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TRANSPLANTOLOGY - A REQUIREMENT OF THE TIME OR THE NEXT EVOLUTIONARY STEP OF HIGH-TECH SURGERY?

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Abstract.

This article presents a brief outline of the history of transplantation service in the Republic of Uzbekistan, which originated in the kidney transplantation Center Academy of Sciences of Uzbekistan. In article highlighted the role of outstanding scientists of Uzbekistan, their works and efforts aimed on creating a separate direction of clinical and scientific medicine. In article presents the achievements of the scientific school of U.A. Aripov and V.V. Vakhidov academicians of the Academy of Sciences of the Republic of Uzbekistan. It reflects the ups and downs of the national service of transplantation nephrology, as well as the birth of the national school of kidney and liver transplantation, held in the State Institution "Republican Specialized Scientific and Practical Medical Center of Surgery (RSSPMCS) named after Academician V. Vakhidov" led by Academician F.G. Nazirov and gave the "second breath" of the national transplant school. Special attention was paid to the current problems of domestic transplantology, there were reflected the moral, ethical and regulatory issues that accompany this scientific and clinical direction, the latest research conducted in the world in this way was indicated. Article presented results of kidney and liver transplantation in Uzbekistan and outlined prospects for further scientific and clinical directions.

Key words: transplantation, kidney, liver, transplant history, living related donors, immunosuppressive therapy.

Innovative and exciting advances in clinical science in the field of solid organ transplantation are constantly being realized in the form of research results, clinical trials, international conferences, consensus conferences, new technologies and discoveries. Salvadori M, Bertoni E. (2014) reviewed the full range of news in the field of transplantology confirmed up to 2013. For each organ, trends in numbers and survival were reviewed, as well as the most pressing issues such as organ preservation, ischemia-reperfusion injury, and rejection, with particular attention to antibody-mediated rejection affecting all solid organs. It has been found that the number and frequency of transplants vary in different countries of the world for various reasons:

(1) Differences in the frequency of target organ diseases. For example, the incidence of end stage renal disease (ESRD) in Norway in 2009 was one third of the incidence in the United States. However, kidney transplant rates were similar in 2010 in Norway and the US, probably due to the very high living donor activity that is common in Norway;

(2) Socio-economic factors [8].

(3) Cultural differences. An example is Japan, with a lower rate of kidney transplants;

(4) Carefulness of transplant reporting, which varies by country. Worldwide, the use of living kidney

donors varies widely, from less than 10% to more than 75%. Liver transplant rates have increased by more than 10% in several countries and decreased in very few countries. Lung transplant rates have remained stable over the past 5 years. Heart transplant rates have changed little in most countries.

Transplantology is one of the youngest and most innovative areas of medicine. Despite the fact that in the history of medicine there are many references to attempts to transplant organs and tissues of a healthy person to a sick person, the actual beginning of scientific transplantology dates back to the 19th century, when the results of experimental and clinical observations of the Italian physiologist Giuseppe Baronio, who in 1804 carried out skin transplantation in a sheep, were published. In 1900, Karl Landsteiner established the presence of blood groups in a person, the principles of blood transfusion from person to person were developed, which formed the basis for the selection of a donor organ in our time. In 1933, the world's first transplantation of a vital organ to a human was performed by Yu.Yu. Voronoy. Taking a kidney from a corpse, he transplanted it into a woman who was dying of mercury poisoning. Technically, the operation was successful, but the kidney did not



function, and the patient died two days later. The first successful kidney transplant was performed in 1954 (Boston, USA) by the famous American surgeon Joseph Edward Murray, who transplanted a kidney to a 23-year-old patient from his twin brother.

The talented Soviet experimental scientist V.P. Demikhov, who made an invaluable contribution to modern medicine, and in particular to transplantology. In 1946, for the first time in the world, he performed a heterotopic heart transplant into the thoracic cavity of a dog and the world's first transplant of the heart-lung complex, in 1947 - the world's first transplant of an isolated lung, in 1948 he began experiments on liver transplantation, and in 1951 he transplanted a dog donor heart, proving that operations of this kind are possible. In 1960 V.P. Demikhov published the monograph "Transplantation of Vital Organs in the Experiment", which for a long time remained the only manual on transplantation in the world.

