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# TRANSPLANTATION OF FETAL STEM CELLS

# AT THE TURN OF THE FIRST AND THE SECOND WAVE OF DEVELOPMENT

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In the history of medicine, the world has not witnessed a more significant and global attention paid by society to a new scientific direction in medicine as what we can observe today towards the transplantation of embryonic/fetal stem cells (ESC/FSC).

The boom began on November 5, 1998 in the USA after publication of articles by James Thomson [1] and by John Gearhart [2] in the "*Science*" magazine and a press conference of "Geron" corporation (which funded both research studies) dedicated to these publications.

Already on December 2, 1998 the US Senate hearings of the first person in medicine of the USA, the Nobel Prize laureate Director of National Institute of Health (NIH) Harold Varmus regarding derived human stem cells and the prospects of their usage in medicine were held [3]. In February of 1999, new Senate hearings were held [4-6], and President Bill Clinton has commissioned NIH to prepare official guidelines for development of this branch.

The said guidelines [7] approved by B. Clinton approximately one month prior to expiration of his presidential term, has been annulled within the first month of George W. Bush's presidency.

The Roman Pope John Paul II interrupted his summer 2001 vacation in order to express his reservations regarding the problem of researching and utilizing human stem cells. President G. Bush addressed the nation with the doubts regarding the problem of human FSC [8]. The parliaments of Germany, Great Britain, and France repeatedly debated the problem of researching and using stem cells.

«Why the excitement?», - Dr.H.Varmus asked at the US Senate hearings. And answered this question: «For the first time, scientists have obtained human stem cells that can give rise to many types of cells in our body.... It is not too unrealistic to say that this research has the potential to revolutionize the practice of medicine and improve the quality and length of life» [3].

In 1998 human stem cells that can give growth to many types of cells in a body were received for the first time as a result of doctor J. Thomson's experiments [1]. Stem cells of animals have been derived in the beginning of 80th years and J. Thomson used the techniques initially developed for mice [3]. «The big step which shows a possibility to grow human FSC in culture was made» [2]. At the same time, J. Thomson, and J. Gearhart have shown reserve making comments on the possible terms of the beginning of clinical application of results of the research. In their opinion, it will take 5-10 years to begin clinical application of stem cells.

Human ESC for cultivation under laboratory conditions were acquired from two sources:

- from internal cellular mass of the viable embryos after artificial in vitro fertilization at the blastocyte stage (age of embryos about 2 weeks) in J. Thomson's work, and
- from a fetal tissue - tissue of embryos from terminated pregnancies (age of embryos of 5-9 weeks) - in J. Gearhart 's work.

When grown in culture, these stem cells appear to be pluripotent and can develop into cells of the three major tissue types. [3].

Since the subsequent discussion gave rise to ethical questions, Dr. Harold Varmus determined the position assumed by NIH regarding each source of embryonic stem cells. In opinion of H.Varmus, Dr. J. Thomson's work in which cells were derived from embryos created by in vitro fertilization, clearly falls within the Congressional ban on human embryo research. NIH could not, and did not, support Dr. J. Thomson's recent work developing this cell line. The same restrictions do not apply to Dr. J. Gearhart's work, who derived his pluripotent stem cells from fetal tissue from terminated pregnancies [3], although it may be governed by other laws and regulations regarding using fetal tissue.

Human stem cells can be obtained from the tissue of an adult human being (peripheral blood, bone marrow, muscles, etc.), from umbilical cord blood of a newborn, from tissues of an embryo or a fetus. The cells are called embryonic by first eighth weeks of gestation, starting from eight week they are called fetal cells.

For transplantation of ESC/FSC, there are two known sources of material, where the second source appeared literally during the last years of the 20th century.

The first source is tissue from non-living human foetuses - fetal tissue.

After the legalization of voluntary abortions (within 12 weeks) in most civilized nations a significant legal work was conducted regarding the regulations of the utilization of cadaveric embryonic/fetal tissue after medical abortions. At the end of 80's Recommendation 1046 (1986) and Recommendation 1100 (1989) of the Parliamentary Assembly of the Council of Europe have formulated legally and ethically acceptable approach toward the using of human cadaveric embryonic/fetal tissue [9,10], which have been accepted in most countries. This is a natural approach from a medical doctor's position. Most research regarding the problem of transplantation of embryonic and fetal stem cells in the 1970s-90s respected this approach [11-14]. With these Recommendations in view, more detailed regulations were developed, among which we would note the guidelines of the Network of European CNS Transplantation and

Restoration (NECTAR), 1993 [15-17]. The legislation for research and applications of human embryonic/fetal tissues, including the therapeutic purposes, was developed in detail by the international community and was adopted by most nations, including the United States [7, 18-21].

The second source has appeared as an attractive by-product of artificial in vitro fertilization.

«When doctors match sperm and egg to create life outside the womb, they usually produce more embryos than are planted in the mother… the additional embryos remain frozen in laboratories», - explained president G. Bush to American citizens [8]. The president pointed out two fundamental questions: «First, are these frozen embryos human life, and therefore, something precious to be protected? And second, if they're going to be destroyed anyway, shouldn't they be used for a greater good, for research that has the potential to save and improve other lives?».

The claim for usage of viable embryos, that remain following artificial in vitro fertilization, raised a protest of the society not only in the USA, but also all over the world. To tell frankly: medical community has never offered to use viable embryos – neither fresh nor preserved - as a medicine or as a source for medicine. The proposition to use embryos after artificial fertilization in the USA did not belong to the medical community as well.

We do not intend this article to contain discussion of philosophical or theological issues regarding the moment of originating of life in an embryo or the moment of a soul embodiment. But regarding the frozen embryo resulted from artificial in vitro fertilization, in our opinion, - it is clearly a «precious human life», - just like his happier brother or sister that was implanted into a mother’s womb. It will also live, if given the right conditions.

For this reason, our answer to President G. W. Bush’s first question is undoubtedly “yes” - this is human life in our opinion.  In this case, it is pointless to ponder the second question.

Moreover, we agree, that the transference of a real possibility and of a legal right for arbitrary control of life (artificial conception) and death (destruction of an embryo) in the setting of laboratories and corporate interests with an undercurrent of financial motivations unequivocally affects interests and safety of humanity.

Commissioned by the USA government, NIH has summarized modern scientific knowledge of Stem Cells in a book «Stem cells: Scientific progress and directions of the future researches. Possibilities and difficulties: with the stress on the future applications of stem cells», published in June, 2001 [22]. This book and the publications of the last three decades (see the bibliography list) gave the basis for our evaluation of the issue, its opportunities and problems.

The English word "stem" has a wide meaning: a trunk, a stalk, a sort, a tribe, a shank, a basis, etc. Each organism develops starting from two initial cells into a complex system of hundreds of types of the specialized cells.

Stem cells are non-specialized cells which are able to reproduce themselves and create a more specialized offspring. There are various types of stem cells, united in a hierarchy of stem cells of different levels of specialization. Progenitor cells, which are categorized between the stem and specialized cell types, produce only specialized offspring and do not reproduce themselves in their original form [22].

Specialized cells are tied to a particular function - in this sense, they are different from the stem cells from which they are created.

Stem cells of adults are non-differentiated (non-specialized) cells; they can occur in differentiated (specialized) tissue, can reproduce themselves, and can also specialize in order to create any specialized type of cell of a tissue from which they descend [22].

A generally accepted classification of stem cells does not yet exist. Several modern classifications of stem cells are incomplete, they contain contradictions and temporary agreements [7, 22].

It is a known fact that cells that exist within a body for the least period of time (first of all – blood and epithelium cells), are provided with stem cells for replenishment of the appropriate cell population during human lifetime. As for other types of cells, there is less clarity of understanding now. For instance, it used to be believed that the nervous tissue of an adult human lacks any stem cells. The results of research studies during the past few years allow us to view the reparative abilities of human body more optimistically [23] due to recent discoveries of new stem cell types (nervous tissue, muscle tissue, and other) in the organism of an adult human being. Moreover, certain types of stem cells exhibit a great level of plasticity and can contribute into a recuperation not only of inherent for them tissue, but also into tissues of other types [24, 25].

Among the stem cells, the haematopoietic stem cell has been studied the best [22].

Sources of the haematopoietic stem cells for transplantation may be: bone marrow, peripheral blood, umbilical cord blood, and fetal hematopoietic system. The quantity of stem cells is 1 for every 10 - 15 thousand cells in bone marrow and 1 for every 100 thousand in the bloodstream [22].

Till now there are not developed exact methods allowing to distinguish stem cells from blood cells or other cells within bone marrow. Stem cells appearance and behaviour in the tissue culture resembles that of ordinary leukocytes. The only “golden standard” of distinction stem cells in a transplant is the following: the transplant is injected into a sub-lethally exposed mouse and, if the regeneration of all three blood growth is observed, it is concluded that the transplant contained stem cells [22].

