

Sketch of the Regenerative Surgery History

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Abstract.

This article gives an account of the basic halting places of the tissue grafting theory development. One has shown that the idea of the regenerative surgery appeared as a natural result of the tissue grafting elaboration. Transplantation in its evolution is distinguished by the author into the following historical landmarks: the substitutive graft surgery stage (N. I. Pirogov), the regenerative graft surgery stage (I.A. Golyanitski), the graft biostimulation stage (V.P. Filatov) and biological graft surgery.

Every stage has been briefly characterized taking into consideration the experience accumulated through experimental findings and clinical observation.

The Alloplant technology has proved to be a historically stipulated stage of home transplantology development and includes the tissue grafting scientific conceptions given above. Moreover the leading factor standing against the background of the Alloplant biomaterials modeling influence is the process of reparative tissue regeneration of a recipient. The authors obtained the findings that allowed them to formulate the regenerative surgery conception on the basis of the Alloplant transplantation technology. (E.R. Muldashev with co-authors, 1975-2002)

Key words: regenerative surgery, Alloplant biomaterials, tissue grafting, tissue bank.

The historical aspects of tissue grafting are considered in many works on the history of medicine. There are a lot of special works such as the well-known monographs by M.B. Mirski (1985), P.P. Kovalenko (1975), V.I. Savelyev (1977) and a number of historical articles and sketches devoted to this problem. However most of the articles represent a chronologic description of life and the creative work of famous scientists contributed in any way to the donor problem, to different historical periods through which the donor problem and the transplantation developed their way. It is a well-accepted approach and will hardly interest a reader of this very sketch. We reckon the history of transplantology can be regarded from a little bit different points of view. In our sketch the evolution of the viewpoint on the tissue grafting problem represents the succession of stages changing one another. We would like to show this extremely interesting field of medicine and biology as “the living of a splendid idea”.

Originally the only purpose of the tissue grafting was substitution. In this case a transplant was considered to be the biomaterial which substitutes an injured part of the organism or of the body. The only aim to perform an operation was to make up for a certain anatomic defect of the body. That is why we conditionally named the present period of tissue graft development as “the stage of substitutive transplantation surgery”. Chronologically this stage falls on the second half of the XIX-th and the beginning of the XX-th centuries. The principal demands that were obligatory to the donor tissue were to provide concordant transplantation. It is wrong, however, to make a statement that the history of tissue grafting began only a century ago. The first ideas to graft, make up for the defect of the recipient’s organ or tissue, perform an operative repair on the surface of the body existed as long as medicine. It is explained by the fact that ancient people often used to apply to mutilating punishments for crime commitment. Ancient Indian doctors who sewed a new nose on a criminal gave birth to tissue grafting. They used to excise a sufficient skin fragment from the forehead and put it over the nasal bone forming the missing organ.

One can come across among safe ancient medical treatises certain statements on the possible usage of the local tissues in different operative repairs. There are separate records left since the medieval times about the attempts to graft donor tissues taken from animals. The only purpose of these procedures was substitution. As an example we can take an operative cranial repair in trepanation. This operation had been performed as it is customary to say nowadays with the help of xenogeneic bone transplant taken from a dog. This fact proves that medical science has always been trying to use donor tissues to repair a certain defected organ. There are facts of donor blood transfusion for the sake of substitution. In each of these cases one can see one aim that is to repair the tissular defect. It is that kind of scientific transplantology which had been formed by the middle of the XIX century. Moreover there were numerous attempts of osseous and dermic transplantations. Various autoplasmic operations used to be performed as well.

There are a lot of researchers who contributed to the development of the substitutive transplantation surgery. Thus the priority in the usage of free bone grafting to repair the mandibular defect belongs to V.M. Zykov, surgeon from Moscow (1900). One should also consider the proposition on teeth transplantation given by the home dentists in the substitutive surgery development. (Mirski M.B., 1985).

K.M. Sapezhko (1986) began to graft lip mucous membrane in order to repair the defects of conjunctiva. First experimentally, then in clinic Y.R. Penski (1983) was a pioneer in the ankylosis transplantation which purpose was to substitute pathologically effected diarthroses.

The development of substitutive transplantation can be seen in different works by such surgeons as V.L. Bogolubov (1908) and P.G. Kornev, V.A. Ooppel (1911) on the fascial and

cranial dura mater grafting. Great many German scientists have made considerable contribution to this problem too, professor Kirsch in particular (18.), who wrote a number of articles, devoted to the tissue transplantation, again with substitutive purpose.

However it was N.I. Pirogov who reached the top of the surgery skill through various types of transplants. His monograph named "About grafting generally and rhinoplasty in particular" (1835) became a handbook of reference for the whole generation of transplantologists and plastic surgeons. Osseous plastic operations on extremities, also worked out by N.I. Pirogov, are known as glory of the home grafting.