The first orthotopic liver transplantation in the clinic was undertaken on March 1, 1963 by a group of American surgeons led by Thomas Starzl (Denver, USA). A 3-year-old child with biliary atresia received a liver transplant from a 5-year-old child who died of a brain tumor. The operation was technically successful, but 5 hours later the child died from complications associated with coagulopathy. Only in 1968 T. Starzl reported the first patient to survive a liver transplant.

For the first time in the world, a successful human heart transplant was performed in South Africa by K.N. Bernard in 1967.

Significant milestones in the development of transplantology in Uzbekistan were the works of outstanding doctors of the 20th century. The history of kidney transplantation in Uzbekistan is closely connected with the name of Academician of the Academy of Sciences of the Republic of Uzbekistan Uktam Aripovich Aripov. In 1964, Ukhtam Aripov, becoming the first deputy minister of health of Uzbekistan, made great efforts to develop specialized medical services, train highly qualified scientific and pedagogical personnel that met the needs of the Republic. Being a polyvalent surgeon performing the most complex operations, he created all the conditions for a comprehensive study of topical problems of abdominal surgery and transplantology. From 1971 to 1984, Ukhtam Aripov, being the rector of the Tashkent State Medical Institute, organized a problematic research

laboratory to overcome tissue incompatibility of transplanted organs and tissues, he was also appointed to the position of head of the first kidney transplant center in Central Asia with a hemodialysis laboratory. On the basis of this center, he formed a team of young talented like-minded scientists, uniting doctors of various specialties. On the basis of the center, the problems of post-transplantation immunity, the creation of domestic immunosuppressants were developed, systems of clinical transplantation and treatment of patients with CRF were organized. As a result, on September 14, 1972, the first kidney transplant was performed in Uzbekistan in a patient with end-stage CRF [1].

In 1974, Ukhtam Aripov was elected an academician of the Academy of Sciences of the Republic of Uzbekistan, and in 1978 - an honorary doctor of the Budapest Medical University. In 1983, for the development and introduction into clinical practice of new improved methods of treating patients with chronic renal failure, the creation of domestic drugs, academician Ukhtam Aripov and a number of his employees were awarded the State Prize of Uzbekistan named after A. Beruniy in the field of science and technology. Thus, in 1972, on the basis of the Problem Research Laboratory for overcoming tissue incompatibility in organ and tissue transplantation of the Tashkent Order of the Red Banner of Labor of the State Medical Institute, the Republican Center for Kidney Transplantation was organized. This center was a medical, consultative, scientific and educational center for the treatment of patients with CRF [3].

The kidney transplantation center for 40 beds was located on the basis of the Clinical Hospital of the Ministry of Health of the Uzbek SSR. The work of the Center was headed by Academician Ukhtam Aripov and Professor N.P. Pack. Two senior and two junior researchers, 11 residents worked at the center. In addition, work at the center was carried out in close cooperation with the Republican Nephrological Center.

The senior researcher and head of the clinical group for kidney transplantation at the Tashkent Kidney Transplant Center was Pak Nikolai Petrovich - laureate of the State Prize in Science and Technology named after Beruniy of the Republic of Uzbekistan, Doctor of Medical Sciences, Professor, Academician of the International Academy of Sciences of Nature and Society, and Academician of the European Academy of Natural Sciences. Pak



N.P. for 19 years he was the chief specialist in hemodialysis and kidney transplantation of the Ministry of Health of the Republic of Uzbekistan. In addition, the initiative and scientific interest of Academician U.A. Aripov allowed to form their own scientific school, to nurture talented students.

Based on the results of the scientific activities of the above-mentioned scientists, materials were formed and subsequently presented regarding the complications of kidney transplantation in the clinic, the results of studying the toxicity of "medium molecules" in chronic renal failure, experimental studies of the mechanisms of action of a number of drugs considered as potential immunomodulators.

A separate contribution to the development of the direction was made by the doctor of the highest category Kholodova Evgenia Grigoryevna, who worked for more than 20 years as the head of the department of hemodialysis and rehabilitation of patients with transplanted organs in the Republican Clinical Hospital No. 1 in Tashkent (early the Kidney Transplant Center). For her excellent work as the head of the Center, she was awarded of the Order of Mekhnat Shukhrati.