In the review of stem cells’ clinical applications [22], the authors limited themselves to application of stem cells only from bone marrow and cord blood for the purpose of treating blood diseases (leukemia, lymphomas, aplastic anemia, hereditary blood diseases), and for restoration of haematopoiesis after a chemotherapy in the course of treatment of oncological diseases. The experience of clinical transplantation of fetal

(embryonic) stem cells from a fetal liver in human for the very same purposes, which has a thirty-year history in a dozen nations, is not mentioned in the book [22].

**Thirty-years experience of clinical fetal stem cells transplantation**

At the same time, transplantation of stem cells [27, 28] from fetal liver of human embryos and foetuses (fetal liver transplantation, further - FLT), was developed namely for regeneration of a haematopoiesis - as an alternative to a complex and expensive method of a bone marrow transplantation [26]. Transplantation of haematopoietic stem cells is the essence of both these methods. This scientific branch was not mentioned in the review [22].

By 1958 there have been shown fetal stem cells' ability to restore devastated immune system of rodents [29].

By 1961 remission was achieved in two out of four patients suffering from chronic pancytopenia who were treated by the transplantation of human fetal cells [30]. There is an array of existing publications issued at the end of 1970s and the beginning of 1980s that describe successful treatment of hematological patients and patients suffering from immune deficiency [31-38]. It is important to note that such work began simultaneously in several nations: the USSR [39-46], the USA [47, 48], India [49-52], Japan [53], France [54, 55], Italy [56-59], China [60-66], Poland [67, 68], Hungary [69] and more.

In 1985 there was held the first international conference on FLT, in which experience of clinical application of this method was presented [47, 49, 50, 56, 63, 65, 70, 71]. Most approaches in these researches were based on experience of bone marrow transplantation, including the use of patient conditioning by means of irradiation or chemo preparations, as well as post-transplant immune suppression to facilitate engraftment of transplanted cells. Both fresh and cryopreserved fetal tissue was used. The characteristics of a tissue were limited to a summary cell count of transplanted cells. The issue of infection precautions was practically not addressed. Some individual very good results were observed. At the same time, overall clinical results and patient survival rates were disappointing. This proved the perspectives of the method, and lack of elaborated technique for its performance.

In 1987 in New Delhi the second conference on FLT problem was held, and the materials were published in the journal "*Thymus*" (1987, 10) [51, 52, 72-76]. In the report, which summarized the world's experience on the matter, the leaders of this scientific branch Gale R.P (USA), Touraine J.L (France) and Kochupillai V. (India) indicated that there were over 300 people that were treated with FLT in cases of aplastic anemia, leucosis and genetic immune diseases [74].

Gale R.P. [77] analyzed international experience of FLT application in cases of severe hematological diseases. According to his data, around the world, FLT has been administered as treatment for at least 122 patients suffering from aplastic anemia and 39 transplants to treat acute leukemia. The improvement of the patient's state was observed in 54% of aplastic anemia cases. In 41% of acute leukemia cases engraftment

of a transplant was observed [77]. At the same time, the treatment results were not always a success, and were sometimes accompanied by significant complications related to immune suppression and patient conditioning. The author's recommendations bore a reserved character: FLT was recommended in situations were there was no appropriate bone marrow donor.

Several publications about unsuccessful treatment of Chernobyl accident victims by means of FLT appeared the next year [78-80].

A large number of publications were issued all over the world, dealing with the use of FLT as a tool in regenerating the immune system of patients suffering from severe hereditary diseases [31- 33, 36, 53, 54, 81-84].

Under J.LTouraine's (France) leadership over the course of 18 years 202 FLT for treatment of 58 children with severe immune deficiencies (24), severe aplastic anemia (2) and inherited metabolic diseases (27) were performed. The good results of treatment during the observation period of 1-16 years were noted in about half of the cases [55, 71, 85]. A unique procedure of FSC transplantation to in-utero patients (unborn patients - 12-28 week old foetuses) was developed, and considerable curative effect was achieved [86, 87].

The authors [22] expressed a predisposition that transplantation of FSC would allow the successful treatment of an entire array of autoimmune diseases. Theoretical outlines that indicate the possibility of successful treatment, particularly, type 1 Diabetes Mellitus were developed. However, there are no references to scientific literature providing appropriate clinical results of treatment of Diabetes Mellitus type 1 by means of FSC.

Authors [22] stress the significant progress regarding the recently developed understanding of recuperative possibilities of a brain in the last years: "Just a decade ago neuroscience textbooks held that neurons in the adult human brain and spinal cord could not regenerate... That dogma that brain tissue could not be regenerated is history" [22, p.77]. Preliminary studies show, that stem cells improve the motion of the paralyzed mice. Since the mid-1980's clinical researches with use of tissues of 7-9 weeks embryos were conducted in several centers of the world, and have shown encouraging results [22, p.81]. Although not all patients improved, in the best cases patients after fetal tissue transplantations have shown clear reduction of their symptoms. In postmortem investigations of such patients whose death was not related to the Parkinson's disease, living neurons were revealed. They were integrated into the normal frames of a striatum.

«A major weakness of these initial studies was that they were all done "open label" », without the double blind control [22, c.81].

By these remark the authors [22] concluded overview of the clinical application of human fetal stem cells in neurology. Though, in our opinion, the history of fifteen-year international experience of clinical FSC application for treatment of Parkinson's disease, - which began in Sweden [88-92] and fell on fertile ground in many other countries (Great Britain [93], the USA [94-96], China [60, 97], USSR [98-100], Czech [101], Poland [102], Canada, France, Spain, Cuba (see [11]), etc., - deserves more attention.

Moreover, at the beginning of the 90's there was established the European Network of the Transplantation and Regeneration of central neural system (NECTAR) [15-17, 103] which quickly united the researchers in this scientific branch and is currently active (see a workshop of 2001 «Neural transplantation in neurodegenerative disease» [104-106]). In 1992 the experience of treatment 120 patients using intrastrial implantation of mesencephalic tissues from embryos of 6-12 weeks gestation (using from 1 up to 16 embryos in each transplantation) was summarized. The majority of patients experienced a positive change in their condition. There were no cases of a negative/unfavourable change in any of the patients [11].

Over the course of fifteen years, enough material has been accumulated to state a significant prospect of the given direction. Transplanted cells survive in the recipient's brain and produce dopamine, which is deficient in patients suffering from Parkinsonism [105]. By 6 to 12 weeks, symptoms of Parkinsonism are reduced, reaching a minimum level in 4 to 5 months. For a year-long period following the transplantation, relative stability of the symptoms [107] is observed. In cases of one-sided implantation, more explicit clinical effects were contralaterally observed [108]. The most part of transplanted neurons (80-95%) dies within 1 to 3 weeks after the transplantation procedure. For this reason, for one transplantation, the mesencephalic tissue of 3 to 5 embryos [109] is used. Functions of the transplanted growth exceed the boundaries of simple dopamine supply. It is functional integration of transplanted neurons in a brain of the recipient needed to obtain clinical convalescence of the patient [110]. The engraftments of transplanted tissue into recipients' brain "without a seam" are remarkable [111]. The two basic preconditions of engraftment are stated: the transplanted tissue should contain both neurons and glial cells; and the second, - there must be the damage of a brain [106].

Thus, over the period of thirty years scientific institutions of the USA, UK, Sweden, Russia, China, Japan, France, Poland, Ukraine, Canada, and more, clinical studies of FSC transplantation were conducted. Basically, there were used fetal stem cells of haematopoietic and nervous tissue - for treatment of patients with disorders of immune system and diseases of haematopoiesis, congenital and inherited diseases, and also Parkinson disease. Results were published in the most prestigious international scientific medical journals [33, 35, 42, 43, 62, 94, 97, 113-126]. The publications provided the analysis of curative action of stem cells from a human fetal tissue, results of a considerable number of successful transplantations. The most complete review of the FLT problem by the beginning of the 90's was made by A. Fine [11, 112]. However, some publications on the matter, a lot of which were published in the USSR, were not included. The regeneration of haematopoiesis, which was observed in the studies - according to "the golden standard" [22], - testified the presence of FSC in transplanted suspensions.

Nevertheless, this significant international clinical experience was mostly omitted in the review publication [22].

### Methodical problems of FSC transplantation

Publications on the problem of stem cells transplantation refer to the following major unsolved scientific problems, methodical limits and technical obstacles:

- tissue incompatibility [5, 6, 127-136];
- necessity of a large quantity of fetal material for transplantations [43, 104, 106, 109];
- infectious safety of transplantation material [137, 138];
- long-term preservation of the material (conservation, cultivation) [39, 116, 139-144];
- methods of administering the transplant (some of which are very sophisticated) [107, 108, 125, 145, 146];
- long-term preservation of vitality and activity of a transplant in recipient's body (including, a problem of engraftment).

In addition to the abovementioned items, certain issues have not yet been established in scientific literature at all, in spite of their importance. These include the following: specifics of fetal material for various forms of pathology [130, 147-149]; the issue of combined utilization of several different types of FSC; the issue of correlation of FSC transplantation with standard methods of treatment; long term maintenance of clinical effects, including repeated transplantations of FSC, etc.