All given above experimental findings and operations performed in clinic are referred to reconstructive surgery where a transplant was used as bioplastic material. In this sense Pirogov's works represent the acme of the grafting skill performed with the aim of substitution.

Speaking about the development of substitutive transplantation surgery it is worth mentioning the ophthalmologist A.F. Shimanovski from Kiev, who worked out an operation on the transplantation of the eyeball anterior segment. He harvested a complete cadaver anterior segment of the eyeball including cornea, part of conjunctiva, sclera, ciliary body. All this complex was grafted to the recipient with the purpose of substitution of the anterior segment of the eyeball. From the present point of view it is obvious that the mentioned operations lacked grounds and transplants lacked transplantability and could not do good to a patient. But nevertheless professor A.F. Shimanovski has performed three operations of the kind and all of them failed. However, at that stage of medicine development the above described operations indicated crisis in the substitutive grafting surgery and stimulated further research.

With the subsequent accumulation of scientific findings grafting surgery acquired a new trend. This period was named as "regenerative surgery stage" after a wit statement said by I.A. Golyanitski (1922). Keeping in mind the present day experience this period can be called "regenerative grafting surgery". At first the only principle with which grafting surgery went on was substitution but later a lot of ways of tissue preparation and grafting had been reconsidered while the regenerative transplantation surgery was developing. I.A. Golyanitski (1922) carried out a great deal of tests under the guidance of S.I. Spasokukotski.

He grafted tissue from one animal species to another, carried out transplantations within the same species, used tissues of animals of different age, tried different tissue beds. He made experiments on orthotopic and heterotopic transplantations. I.A. Golyanitski used any kinds of the vessel bed with different vascularization level, comparing graft findings through numerous tests. The author noticed that in all cases a transplant compels the tissue bed to begin the reparative process. In his opinion, a transplant induces the process of reparative regeneration which is one of the basic grafting factors.

This finding allowed I.A. Golyanitski to define methods of grafting as regenerative surgery. Here are the conclusions made by I.A. Golyanitski (1922):

I. Good transplantability is provided on condition that:

1. transplant keeps viable
2. transplant is taken from the same animal that is operated on (autotransplant)
3. sticking to aseptic rules
4. transplant comes from a young animal
5. transplant (its tissue) is poorly differentiated
 - a) phylogenetically
 - b) ontogenetically
6. transplant can be rapidly vascularized
7. when grafted transplant doesn't change its nutrition conditions
8. transplant is to perform its usual function
9. transplant shows early functioning
10. functional demands don't exceed its efficiency
11. transplant is resistant to:
 - a) irregular nutrition
 - b) infection
12. factors causing unidentified consequences. Among them these are: predisposition, immunity, sex, race, physiological state, nutrition quality and so on.

II. Conditions providing bad transplantability:

1. transplant keeps unviable (kept long in bad conditions)
2. transplant belongs to some different animal
3. infection
4. transplant comes from a mature or old animal
5. transplant is greatly differentiated
6. only one of the transplant's sides is capable to get nutrition (skin, walls of cavities organs and so on.)
7. transplant cannot be rapidly vascularized (the vessels are still not sutured, surrounded by a capsule and so on)
8. transplant is placed in unusual conditions of nutrition and functioning
9. transplant acquires some other functions or doesn't function at all.
10. transplant is unable to perform its function
11. transplant cannot resist to:

- a) irregular nutrition
- b) infection

Most of the given conclusions remain urgent these days.

Later most of researchers considered grafting in the light of regenerative surgery. Thus, the founder of the first tissue bank in Europe R.Klen (1961) investigated biological activity of transplants and pointed out that tissue bed stimulated reparative process. He referred such transplants to allostatic ones. This approach was further developed in the works of the Priorov's CITO collaborators and tissue bank founded on its basis. Formalinized transplants were researched in the same direction. (Parfentyeva V.F., 1986) Different aspects of tissue regeneration are considered in a number of works devoted to lyophilized and cryoconservative grafting. (P.P. Kovalenko, 1961; A.S. Imamaliyev, 1964; P.P.Kovalenko, V. A. Emelyanov, 1966).

All amount of findings received in the XIX century naturally resulted in the considered regenerative transplantation surgery stage. Hence, in our country Y.I. Bogdanovski (1861) was the first to carry out osseous homografting tests and work out the principle steps to perform such operations. All these findings analyses made in those days show that it was Russia where together with allotransplantation bone tissue regeneration experiments were carried out. (Mirski M. B., 1985).