During the existence of the center, the employees of the hemodialysis laboratory have introduced such progressive and economic forms of treatment of patients as the creation of various modifications of the imposition of arteriovenous fistulas, the transfer of some patients to outpatient hemodialysis, the widespread use of special methods of hemodialysis: diafiltration and hemosorption. The Kidney Collection and Preservation Group had a close relationship with the intensive care, traumatological and neurosurgical departments of the city hospitals, carried out the collection and conservation of kidneys for subsequent transplantation. The group of postoperative management of patients was directly involved in nursing patients after surgical interventions, issues of immunosuppressive therapy and prevention of its complications. The patients spent their first month after kidney transplantation in wards of increased sterility of the boxed type with a round-the-clock post of a doctor, nurse and nurse. The group of tissue typing and immunological control conducted an immunological study of potential recipients, dealt with the selection of donor-recipient pairs, and carried out postoperative monitoring of the effectiveness of immunosuppressive therapy.

With the direct assistance and participation of the staff of the Center, hemodialysis departments were

opened in Samarkand, Fergana, Andijan, Bukhara, Alma-Ata, Ashgabat, Dushanbe, Chimkent. The Center had a close relationship with the Alma-Ata Kidney Transplantation Center, with which the exchange of donor kidneys and information about recipients was carried out [3].

The Center provided advisory assistance in all regions of the republic, as well as in the regions of the neighboring republics of Central Asia. Annually, the employees of the Center provided up to 200 air ambulance calls. Scientific research by the staff of the Center was carried out according to a comprehensive plan to the task of the State Committee for Science and Technology under the Council of Ministers of the USSR, the Ministry of Health of the Uzbek SSR and the All-Union Scientific Council for Transplantation and the Creation of Artificial Organs.

One of the urgent problems of transplantology was the search for and introduction into clinical practice of new immunosuppressive drugs. The accumulated experience allowed the national transplantation school not only to study the action of pharmaceutical preparations and their influence on the mechanisms of immunosuppression, but also to synthesize their own. So in the 80s, the Institute of Bioorganic Chemistry of the Academy of Sciences of the Uzbek SSR already had 10 names of its own immunosuppressants in its arsenal. In turn, the drugs batriden and megosyn were selected for clinical study, the first of which, having passed clinical testing, was approved for medical use as an immunosuppressant in kidney transplants and for clinical study in autoimmune diseases.

To solve the problems of prevention and treatment of complications of immunosuppressive therapy in patients after KT, the Kidney Transplantation Center, together with the Institute of Bioorganic Chemistry of the Academy of Sciences of the Uzbek SSR and the Laboratory of Physicochemical Research Methods of the Central Scientific Research Laboratory, studied the metabolic pathways of immunosuppressants, target organs for aggressive metabolites of these drugs, the search for possible protectors from side effects of immunosuppressants.

On the basis of the Tashkent Center for Kidney Transplantation, in 1977, a meeting of experts of members of the CMEA (Council for Mutual Economic Assistance) on the problems of KT was held, and in 1979, the All-Union Conference "Immunosuppression

in allotransplantation" was held. Separately, it should be noted the number of procedures performed, so if in the Center in 1972 2 TP were performed, and hemodialysis sessions were 300, then by 1981 the number of kidney transplants reached 227 (20 - 25 operations per year), and the number of hemodialysis was up to 25,500. The median survival rate at 6 months was 65%.

The center often visited by foreign delegations; there were connections with the Budapest Medical University (an agreement on scientific cooperation was signed), kidney transplant centers of the GDR, Poland and Czechoslovakia. During the period of operation of the Kidney Transplant Center, 358 kidney transplants performed. In 311 cases, cadaveric kidney transplantation, 47 patients underwent kidney transplantation from a living related donor.

Unfortunately, the adoption of the "Criminal Code of the Republic of Uzbekistan" in the new edition of 1994 significantly affected the entire kidney transplant service. Thus, the new law allowed the removal of organs from a corpse only with the permission of relatives or the lifetime consent of the deceased, which completely stopped kidney transplantation in our country.

Only in 2002, the Ministry of Health of the Republic of Uzbekistan issued an order to allow kidney transplantation from a living related donor, which launched a new program - lifetime donation. The first such operation was performed at the Kidney Transplantation Center (current Republican Clinical Hospital No. 1). However, already 4 years later, this order was withdrawn and surgical interventions of this kind stopped again. The current situation, due to the lack of regulatory support for the program, forced patients to seek help abroad.