Without solving these issues, FSC transplantation would not be able to become a routine clinical method.

These serious unresolved problems considerably reduced initial enthusiasm of the 80's, caused skepticism in the leaders of this scientific branch, and led to absence of the special conferences on a problem in the 90's. From the beginning of 90's, there can be observed the decrease of activity in the area of clinical application of FSC according to reduction of number of appropriate publications in the scientific literature. Only five such clinical works on FSC application were presented at the 4-th Congress of the International Cell Transplant Society in 1999 (Montreux, Switzerland), [150, 151]. Only one such work was presented at the first European Conference on cellular therapy in 2000 in Pasteur Institute in Paris [152].

## Experience of clinical fetal stem cells transplantation at Embryonic Tissues Center EmCell

On the background of general decrease of scientific activity in the area of clinical FSC transplantation caused by methodical and scientific obstacles, in the 90's there appeared a scientific school that managed to practice daily clinical application of FSC transplantation, having overcome the majority of the mentioned problems. Worldwide, it is known as EmCell (www.emcell.com) [153].

Since the beginning of the 1990s, clinical effects of FSC transplantation are regularly studied at the National Medical University and EmCell, Kiev, Ukraine, under supervision

of Prof. A.I.Smikodub. Among the first patients, under the influence of J.L.Touraine [126] and Gale R.P. [47, 48], there were patients with serious haematological diseases [154], immunodeficiency [155, 156], Diabetes Mellitus [150.]. Encouraging results were received in treatment of aplastic anemia [154], agranulocytosis after chemotherapy in patients having leucosis [157] and solid tumors [158], AIDS patients [159, 160], Diabetes mellitus patients [161, 162], etc.

In 1994 a specialized Cell Therapy Clinic devoted solely to FSCT was established jointly by National Medical University, Council of city of Kiev and Embryonic Tissues Center EmCell.

The development of FSC transplantology was supported by the Academic Council of National Medical University. During 1994-2001 it has allotted eight post-graduate Medical Doctors and planned six multiyear researches for Ph.D. degree on clinical problems of FSC transplantation. The application of FSC transplantation was studied in complex treatment of immune and hematological disorders, in patients who suffered from Diabetes Mellitus [160, 162], from cytostatic myelodepression [157, 163], cancer of pancreas, complicated with a mechanical jaundice [164], AIDS [155, 156, 165], complex treatment of oncological diseases [156, 158], nonspecific ulcerative colitis and Crohn's disease [152].

By the end of 2001 the doctors of the Cell Therapy Clinic and EmCell have published about 100 scientific works in medical journals, materials of international congresses and conferences. Eleven patents were granted, including five patents of Ukraine and two patents of the USA. Guidelines for treatment of several diseases and conditions using FSC transplantation were developed and approved in a due course by Ministry of Health of Ukraine and Academy of Medical Science of Ukraine for wide practical use [167-169].

At present, Ukraine apparently possesses a higher level of preparedness for wide-scale use of FSC transplantation than any other country. Clinical experience of application of FSC transplantation exists for a wide range of diseases and states, and due legislation is in place.

Below are reviewed clinical results of two completed and published scientific researches, ended by dully approved Guidelines for clinical use of the elaborated FSCT methods.

**FSC Transplantation in treatment of oncological and hematological patients**

During 1994-2001 the research on application of FSC transplantation for treatment oncological and hematological diseases were conducted by EmCell jointly with National Medical University, Institute for Oncology and Radiology of Ministry of Health of Ukraine, Institute for Hematology and Transfusiology of Academy of Medical Science of Ukraine, Central Army Hospital of Ministry of Defense of Ukraine, Republican children's hospital " Ohmatdet" and the Kiev Medical Academy for Postgraduate Education. About 200 patients were studied during this period.

It was determined, that FSC transplantation in complex treatment of oncological and hematological diseases is indicated in all phases of the disease, and at all stages of the treatment process [151, 157, 163, 166, 167, 170, 171, 172].

***In the initial phase***

Transplantation of FSC facilitates preparation of patients in critical condition for surgical treatment, in particular: provides a considerable improvement of general state, reduces asthenia, fatigability, depressions. The transplantation allows regain body mass of emaciated patients; it is possible to stabilize weight of patients with cachexy. Anemia disappeared in 94% of cases during 2 weeks. The risk of complications resulting from a hemorrhage is reduced. Postoperative recuperation proceeds more rapidly.

FSC transplantation was observed to have a positive influence on the immune system, which consisted of significant 1-month-long growth of the quantity of CD4+ lymphocytes and a tendency toward the increase of the total population of lymphocytes and CD3+, CD8+, CD19+ sub-populations, as well as natural killer cells within 2 months [171].

The improvement of immune protection of patients results in lower risk of postoperative infectious complications, reduction of dissemination of tumor cells and metastasizing. Patients who received FSC transplantation prior to the operation had less difficulty tolerating chemotherapy and radiotherapy treatments.

***In the Process of Chemotherapy and/or Radiotherapy***

In oncological patients with myelotoxic agranulocytosis, FSC transplantation allows for much more rapid regeneration of peripheral blood count.

It is especially important to note, that following FSC transplantation the time of neutrophils level regeneration sharply shortens to a 5-7 day period [170], compared to the typical 30 days in a control group (Fig.1). During febrile neutropenia, clinical improvement is observed almost immediately - for the duration of 1-3 days, still prior to a significant increase of neutrophils in the blood formula. The body temperature is normalized, intoxication syndrome is diminished, and manifestations of stomatitis are reduced [172].

Rapid exit from agranulocytosis guarantees a significant (2 or 3-fold) reduction in the quantity of complications related to infection [163]. The gravity of such complications is also significantly diminished (Fig.2). The rapid regeneration of the quantity of thrombocytes (Fig.3) facilitates the reduction of manifestations of hemorrhagic syndrome, risk of cerebral haemorrhages, and other complications associated with thrombocytopenia. Transplantation of FSC allows to effectively conquering even a persistent thrombocytopenia.

Fig.1a RECOVERY DYNAMICS OF TOTAL LEUKOCYTES AND OF NEUTROPHILS IN HAEMATOLOGICAL PATIENTS WITH SEVERE POST-CHEMOTHERAPY NEUTROPENIA AFTER EMBRYONIC STEM CELLS TRANSPLANTATION (N=16). Abs.num.

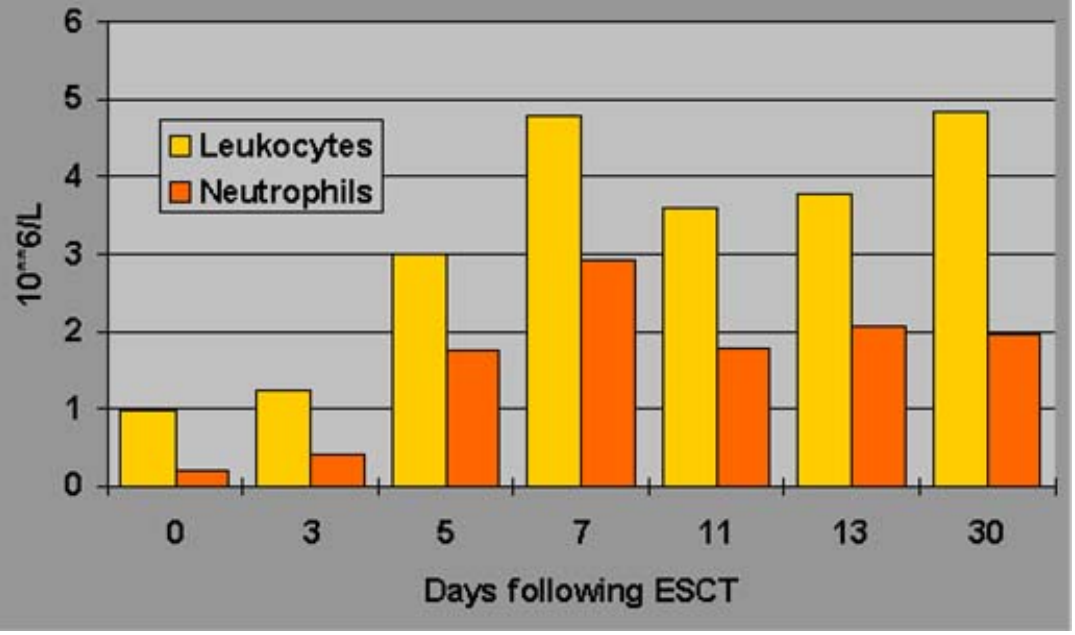
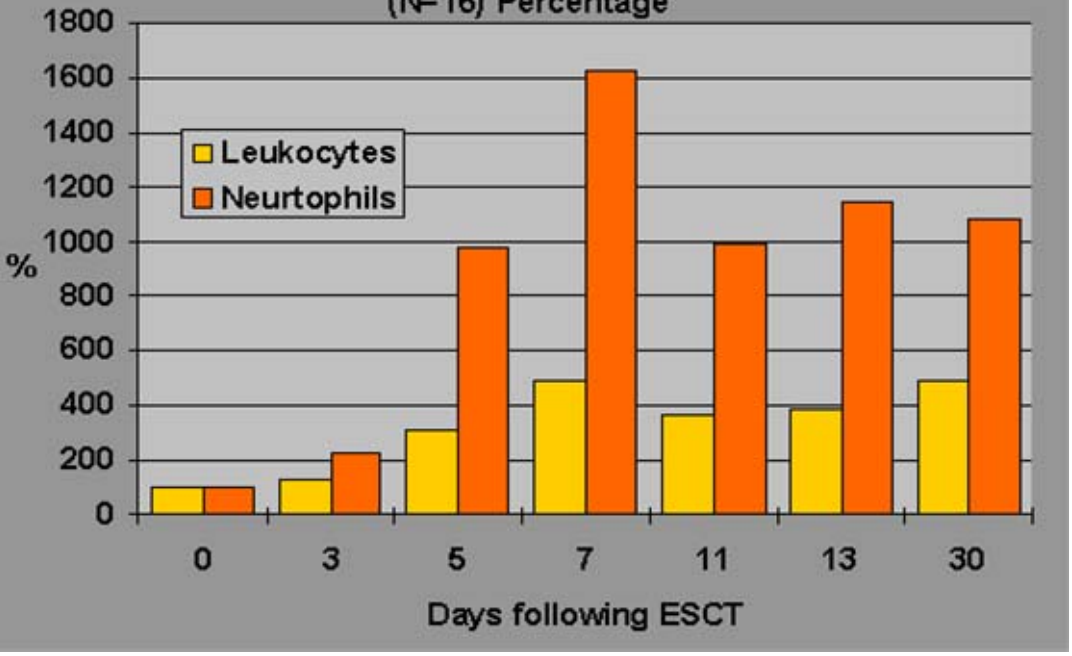