However all these facts on the research tissue regeneration need summarizing into one general theory. Only I.A. Golyanitski has formulated in his works the regenerative surgery conception as a scientific theory. At the same time clinical practice did not turn out to be ready to accept the new idea. It happened first of all because of the lack of adequate method of conservation, storage and morphological testing of transplants. As a result scientific researches that overtook their time were not widespread in clinical practice.

In 1920s V.P. Filatov performed a number of innovatory cornea grafting operations. Originally it used to be a substitutive transplantation as donor cornea was used as orthotopic biomaterial grafted onto the identical bed. The main purpose of this transplantation was to keep grafted cornea transparent.

While working out this problem V.P. Filatov paid attention to the fact that a donor cornea influences the tissue bed not only locally but also makes some positive structural changes on pathological segment of the fellow eye which did not undergo an operation.

Out of these findings V.P. Filatov has made an exceptionally important conclusion that grafting transplants exert systemic influence over the organism and that is why it is not enough to consider the problem of grafting only from the point of view of substitution or regeneration.

While regenerative conception examines transplantation locally, that is only tissue bed zone, V.P. Filatov looked at this matter from a quite different angle, he saw it as an interaction of the transplant-recipient system. The author named this conception “tissue therapy” Plainly speaking there appeared a new trend taking into account all reactions of an organism to grafting.

What was in the basis of this theory? V.P. Filatov believed that when tissue is taken from a donor and kept under certain conditions it accumulates some special substances that he called biologically active. When grafting is finished these substances get into the general blood channel and display their biostimulating effect. There are five cases described by V.P. Filatov when patients recovered from diabetes with the help of skin allografting. To carry that out he used to take donor skin allotransplant and grafted it on a diabetic recipient’s lumber region. After that one could watch partial or complete stabilization of carbohydrate exchange. V.P. Filatov also cured several patients with chronic cavernous pulmonary tuberculosis. Moreover he grafted skin allotransplants that resulted in cavernous cavities obliteration. He considered these findings as the result of general biological and systemic influence that transplants exerted on the organism. V.P. Filatov thought that when tissue transplant grafting is through, biologically active substances contained in donor tissues begin to positively effect on the recipient’s organism. Besides he showed that cadaver donor is not the only source of biologically active substances. V.P. Filatov reckoned that any biological structures when they are already out of general metabolism enter the state of reliving and it did not matter what the source of donor material was. And that is why he got his biostimulator from any other different sources: plants, microorganisms. Academician V.P. Filatov in particular used estuary dirt that contains microorganisms. He put it in special conditions for reliving and he got an extract with biologically active substances. In the same way aloes extracts were created and they went through this process of reliving. The theory of tissue therapy was a new level of interpreting the problem of transplantation. It was revolution in understanding the interaction between the transplant and the recipient. It became clear that that all integrative systems of the organism take part in this interaction: nervous, immune and endocrine system. Thus a lot of systems of an organism take part in retaliatory reaction to the allografting. V.P. Filatov founded the basis of this conception which developed on successfully in the works of other scientists. Let us take a monograph written by V. I. Savelyev (1997) “ The reaction of the organism to the osseous grafting” (1997) in which one can see that the author works on with idea of the systemic reaction of the organism to the tissue grafting. There are several research works made by P.P. Kovalenko in the same trend too. (1970, 1975, 1976).

Further evolution of the grafting idea could not avoid historical collisions. In 1960s the whole world witnessed birth of new polymer chemical technologies. Polymers began to appear

with different mechanical features, well modeled, and which seemed to be inert while grafting was performed. And most researchers came to the conclusion that this tissue grafting epoch was coming to an end. The mankind created polymers which were going to be used instead of donor tissue in plastic operations on the human body surface, surgeons would be able to fix inner organs, to cure progressive myopia, to perform many other operations. These principles were put into the basis of a new trend in medicine. Metal constructions and polymers were adopted by traumatology and orthopedia, ophthalmology acquired an artificial chrySTALLINE lens which gave rise to an eye surgery epoch. The priority in this field belongs to the famous ophthalmologist academician S.N. Fyodorov who worked out an original chrySTALLINE lens model which was well introduced to the clinical practice. Donor tissues were replaced by artificial joints and many other explants. There was a tendency of traditional donor service reduction and disappearance.

These viewpoints happened to be untimely. After a couple of decades of decline, tissue grafting together with tissue bank service restored to life. A long period of polymer clinical tests shows that the clinical practice cannot get on without donor tissues at present. In comparison with donor tissue synthetic tissues are unable to perform all those after-graft functions. So tissue grafting revives with the network of tissue banks and with all this store of experience accumulated in the XIX century.

Why could not explants justify hopes medicine theory and practice originally had? The reason of it lies in the fact that synthesized “biological tissue equivalents” neglect regenerative surgery principles and associate grafting with substitutive surgery.