Thus, as in other countries of the world, the formation of the organ and tissue transplantation service in Uzbekistan went through a series of difficult moments in its development. The difficult material, technical and political situation in the countries of the post-Soviet space in the late 80s and early 90s led to the complete loss of the previously created fundamental base and accumulated experience. Attempts to rehabilitate the transplant service faced the lack of clearly formulated legislative acts, a complex moral and ethical background, excluding organ transplantation from donors with "brain death".

Kidney transplantation

As is known, kidney transplantation (KT) is the only radical way to help patients suffering from chronic progressive kidney diseases. According to WHO, today the number of patients suffering from terminal kidney diseases in the world exceeds 4 million people, at the same time, the number of surgical interventions aimed at replacing an organ that has lost its function is steadily growing. With the improvement of surgical technique, as well as a more detailed understanding of the mechanisms of immunosuppression, KT allows achieving five- and ten-year survival equal to 90% and 74%, respectively (according to UNOS, USA) [14].

At the same time, the incidence of chronic progressive kidney diseases, leading to chronic renal failure (CRF) in its later stages, does not tend to decrease. In addition, due to the constantly expanding nosological range of diseases requiring KT, the shortage of donor organs is still an acute actual problem. In connection with the above, the use of kidney transplants from living related donors has acquired particular relevance. Immediate restoration of the function of the transplanted kidney and rare crises of rejection in related transplantation, in addition to the best immediate results, certainly make it possible to predict a higher long-term survival of grafts and patients than with cadaveric organ transplantation. This is associated not only with a greater degree of immunological compatibility of the donor and recipient, but is also largely determined by a reduction in the time of cold ischemia and, accordingly, a decrease in the severity of reperfusion injuries [2].

Closely related transplantation remained the only available option for large families in Uzbekistan. Repeated attempts by academician Vasit Vakhidovich Vakhidov, director of the country's leading center of surgery, to implement this direction were unsuccessful, more and more potential patients with the need for this type of surgical treatment continued to leave for foreign clinics. Only a decade later, his talented student, surgeon and public health organizer, Academician Feruz Gafurovich Nazirov, managed to move this problem forward. At the cost of his colossal efforts, transplantation in Uzbekistan has gained a "second wind". On the basis of the State Institution "Republican Scientific and Practical Medical Center for Surgery named after A.I. Academician V. Vakhidov, the organ transplantation program was not only reanimated, but also acquired



completely different features.

Specialized departments were created, in particular, the “Department of Vascular Surgery and Kidney Transplantation”, which is still headed by Professor Bakhritdinov Fazlitdin Shamsitdinovich. The material and technical base has been strengthened, retraining of personnel has been carried out in leading foreign clinics, the indications for surgical intervention have been expanded, and a solid foundation has been created for scientific work in an acutely relevant direction for the country. All of the above is reflected not only in an increase in the number of interventions performed, but also in a direct improvement in their quality. Transplantation began to be performed in patients with diabetes mellitus and other concomitant diseases that previously did not allow one to count on a favorable outcome of the intervention.

Thus, starting from 2010, in the State Institution “RSSPMCS named after. acad. V. Vakhidov” kidney transplantation operations were resumed, and in February 2018, after the draft law “on closely related kidney and liver lobe transplantation” was published, Academician F.G. Nazirov performed the first liver transplantation in the country from a living related donor. In addition, by the end of 2021, the number of kidney transplants in the State Institution “RSSPMCS named after. acad. V.Vakhidov” reached 540.

At the same time, not only new areas of clinical transplantation were created, but also already developed techniques were modified and improved. Thus, in 2015, the center performed the first kidney transplant using laparoscopic donor organ sampling.

Achieved in the State Institution “RSSPMCS named after. acad. V.Vakhidov” success not only showed safety, but also clearly demonstrated the need for further development of the transplant service in the country, being an incentive for further improvement of the legislative and regulatory framework. So, already in December 2019, amendments and additions were made to the draft law “on the procedure for closely related transplantation of a kidney and (or) liver lobe” significantly expanding the donor pool. Currently, in Uzbekistan, the removal of organs for transplantation is possible only from living donors who are relatives of the recipient, and with their voluntary consent. All patients with a transplanted kidney living in the Republic of Uzbekistan are under dispensary registration in the department of hemodialysis and

rehabilitation of patients with transplanted organs in the Republican Clinical Hospital No. 1 in Tashkent.