Fig.1b
RECOVERY DYNAMICS OF TOTAL LEUKOCYTES AND OF NEUTROPHILS IN HAEMATOLOGICAL PATIENTS WITH SEVERE POST-CHEMOTHERAPY NEUTROPENIA AFTER EMBRYONIC STEM CELLS TRANSPLANTATION (N=16) Percentage



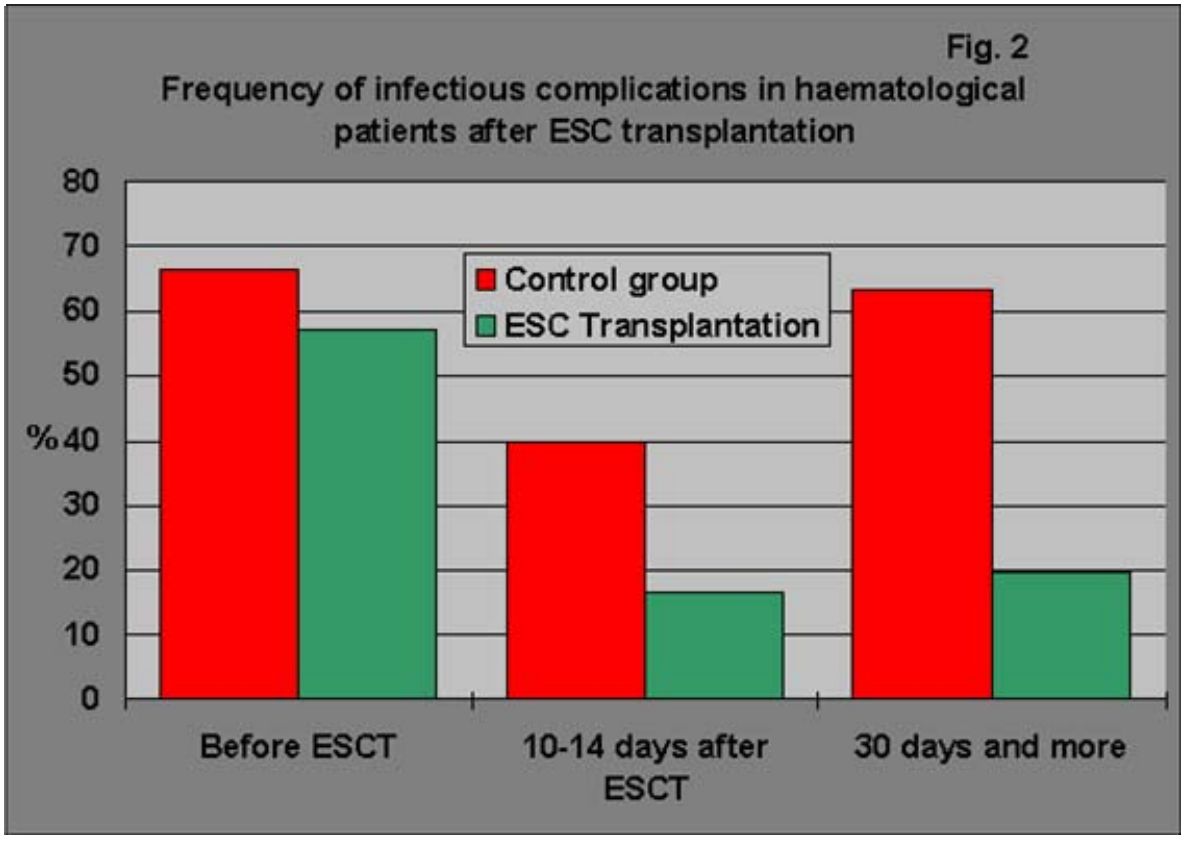


Fig. 2
Frequency of infectious complications in haematological patients after ESC transplantation
80
70
60
50
%40
30
20
10
0
Control group
ESC Transplantation
Before ESCT
10-14 days after ESCT
30 days and more

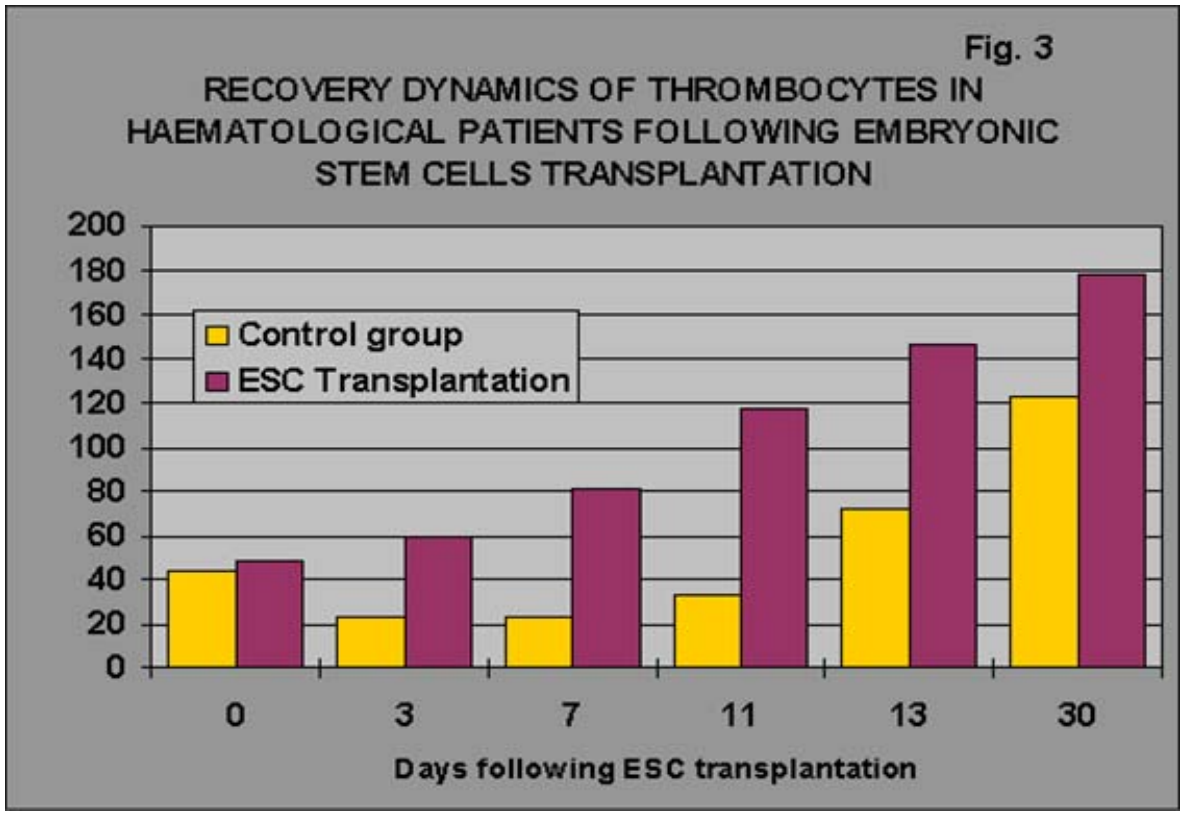


Fig. 3
RECOVERY DYNAMICS OF THROMBOCYTES IN HAEMATOLOGICAL PATIENTS FOLLOWING EMBRYONIC STEM CELLS TRANSPLANTATION
200
180
160
140
120
100
80
60
40
20
0
Control group
ESC Transplantation
0
3
7
11
13
30
Days following ESC transplantation

Rapidly bringing the patient out of the risk zone in cases of cytostatic disease and expressed agranulocytosis, thanks to FSC transplantation, allows one to conduct a more aggressive chemotherapy treatment, with lower risk to the patient's life. This significantly increases effectiveness of chemotherapy courses in treatment of oncological diseases, as well as in prophylaxis of metastasizing and relapses [167, 171].

