum dots”, can be an enormous progress in medicine because they have unique potential to transport molecules of a drug and deliver it to the damaged cells and tissues. Dendromers which can be transported with the drug into the interior of a cell will also release proper dose of the drug in the required place under the stimulation of light [42–45].

Owing to nanotechnology one may hope that in 10 or 20 years we can produce computers for conducting complicated analyses inside the body of a patient. Those “genetic” computers will be constructed with DNA and enzymes and can detect prostate and pulmonary cancer basing on changes

in genes activity. But now the research is being carried out in the phase of *in vitro* experiments [42–45].

What if we, however, will manage to overcome cancers, cardiovascular diseases genetically and many others? Nature abhors a vacuum. Certainly new illnesses will arise that we cannot even imagine. Forecasts concerning the length of the human life may so show themselves incorrect as they are based on results from recent years. It is difficult to predict whether an unexpected epidemic breaks out in several dozens of years or we are infected by new viruses.

The present situation is defined exceptionally well and the following words point the cause of our fears out: “World which is coming into existence at present is sighing still to remains of what is breaking down now. And nobody can during the violent confusion say, loam will come into existence from old institutions and customs, loam whereas will die without trace“. This diagnosis wrote Alexis de Tocqueville in 1840 [50].

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