What are the principles of the present day transplantation theory and what is its foundation stone. First of all the three evolution stages mentioned above are included into modern tissue grafting conception which in our opinion successfully absorbed all historically formed principles. Now grafting any material at the first stage we count on its substitutive function. The “substitutive” theory however shows its other side and is considered from a different angle. It can be applied only at that stage of the post grafting period if the donor tissue preserves its structure. The substitutive stage claims for selection of transplants with adequate plastic and biomechanical features that allows to model body outline, to revive anatomic unity of the segment.

Later the principles of regenerative surgery came forward and in the place of a transplant there appeared a regenerate with characteristic features. Now one can be certain that the basic mechanisms that have a concrete influence on different tissues regeneration are revealed. (E.R. Muldashev, 1994; S.A. Muslimov, 2000; V. U. Galimova, 2000) These processes are defined by a large number of factors which were investigated in the works by P.P. Kovalenko (1970, 1975, 1976), V.I. Savelyev (1985) and presented in scientific editions of the Central traumatology and

orthopedia institution and also tissue banks of Novosibirsk, Ekaterinburg and Saint Petersburg and others.

According to V. P. Filatov the tissue therapy conception underwent great changes too and had been perfected on the basis of the big store of experience and at the present moment this conception should be considered keeping in mind immune, nervous and endocrine system reactions. Retaliatory reaction mechanisms work under the influence of these three systems when a grafting operation is performed. As this takes place, the local reactions are secondary and obey those of the systemic ones. It is worth paying attention to the fact that retaliatory reaction can differ. It can result in classical biostimulation discovered by V.P.Filatov and in concrete influence on the nervous system, in immunomodeling influence making an effect on the hormonal factors.

The systemic reaction of an organism to the transplant introduction is described in the well known works by V.I. Savelyev (1997), demineralized osseous matrix in particular. The author marked the appearance of hemagglutinin and complementbound antibodies in a recipient's serum the increase of their titers in blood and thus serum complement activity. The author made an accent of the immunological rebuilding of an organism which causes a disorder of the natural tolerance, lymphoid cells stimulation and antibody generation. (Savelyev V. I., 1985). All substances found in a transplant are considered to be biologically active as each element exerts its own influence on grafting reaction of an organism. The Russian Eye and Plastic Surgery Centre worked out a method of the Alloplant biomaterials introduction into the biologically active segments. This method is as a matter of fact the evolution of transplant-recipient systemic interaction idea. (E.R. Muldashev, 2000)

All the given aspects are taken into consideration while Alloplant biomaterials grafting, and this fact allows to speak about a successful combination of the store of experience accumulated by substitutive grafting, regenerative grafting and finally biostimulation or systemic biomaterials on a recipient organism in the conception of modern tissue transplantation. At the borderline of these three historically moving on trends in our opinion a modern Alloplant grafting technology had been formed. At present combined by one theory they make up the basis of the modern biological grafting stage. We call it biological because of the factor of the substitutive biomaterial function and the factor of reparative regeneration with various kind of aspects. Here one includes different mechanisms of cells differentiation, transplant structure replacement and rebuilding forming an adequate regenerate in its place. This is an extremely broad spectrum of biological interactions that take place not only in a tissue bed but also in a transplant itself. Moreover local processes are realized under the regulating influence of neuroendocrine mechanisms, humoral factors, immune system that altogether realize the whole

complex of the local processes. All the given above interactions we define as transplant-recipient system and refer to biological grafting.

We are also certain of the fact that it is regenerative surgery that founds general biological approach in grafting. There are several reasons for that. First of all the structure of a regenerate is formed in the place of biomaterial along with the trend and dynamics of the local reparative processes. It is well known that its morphological peculiarities in many ways depend on the structure and histochemical composition of a grafted biomaterial. (E. R. Muldashev, 1994, S.A. Muslimov, 2000). On the other hand reparative process in the sphere of allografting is provided by a complex of central mechanisms (R.T. Nigmatullin, 1996; V.U. Galimova, 2000; Y.I. Kiyko, 2002). We are speaking here about the factors which are in a limited way referred to the sphere of “grafting biostimulation”. In other words, the process of the reparative regeneration interpret all local systematic interactive mechanisms that gives us an opportunity to consider the regenerative surgery as the main link of modern biological approach in surgery.

The given above aspects of regenerative and biological surgery when Alloplant grafting bio materials are viewed in detail in the works written by E.R. Muldashev and his collaborators (1975-2002). The findings constituted theoretical basis when working out a new generation of biomaterials which are successfully used in all fields of medicine. Next issues of this periodical will give an account of the grounds for different kinds of Alloplant biomaterials, the way they are adopted in different surgery branches.

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