***In the final stage of treatment***

After completing chemotherapy or radiotherapy courses, there is still a remaining problem of regenerating activity of the patient's immune system, which insufficiency, in fact, allowed for the development of tumor disease [173, 174]. In patients with a manifested secondary immune deficiency after radical treatment of solid tumors, the CD4+, CD8+, CD3+ and CD19+ lymphocyte quantity indices, due to the transplantation, showed increasing amounts during a two month period, with the total doubling by the end of the period. Although the quantities did not reach normative levels, the reached amounts remained at the new higher levels for approximately one year of observation [171].

An important effect of FSC transplantation is the rapid and stable improvement of psychological, emotional, and psychophysiological nature. The patients' condition changes within a few hours after the transplantation procedure: patients experience a better mood and a sense of willpower, strength of mind, followed by an improved emotional and mental condition. Subsequently, depressive tendencies are significantly reduced, emotional stability is increased, etc. [156].

Phobias, apathy, depressions, general weakness, insomnia are typical in critically ill oncological and hematological patients. Positive psychological and psychophysiological changes after FSC transplantation assist such patients to go through many trials related to a disease. The improvement of psychoemotional state of patients in grave conditions, including incurable ones, is the important contribution to improving the quality of perhaps the last period of life of these patients.

After FSC transplantation a frequency of relapses considerably diminishes. In particular, patients suffering from cancer of the neck of the uterus, the percentage of relapses was reduced by more than one-half of incidents after transplantation (23% in a control group and 10% after FSC transplantation) during a 2-year-long observation period [163, 174]. There was noted a significant increase of survival period of incurable patients, who underwent the palliative operations to treat cancer of pancreas, complicated with an icterus [164].

***Prophylaxis of oncological diseases***

There are no factual clinical data regarding prophylaxis of oncological diseases by means of FSC transplantation. At the same time, theoretical consideration and experimental results [158] suggest a significant preventive effect of FSC transplantation in case of oncological diseases. So, experimental results of FSC transplantation in mice with Lewis's carcinoma prove a considerable (approximately three-fold) reduction of a risk of

metastasizing: their numbers (1.2±0.2 compared with 4.5±0.3 in the control) and masses (1.1±0.4 мм$^3$ compared with 3.7±0.5 мм$^3$ in the control)) [158, 174].

Thus, application of FSC transplantation in treatment of oncological patients allows for preparation of critically ill patients for the operation, provides for a higher tolerance of chemotherapy and a more rapid recuperation after chemotherapy treatments, allows for the regeneration of an antitumor immunity, and lowers metastasising and relapsing [171].

**FSC transplantation in treatment of Diabetes Mellitus**

Publications of the 80's expressed assumptions of the probable curative influence of FSC transplantation in cases of Diabetes Mellitus I type. However there were no publications with the actual clinical results of such treatment.

An original method for Diabetes Mellitus treatment with the use of FSC transplantation was developed [150, 161, 162, 169]. According to the method, transplanted cell suspensions do not contain β-cells, which appear in later stages of embryogenesis. Analyses of the patent applications in patent offices in Washington, Hague and Moscow have shown complete novelty (level A) of this method. The method proved to be effective in treatment of Diabetes Mellitus of type I, as well as of type II. EmCell's experience of successful application of FSC transplantation covers 150 patients having Diabetes Mellitus.

FSC transplantation is especially effective in complex treatment of patients suffering from an initially manifested insulin-dependent diabetes and leads to stable compensation of the disease [162]. Practically all patients, after undergoing FSC transplantation, experienced a decrease in the required daily dose of insulin (by 20-100%, by 40.8% on average) for the duration of 2 - 3 months (Table 1, Fig.4). The return to initial required dose of insulin was not observed within at least a year. FSC transplantation allowed slowing down development of the diabetes mellitus type 1. The course of the disease became gentler; the periods between relapses grew to 5 - 14 months [162].

Apparently, the most important curative action of FSC transplantation in the initially manifested Diabetes is essential weakening or interruption of autoimmune aggression resulting in discontinuation of insulitis and partial reparation of insulin production. The probability of this very mechanism is hinted at by the reestablishment of specifically immune indicators of the patient after the transplantation procedure. This way, after 14 - 28 days, the researchers observed an increase in the absolute quantity of lymphocytes (on average 35.9 ± 10.7%), quantity of T-lymphocytes: CD3+ cells – by 58.1 ± 17.2%, CD4+ cells – by 54.9 ± 24.2%, CD8+ cells – by 57.7 ± 13.1%. This effect was retained in repeat observations held 2-3 months after the transplantation: quantity of CD3+ cells – by 43.0 ± 12.7%, CD8+ cells – by 56.2 ± 15.4%. The quantity of B-lymphocytes was reduced: CD22+ cells – by 28.4 ± 13.9%.

Table 1

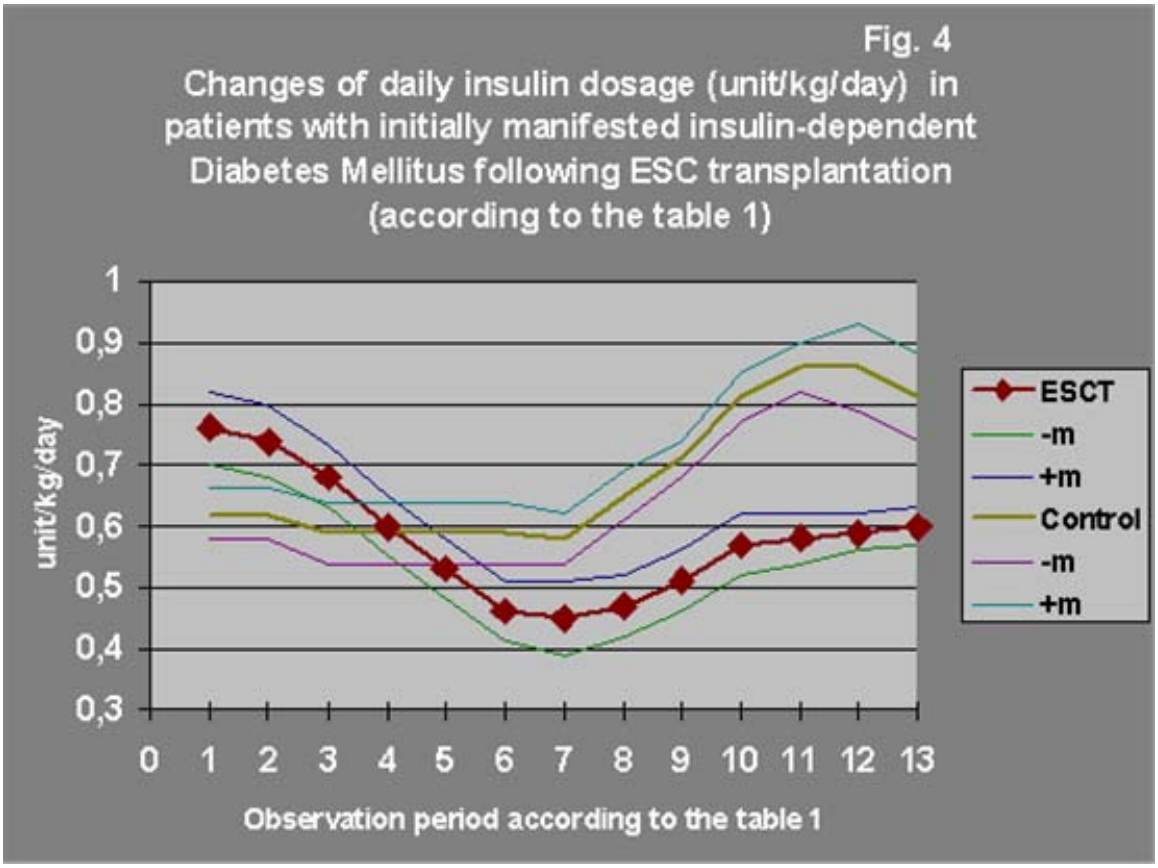
**Changes of daily insulin dosage (unit/kg/day) in patients with initially manifested insulin-dependent diabetes mellitus following FSC transplantation**