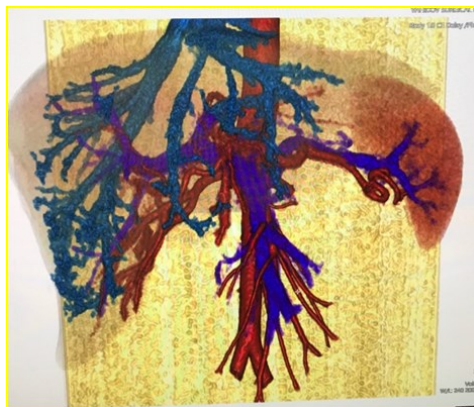
Additional opportunities in terms of the development of this direction, so in the future, the possibility of transplanting the heart and cardiopulmonary complex, pancreas and lungs is considered. In addition, organ and tissue transplantation has already begun performing in several medical and preventive centers in the country. Therefore, thanks to the efforts of Khadzhibaev A.M., since 2018, the kidney transplantation program has launched at emergency center, and the results achieved by the collective center correspond to leading international clinics.

Despite the progress made in the field of transplantation, a number of unresolved issues remain in the country. Among these, a special role occupied by the acute shortage of highly specialized specialists qualified in the field of transplantology. It has known that the transplantation service based not only on transplant surgeons; morphologists, immunologists, specialists in the field of interventional interventions, and many others are need for the successful implementation of the program. Thus, despite the work done, the development of this area of clinical medicine undeniably requires even greater efforts aimed at creating and strengthening a solid material and technical base of specialized departments, improving our own scientific and clinical school. In addition, one of the priority tasks considering the creation of a domestic transplant center, which allows not only to unite specialists of various profiles specializing in clinical transplantology, but also to significantly consolidate efforts aimed at developing the domestic transplant service.

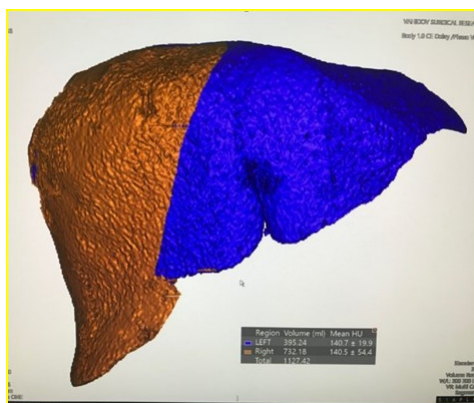
Thus, related kidney transplantation, which opened the era of clinical transplantation of vital organs in the last century, has now acquired a second wind. The prospects for kidney transplantation in Uzbekistan in the 21st century are associated with overcoming the ethical problems of organ transplantation, improving the tactical and technical aspects of transplantation, opening new transplantation centers and centers for the rehabilitation of patients after organ transplantation, which have all modern capabilities for examining and treating seriously ill patients.

Liver transplantation

The increasing number of operations performed every year (up to 30 thousand annually worldwide) is evidence of the recognition of liver transplantation as the method of choice. Once rightfully categorized as one of the most complex transplant surgeries over the past two decades, this operation has become a routine procedure in many centers around the world. The need for liver transplantation occurs annually in at least 20-40 people per 1 million people. The growing shortage of donor organs has led to the successful clinical implementation of alternative technologies: split transplantation, transplantation of liver fragments from a living donor, the use of organs from suboptimal post-mortem donors. Liver transplantation indicating for patients with irreversible, progressive liver damage, when there are no other effective methods of treatment. However, you should be aware that liver transplantation is a complex and difficult operation, during and after which there may be complications.



Intraparenchymal angioarchitecture and sectoral anatomy of the donor liver



Planned resection line

After graft sampling, taking into account the anatomical features of the vessels and biliary ducts

on the “Back table”: in three cases, additional reconstruction of the segmental hepatic veins (with a diameter of at least 6-8 mm) was performed using the Gortex prosthesis, in one case, the connection of the right hepatic vein and the additional segmental veins. In three cases, the presence of three biliary ducts was established, the diastasis between them was 2-3 mm, in connection with which the ducts were connected to each other.