(corresponding graph in Fig.4)

| | Period of observation | | Quantity of patients | M | m | P (P<0.05) |
|---|---|---|---|---|---|---|
| 1 | **Before transplantation >** | | 20 | **0.76** | 0.06 | |
| 2 | | **1-7** | 20 | **0.74** | 0.06 | 0.85 |
| 3 | | **7-14** | 20 | **0.68** | 0.05 | 0.37 |
| 4 | **Days** | **14-28** | 20 | **0.60** | 0.05 | 0.06 |
| 5 | **following** | **28-45** | 20 | **0.53** | 0.05 | **0.01*** |
| 6 | **transplantation** | **45-60** | 20 | **0.46** | 0.05 | **0.00*** |
| 7 | | **60-90** | 20 | **0.45** | 0.06 | **0.00*** |
| 8 | | **90-180** | 20 | **0.47** | 0.05 | **0.00*** |
| 9 | | **180-270** | 19 | **0.51** | 0.05 | **0.00*** |
| 10 | | **270-365** | 15 | **0.57** | 0.05 | **0.03*** |
| 11 | **Years** | **2** | 9 | **0.58** | 0.03 | 0.06 |
| 12 | **following** | **3** | 6 | **0.59** | 0.03 | 0.13 |
| 13 | **transplantation** | **4** | 5 | **0.60** | 0.03 | 0.20 |

Fig. 4

Changes of daily insulin dosage (unit/kg/day) in patients with initially manifested insulin-dependent Diabetes Mellitus following ESC transplantation (according to the table 1)



The intensity and the duration periods of between relapses depended on the time between initial manifestation of diabetes mellitus and FSC transplantation: in cases where the transplantation was completed within a maximum of 2 months after the detection of the disease, treatment results were significantly superior to those achieved with a longer waiting period of 2-5 months between detection and FSC transplantation. This also supports the supposition that FSC transplantation interrupts autoimmune insulitis and protects the patient's pancreatic β-cells, which survived until the time of FSC transplantation, from destruction.

In patients suffering from Diabetes Mellitus complicated by diabetic I-II stage nephropathy, from chronic kidney insufficiency of I-II degree, or from anaemic syndrome - FSC transplantation allowed for regeneration of red blood cell indices within 30-45 days with a subsequent stable period that lasted 2-11 months. Within the same time frame, the oppressed cellular immunity also experienced significant regeneration: the absolute quantity of leucocytes – on average by 50.7 ± 14.5%; of T-lymphocytes – CD3+ cells by 72.3 ± 11.5%, CD4+ cells by 62.7 ± 11.9%, CD8+ cells by 84.3 ± 21.2%. Within the next 2-3 months the abovementioned indices rose by an additional 5 - 12% [162].

The kidney function in this group of patients following FSC transplantation either improved or stabilized: the patients experienced a significant reduction in the daily proteinuria with the maximum level of reduction being reached by 2 months; additionally, the creatinine level stabilized; finally, there was a marked improvement of protein metabolism with a higher content of albumins and a higher protein coefficient after 1-2 weeks.

Stabilization of hemodynamics was noted, specifically the decrease of blood pressure - first on the initial dose of hypotensive medications and later also in view of their lowered dose or partial cessation of medication. Duration of the hypotensive effect following FSC transplantation was 5-9 months in patients suffering from diabetes with I degree chronic kidney insufficiency and 2-4 months in patients suffering from diabetes with II degree chronic kidney insufficiency.

Glycemia indices showed lowed levels and were stabilized. Following FSC transplantation, the daily dose of insulin was lowered by almost 20% for the duration of 2-3 months in this group of patients.

The patients having diabetes experienced the reduction of dystrophic symptoms; the working capacity [161, 162] has increased.

Thus, the FSC transplantation appeared to be an effective treatment of diabetes and its numerous complications.

The specific medical action of FSC transplantation in Diabetes Mellitus patients is the hypoglycemic effect, which is manifested by decrease of a glucose level in blood, of glucose contents in urine and allows for one to reduce doses of hypoglycemic medication, including insulin [150, 161, 162].

FSC transplantations in patients suffering from Diabetes Mellitus provide the complex curative effect [162] consisting of:

- immune status correction,
- decreasing or interruption of autoimmune aggression,
- improvement of protein, carbohydrate and mineral metabolism,
- improvement of haematopoiesis,
- improvement and stabilization of hemodynamics,
- decrease of micro- and macroangiopathy manifestation
    - diabetic trophic lesions,
    - diabetic neuropathy,
- improvement of kidney function,
- improvement of vision,
- decrease of frequency and depth of infectious complications,
- improvement of general state of health,
- improvement of mental and physical capacity,
- optimization of psychoemotional condition.

The FSC transplantation ensures a significantly milder course of Diabetes Mellitus, longer and deeper remissions, lower rate of the disease's progression, prophylaxis of complications, and more favorable life prognosis. The repeated FSC transplantations provide long-lasting maintenance of FSC curative effects.

The given result exceeds the boundaries of problems associated with diabetes alone - in fact there is no available method for discontinuation of an autoimmune aggression in any autoimmune disease now (chemotherapy and hormone therapy, which are applied now to suppress activity of autoimmune process, are palliative methods with severe side effects).

Effect of correction of immune system behavior in autoimmune diseases was revealed in treatment of several other diseases with autoimmune genesis (unspecific ulcerative colitis [152, 176, 177], multiple sclerosis [153], rheumatoid arthritis, etc).

**Conclusion**

The clinical experience of Cell Therapy Clinic of National Medical University and Center of embryonic tissues EmCell  allows to conclude, that the essential scientific and technical obstacles, which were indicated by researchers of FSC transplantation, have been successfully surmounted. In particular: problem of a graft rejection, danger of contamination of the patient, a possibility of long cryopreservation of cell suspensions, rational ways of delivery of the transplanted cells to the lesion, the possibility of repeated (sometimes, multiple) transplantations, ensuring the long-term survival of a transplanted material in the recipient, and long-lasting clinical action of provided curative effects, etc. [168, 169, 207].

It should be stressed, that in absence of a methodical solution for any of the abovementioned issues, FSC transplantation would not become reality and the presented results could not have been achieved.

We consider that fetal tissue may completely cover the current demand for FSC needs for investigations and clinical application at the present stage of FSC transplantation development as a scientific clinical branch.

The legislation, which allows and regulates using of fetal material in scientific and therapeutic purposes, is accepted in the majority of the developed countries of the world [3, 9, 10, 20, 21, 177, 178]. The use of this material demands very delicate ethical approach. The mostly complete and elaborated ethical guidelines for FSC transplantation, in our opinion, were developed by NECTAR [15], and may be recognized, accepted and respected worldwide.

Thus, we are the witnesses and participants of the birth of a new branch of transplantology – clinical Embryonic Stem Cell Transplantation. It allows

- essentially extend clinical means for treatment of many diseases,
- considerably contribute into prophylaxis of many diseases (cancer, cardiovascular, etc.),
- retard premature ageing,
- increase quality of life of elderly and ill people.

The peculiarity of FSC transplantation, is the fact that transplanted is a small amount of rather universal cells (stem cells may have different degree of specialization), and the curative effects are provided by their specialized posterity. Differentiation and multiplying of this posterity is guided by systemic regulation of the recipient's body, in regard of maintaining its weakened or impaired, ill or lost functions.

Main curative effects observed in patients following FSC transplantation encompass all levels of organization and functioning of human body [153], and are arranged in a systemic way:

- Rapid and substantial improvement of volitional, mental and physical activity of patients, stabilization and improvement of mood, positive psychophysiological changes, particularly in such areas as attention, memory, and mental performance;
- Restoration of suppressed haematopoiesis (normalization of erythrocytes, leukocytes, lymphocytes, and thrombocytes counts);
- Stimulation, correction, or suppression of immune system (depending on what is beneficial for the patient in his/her current condition, or stage of the disease);

- Stimulation of trophic functions in tissues and organs, improvement of deteriorated tissues, impaired, weakened and faded functions, retardation of premature ageing, vivid systemic effect of functional "rejuvenation";
- Normalization of homeostasis (normalizing of glycaemia, lipidemia, creatinemia, protein, carbohydrate, mineral metabolism, blood pressure, improvement of blood circulation, etc.).

Not all these effects are universally revealed in each case. Sufficient results of treatment can be achieved mostly by combined use of different kinds of Stem Cells, depending on mechanisms of pathological processes, current patient's condition, individual problems of treatment, stage of disease, phase of treating process and particular tasks of treatment in certain case.

Modern fashion for cell therapy and certain simplicity of technical procedures of FSC transplantation may cause in a way careless attitude to the FSC transplantation. At the same time, the simplicity of FSC transplantation should be related rather to an idea of FSC transplantation, than to the actual clinical methods for treatment specific diseases.

You may recollect the similar history of blood transfusion, which despite an obvious idea took about two millennia to develop a clinical method. It was used occasionally in Europe from the middle of XVII century, but being deadly dangerous was prohibited, until breakthrough in XX century, when it became routine effective clinical method. Less than only a hundred (!) years ago.

Among all components of FSC transplantation, fetal stem cells are the most available one. The most scarce and demanded component, from a point of view of a reputable doctorial community, - is the knowledge, elaborated and approved methods for FSC application in particular clinical cases in different diseases.

During recent years two waves of interest toward FSC transplantation were observed.

The first wave developed more than 30 years ago when FSC was investigated as the possible alternative for bone marrow transplantation in cases of irradiation injuries and diseases related to haematopoiesis. The pioneers of these studies were G. Lucarelli in Italy [109-111], J.L. Touraine in France [27, 85-87, 179], K.M.Abdulkadyrov in the USSR [180, 181, 183], Wu S.T., Ye G.Y., Meng P.L. in China [37, 65, 69, 76], R.P. Gale in the USA [47, 48, 77, 80, 182], etc.

The peak of the first wave occurred in the 70-80's. A. Fine's review [11] provides the most complete analysis of studies and results of this branch during the first 20 years of its development. Investigations on FSC transplantation started, practically, simultaneously in about 20 countries. Haematopoietic stem cells first among other kinds of stem cells attracted the main interest (fetal liver transplantation). Later it involved nervous system FSC (since O.Lindval in Sweden [183-189]). During this (first, initial)

wave of interest the basic clinical results were gained. High curative potential of FSC transplantation was confirmed. Major scientific and technical obstacles were revealed.

During the same period - the end of 80's beginning of 90's - the progress concerning ethical and legislative problems of the use of cadaveric fetal human tissues was achieved [9, 10, 15, 20, 21, 123, 190, 191].

At that time complex solution for major scientific problems of FSC clinical application was not available, including histocompatibility, infectious safety, amount of applied material, age of fetal tissue, etc., though the ways for overcoming most of these obstacles were found during that initial period.

To make a successful transition toward a routine daily clinical practice it was necessary to solve not only one or several problems, but all (!) these scientific problems-obstacles simultaneously. The absence of the complex solution of these problems retarded development of FSC transplantation as a scientific clinical branch. The number of publications on this scientific direction has sharply declined by the second half of the 90's.

The second wave of interest to ESC/FSC emerged in 1998 after publication of the research on the possibilities of human embryonic stem cells cultivation in laboratory conditions, [1] which evoked a hope for receiving embryonic tissue in unlimited quantity [2].

Anticipation of medical consequences of huge curative promise of ESC/FSC elicited acute reaction from society. However, world community reacted not only to the medical side of this issue, but also to the ethical aspect. For the first time mass media arose and debated permissibility of using human viable embryos as a source for production of a medicine.

The scientific and popular literature of the second wave provides an important theoretical basis of potential curative action of FSC concerning different diseases in relation with specificity of their etiology and pathogenesis, but there are no attempts of treatment and even of analysis of experience of the FSC clinical application received by researches of the first wave in the 70-80's.

The potential solution of a remote marketing problem (a huge supply of embryonic tissue for FSC transplantation) hindered the top-priority problem of creation and development clinical methods for FSC application.

The basic result of the second wave for clinical purposes so far was the significant attention of the society to the development of a new branch of transplantology.

It is necessary to mention, that the first wave of FSC research did not pass away completely, and its further development brought forth certain scientific and practical results. In particular, clinical researches of FSC transplantation were conducted in a Cell Therapy Clinic of National medical University and Center EmCell in Kiev, Ukraine [153] from the beginning of 90's. FSC transplantation was applied for treatment of

hematological, oncological diseases, Diabetes Mellitus, AIDS/HIV-infection and several other diseases and conditions. Different clinical models facilitated better understanding of mechanisms of FSC curative actions and clinical results.

Over the course of ten years almost 2000 transplantations were performed for treatment of a wide range of diseases. Clinical researches were done in leading scientific institutions of the country on each of the diseases, with the participation of the recognized experts in particular medical field. During these years about 100 scientific works were published, materials were presented at 12 international and 8 domestic conferences and congresses, guidelines for treatment of several diseases and conditions with the use of FSC [167-169] were elaborated and approved in due course by Ministry of Health of Ukraine and Academy of Medical Sciences of Ukraine.

Granted were 11 patents for methods of treatment with the help of FSC transplantation, including two USA patents (in 1998 and 2001) [155, 156]. Patent offices in Washington, Hague and Moscow gave the highest possible assessment of their novelty. For this reason, it is not a surprise that many physicians know little of such methods - these techniques are only now becoming the property of medical community.

The methods of treatment with application of FSC transplantation have a high level of potential. They would, probably, have much in common for the tissue from both sources – directly from human fetal tissue, and also from embryonic tissue that will be cultivated under laboratory conditions.

FSC from human fetal tissue can already be used in clinical practice. Currently human fetal tissue serves as the only source for development of clinical methods for treating various diseases with the use of FSC transplantation in human.

There is a long way from defining a source of FSC, elaborating a method for their manufacturing - up to creation and approval of an efficient clinical method for treatment of a certain disease. For several diseases and conditions such work has been already completed in Ukraine.

At present, the recognition and distribution of the developed methods of treatment using FSC transplantation may proceed more effectively in case of arranging joint research studies of Ukrainian specialists (who possess clinical expertise of using FSC transplantation and several approved guidelines) with Western colleagues who would like to appropriate these progressive methods. Cooperative work will allow widening the methodical and financial foundation for such scientific research studies. It may also help to acquire new data that will guarantee a greater level of confidence regarding the data achieved earlier. This may open the road to the world recognition of a clinical FSC transplantation in treating of a wide range of diseases and conditions, prophylaxis of certain diseases, improvement of life quality and longevity.

**References**


1. Thomson J.A., Joseph Itskovitz-Eldor, Sander S. Shapiro, Michelle A. Waknitz, Jennifer J. Swiergiel, Vivienne S. Marshall, and Jeffrey M. Jones Embryonic Stem Cell Lines Derived from Human Blastocysts // Science. – 1998. - V.282. N5391. – P.1145-1147.
2. Gearhart J. New Potential for Human Embryonic Stem Cells // Science. – 1998. – V.282. – N5391. - P.1061-1062.
3. The Director's Congressional Testimony on Stem Cell Research // NIH Stem Cell Information Archives, December 2, 1998 // http://www.nih.gov/about/director/120298.htm
4. The Director's Congressional Testimony on Stem Cell Research // NIH Stem Cell Information Archives, January 26, 1999 // http://www.nih.gov/news/stemcell/statement.htm
5. NIH: What would you hope to achieve from human pluripotent stem cell research? // NIH Stem Cell Information Archives, April 26, 2000 // http://www.nih.gov/news/stemcell/achieve.htm
6. NINDS and NIDDK Directors' Congressional Testimony on Stem Cells // NIH Stem Cell Information Archives, April 26, 2000 // http://www.nih.gov/news/stemcell/State.htm
7. National Institutes of Health Guidelines for Research Using Human Pluripotent Stem Cells // NIH Stem Cell Information Archives, August 25, 2000 (corrected November 21, 2000) // http://www.nih.gov/news/stemcell/stemcellguidelines.htm
8. The President's Address to the Nation // NIH Stem Sell Information, August 9, 2001 // http://www.whitehouse.gov/news/releases/2001/08/20010809-2.html
9. Parliamentary Assembly of the Council of Europe (1986) On the use of human embryos and foetuses for diagnostic, therapeutic, scientific, industrial and commercial purposes // Council of Europe. – Strasbourg. –1986. - Recommendation 1046
10. Parliamentary Assembly of the Council of Europe (1989) On the use of human embryos and foetuses for scientific research // Council of Europe. – Strasbourg. – 1989. - Recommendation 1100
11. Fine A. Human fetal tissue research: practice, prospects, and policy. [Review] // Cell Transplantation. – 1994. - N3. – V.2. – P.113-145
12. Hovatta O, Ahrlund-Richter L. [Ethical aspects of stem cell research. Legislation and guidelines in Europe] // Lakartidningen. – 2001. - V.98. - N34. – P.3515-3519
13. Hurd R.E. Ethical issues surrounding the transplantation of human fetal tissues [Review] // Clinical Research. – 1992. – V.40. - N4. – P.661-666
14. King P, Areen J Legal regulation of fetal tissue transplantation // Clin Res. – 1998. – N36. – P.205-208
15. Boer G.J. Ethical guidelines for the use of human embryonic or fetal tissue for experimental and clinical neurotransplantation and research // Network of European CNS Transplantation and Restoration (NECTAR). - J Neurol. – 1994. – V.242. – N.1. – P.1-13
16. Boer G.J. Notes for the discussion on the ethical issue of clinical neurotransplantation // Report at Founding meeting Network for European CNS Transplantation and Regeneration (NECTAR). - Le Vésinet. - 1991
17. Boer GJ. Ethical issues in neurografting of human embryonic cells // Theor Med Bioeth. – 1999. – V.20. – N.5
18. Bauer A.R. Fetal tissue transplantation: legal and ethical implications of a "magic bullet" [Review] // Legal Medicine. – 1991. - P.245-267
19. Bell N.M. Regulating transfer and use of fetal tissue in transplantation procedures: the ethical dimensions // American Journal of Law & Medicine. – 1994. – V.20. - N3. – P.277-294
20. National Consultative Ethics Committee for Life Sciences and Health (CNESVS) (1984) Recommendation on the use of embryo tissue as well as tissue of dead foetuses for therapeutic, diagnostic and scientific purposes