During the reconstruction of the hepatic-caval anastomoses, fourteen patients underwent monovenous hepatic-caval anastomoses. In three cases, hepatic-caval anastomoses were performed after reconstruction of the hepatic veins using a PTFE graft.

All patients underwent standard porto-portal terminal-terminal anastomoses. Arterial reconstruction was performed with the imposition of direct anastomoses with the proper hepatic artery in 16 cases, with splenectomy in one case, and reduction of blood flow through the splenic artery by ligation in six cases (to prevent the Steal syndrome). In 1, an inverted splenic artery was used. In 9 cases, biliary reconstruction was performed with the imposition of biliary anastomoses, in 8 patients, the imposition of biliary-biliary anastomoses was performed.

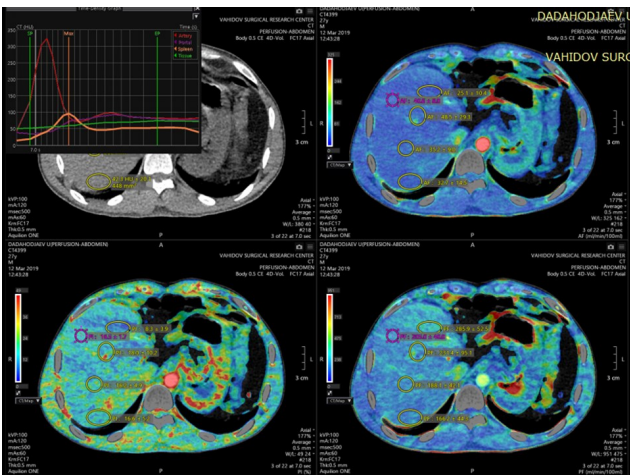
In the immediate postoperative period, complications were observed in 3 recipients in the area of the arterial basin of the anastomosed hepatic artery. The postoperative period was the most difficult in one recipient, in whom an inverted splenic artery was used for arterial reconstruction. On the 4th day, thrombosis of the arterial anastomosis developed. An endovascular intervention with recanalization, dilatation of anastomosed vessels, lysis of thrombotic masses, and complete restoration of blood flow was performed. However, the intervention was complicated by profuse intra-abdominal bleeding, relaparotomy - a solitary source of arterial bleeding was found at the site of the clip on the tributary of the splenic artery. Hemostasis.

In 2 cases, when applying an arterial anastomosis due to a discrepancy between the diameters of the arteries of the recipient and the donor, a sharp decrease in the arterial blood flow velocity was noted on the 1-2 day after the operation. Produced selective angiography of the hepatic artery with balloon dilatation of the anastomosis. The blood flow has been restored.

In 6 recipients, the following complications were observed in the long-term period: in 2 cases, after biliary-biliary reconstruction, the stricture at the level of the biliary-biliary anastomosis was resolved by endoscopic stenting, in 1 patient with a bigepatic anastomosis, a stricture formed only on one of the anastomoses with complete patency of the second anastomosis. With technical difficulties, endoscopic stenting was performed, 2 patients had prolonged bile leakage with the formation of an external biliary fistula, which closed spontaneously within 4 to 6 months.

After repeated attempts to stent the formed stricture in one patient, a year after transplantation, a second intervention with biliary reconstruction was performed - hepaticoenteroanastomosis was applied.

Introduction to the Center of Surgery named after acad. V. Vakhidov of such a high-tech operation as liver transplantation and our first experience of such a range of operations showed that related liver transplantation is a multi-stage surgical intervention, which is rightly considered the most difficult in abdominal surgery. It should also be noted the complexity and complexity of the problem, including medical, legal, ethical and economic issues that arise when performing related liver transplantation.



13 months after surgery - perfusion MSCT of the liver

What lies ahead for surgery? With the advent of new technologies, tissue engineering and regenerative medicine, many organs may receive an artificial equivalent: thanks to retinal implants, some blind people can visualize stimuli, an artificial heart can be offered in case of heart failure while waiting for a heart transplant. An artificial larynx allows laryngectomy patients to lead near-normal lives, while a diabetic can gain glycemic self-regulation

controlled by smartphones with an artificial device. Dialysis devices are becoming portable, as are oxygenation systems for end-stage respiratory failure [12]. Bright prospects are being explored or may appear in the near future. For a long time, research aimed at compensating for visceral insufficiency and the shortage of donor organs with artificial organs. Dialysis and oxygenation devices for end-stage respiratory failure are becoming portable. Good prospects exploring or may see light in the near future, but hindsight is not enough to assess the side effects, and the cost of these new devices is not negligible, even if the advent of 3D printers may reduce the sums.

Regenerative medicine technologies aiming at restoring and regenerating poorly functioning organs. One goal is to achieve a state without immunosuppression to improve quality of life, reduce complications and toxicity, and eliminate the cost of lifelong anti-rejection therapy. Innovative strategies include decellularization to fabricate cell-free scaffolds using as a matrix for organ production, 3D printing, and interspecies complementation of blastocysts. The future of organ bioengineering depends on further understanding of organogenesis, in vivo regeneration, regenerative immunology, and long-term monitoring of implanted bioengineered organs [7].

New technologies are rapidly changing traditional approaches to organ transplantation. In the modern era, key transplant issues include:

- (1) how best to individualize and possibly eliminate the need for lifelong immunosuppression
- (2) how to expand the pool of donors suitable for human transplantation [5].

Tolerogenic nanoparticles with regulatory molecules and donor antigens are able to influence the host's immune responses with great precision, which in some cases leads to donor-specific tolerance. Third, the CRISPR/Cas9 gene editing technology allows precise removal of immunogenic molecules while inserting the desired regulatory molecules. This technology is particularly useful in creating genetically engineered pigs for xenotransplantation to address the shortage of human organs. Together, these new technologies are enabling the transplant community to make major breakthroughs that will greatly advance transplant medicine. Tolerogenic nanoparticles with regulatory molecules and donor antigens are able to influence the host's immune responses with great precision,

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The creation of biobanks, together with high-throughput technologies such as genomics, transcriptomics and proteomics, has opened up new horizons in the discovery of biomarkers and the development of systems biology approaches to identify key pathways that can be used to improve the results of solid organ transplantation [9]. One of the main problems of organ donation has been the lack of access to large-scale, well-characterized materials to facilitate projects aimed at characterizing donor organ damage and identifying biomarkers. This could hamper organ donation research by preventing researchers from obtaining high quality materials with less preanalytical variability.

Bio-banking is not a new phenomenon. For many years researchers and clinicians, usually as part of academic institutions, have held collections of samples from research subjects [10, 15]. Over the last 30 years, but particularly since the implementation of legislation such as the Human Tissue Act 2006 in England, this has developed in to a more complex but refined procedure, involving larger collections including national bio-banks, such as the UK bio-bank, or disease and population specific bio-banks, such as that for prostate cancer [16]. An emerging area of science looking into sample quality, specimen handling and bio-banking infrastructure has emerged as a consequence [17]. Alongside this a number of important ethical and regulatory issues have emerged, specifically with regards to genetic information, obtaining samples and sample storage [11]. Accountability, anonymisation and data protection are also emerging as key areas for consideration for biobanking [6].

Immunological monitoring during organ transplantation basing mainly on the determination of laboratory parameters as surrogate markers of organ dysfunction. Structural damage caused by all reactivity can only be detected by invasive graft biopsy, so inevitable episodes of rejection are

diagnosed at an advanced stage. Beckmann JH, (2017) believes that new non-invasive specific markers are needed that will allow transplant doctors to identify rejection episodes at an earlier stage, at the molecular level [4]. Accurate identification of rejection episodes and establishment of operational tolerance allow early treatment or, accordingly, controlled cessation of immunosuppression. In addition, new predictive biological markers expecting to allow risk stratification before transplantation, which will affect organ allocation and immunosuppression regimens. New high-throughput screening methods can simultaneously examine hundreds of characteristics and generate specific biological signatures that can provide specific information about acute rejection, chronic dysfunction, as well as tolerability of surgery. Despite the fact that numerous studies and various publications report important advances in this area, almost no new biological marker introducing into clinical practice. However, new technologies such as genome, transcriptome, and proteome and metabolome analysis will make personalized transplant medicine possible, further improve long-term outcomes, and graft survival rates.

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