21. National Consultative Ethics Committee for Life Sciences and Health (CNESVS) (1990) Statement on intracerebral graft of mesencephalic tissue of human embryo origin in patients with Parkinsonism for therapeutic experimentation
22. Stem Cells: Scientific Progress and Future Research Directions // National Institutes of Health Stem Sell Information. - July 2001 // http://www.nih.gov/news/stemcell/scireport.htm
23. Bjorklund A, Lindvall O. Self-repair in the brain //Nature. – 2000. – V.22. - N405(6789). – P.892-893, 895
24. Metcalf D. Stem Cells, Pre-Progenitor Cells and Lineage-Committed Cells: Are Our Dogmas Correct? // Annals of the New York Academy of Sciences. – 1999. - N872. – P.289-304
25. Metcalf D., Moore, M.A.S. Embryonic aspects of hemopoiesis // Frontiers of biology: Hematopoietic cells (Neuberger, A., Tatum E.L. eds). – Amsterdam. – 1971. - North Holland Publising Co. – P.172-271 (Цит. по Fine A., 1994).
26. Hematopoietic Cell Transplantation. Edited by E.D.Thomas, K.G.Blume, S.J.Forman. – Blackwell Science, Inc., 1999, II edition. – 1260 p.
27. Touraine J.L. The fetal liver as a source of stem cells for transplantation into fetuses in utero // Curr Top Microbiol Immunol. – 1992. N177. - P.187-193 (Review)
28. Transplantation of stem cells from fetal liver. - Lancet. – 1981. – V.1. - N8231. – P.1193-1194
29. Uphoff D.E. Preclusion of secondary phase of irradiation syndrome by inoculation of fetal hematopoietic tissue following lethal total body X-irradiation // J.Natl. Cancer Inst. – 1958. – N.20. – P.625-632 (Цит. по Fine A., 1994)
30. Bodley Scott R., Matthias J.Q., Constandoulakis M., Kay H.E.M. Lucas P.F., Whiteside J.D. Hypoplastic anemia treated be transfusion of foetal haemopoietic cells // Lancet. – 1961. - N2. – P.1385-1388 (Цит. по Fine A., 1994)
31. Adams B. Restoring hope: lifting the ban on fetal tissue transplantation research // Academic Medicine. – 1992. – V.67. - N4. – P.246-247
32. Kansal V., Sood S.K, Batra A.K, Adhar G., Malviya A.K., Kucheria K., Balakrishnan K. Fetal liver transplantation in aplastic anemia // Acta Haematol. – 1979. – V.62. - N3. – P.128-136
33. Keightley R.G., Lawton A.R., Cooper M.D., Yunis E.J. Successful fetal liver transplantation in a child with severe combined immunodeficiency // Lancet. – 1975. – V.2. - N7940. – P.850-853
34. Kelemen E. Recovery from chronic idiopathic bone marrow aplasia of a young mother after intravenous injection of unprocessed cells from the liver (and yolk sac) of her 22 mm CR-length embryo // A preliminary report. Scand J Haematol. – 1973. – V.10. - N4. – P.305-8
35. Lane H. C., Masur H., Longo L., Klein H. G., et all. Partial immune reconstitution in a patient with the acquired immunodeficiency syndrome // N. Engl. J. Med. - 1984. - V. 311. - N17. - P.1099-1103.
36. Pahwa R., Pahwa S., Good R.A., Incefy G.S., O'Reilly R.J. Rationale for combined use of fetal liver and thymus for immunological reconstitution in patients with variants of severe combined immunodeficiency // Proc Natl Acad Sci U S A. – 1977. – V.74. - N7. – P.3002-3005
37. Ye GY. [Fetal liver transfusion (FLT) in the treatment of aplastic anemia] // Zhonghua Nei Ke Za Zhi. – 1983. – V.22. - N2. – P.71-73
38. Баранов А. Э., Гуськова А. К., Селидовкин Г. Д. и соавт. Опыт трансплантации костного мозга, лейкомассы и клеток эмбриональной печени человека больным гемобластозами (Ин-т биофизики МЗ СССР, Москва) // Терапевтический архив. – 1986. - т.58, N9, С.9-18.
39. Simonova L.I., Shantyr' V.I., Morozov I.A., Lakiza B.S., Trunov N.P. [Processing and transplantation of preserved (-196 degrees) fetal hemopoietic tissue]// Probl Gematol Pereliv Krovi. – 1976. – V.21. - N12. – P.20-23

40. Каргин В. Д., Абдулкадыров К. М. Применение трансплантаций эмбриональных гемопоэтических и лимфоидных органов и клеток при лечении заболеваний системы крови // Гематология и трансфузиология. – 1983. - N7. - С.16-22.
41. Пяткин Э. К., Баранов А. Э., Гордеева А. А. и др. Цитогенетический контроль трансплантации клеток эмбриональной печени больным гемобластозами после лечения цитостатиками в больших дозах и тотального гамма-облучения // Мед. Радиология. – 1982. - т.27. - N11. -С.19-24.
42. Шерешков С. И., Алексеев Л. П., Ярцев М. Н. Трансплантация эмбриональной печени при тяжелой комбинированной иммунной недостаточности (Обзор) // Терапевтический архив. – 1988. - N5. - С. 36-42
43. Шерешков С. И., Бугаидзе Л. И., Баранов А. Э. Трансплантация клеток фетальной печени от многих эмбрионов больным гемобластозами, кондиционированным общим облучением и химиопрепаратами // Гематология и трансфузиология. – 1984. – т.29, N4. - С.9-15.
44. Бубнов А. Н., Абдулкадыров К. М., Балашова В. А. и др. Методика получения и некоторые морфофункциональные характеристики гемопоэтических клеток фетальных органов // Проблемы гематологии – 1982. – т. 27. - N5. - С.12-16
45. Кулаков В.И., Сухих Г.Т., Молнар Э.М. Иммунноцитотерапия. Новое направление в трансплантации фетальных тканей .. Бюлл. эксп. биол. и мед. – 1994. - т.117. - N4. - С.412-417
46. Кулаков В.И., Сухих Г.Т., Молнар Э.М. Трансплантация фетальных тканей человека; анализ состояния проблемы и перспективы развития // Трансплантация фетальных тканей и клеток человека. – 1996. - С.5-10.
47. Gale R.P. Fetal liver transplantation in hematologic disorders // Prog Clin Biol Res. Fetal Liver Transplant. - Alan R. Liss, Inc. – 1985. – N.193. – P.293-297
48. Gale R.P. Fetal liver transplants // Bone Marrow Transplant. – 1992. - N9. – P.118-20 (Review)
49. Kochupillai V., Sharma S., Francis S., Mehra N.K., Nanu A., Kalra V., Menon P.S., Bhargava M. Bone marrow reconstitution following human fetal liver infusion (FLI) in sixteen severe aplastic anemia patients // Prog Clin Biol Res. Fetal Liver Transplant. - Alan R. Liss, Inc. – 1985. – N.193. – P.251-265
50. Kochupillai V., Sharma S., Francis S., Mehra N.K., Nanu A., Verma I.C., Takkar D., Kumar S., Gokhale U. Fetal liver infusion: an adjuvant in the therapy of acute myeloid leukemia (AML) // Prog Clin Biol Res. Fetal Liver Transplant. - Alan R. Liss, Inc. – 1985. - N193. – P.267-279
51. Kochupillai V., Sharma S., Francis S., Nanu A., Mathew S., Bhatia P., Dua H., Kumar L., Aggarwal S., Singh S., et al. Fetal liver infusion in aplastic anaemia // Thymus. – 1987. – V.10. - N1-2. – P.95-102
52. Kochupillai V., Sharma S., Francis S., Nanu A., Verma I.C., Dua H., Kumar L., Aggarwal S., Singh S. Fetal liver infusion in acute myelogenous leukaemia // Thymus. – 1987. – V10. - N1-2. – P.117-124
53. Seto S., Miyake T., Hirao T. Reconstitution of cell-mediated immunity in severe combined immunodeficiency following fetal liver transplantation // Tokai J Exp Clin Med. – 1985. – V.10. - N2-3. – P.233-238
54. Betend B., Touraine J.L., Hermier M., Francois R. Restoration of mixed and severe immunologic deficiency, by fetal liver and thymus graft // Arch Fr Pediatr. – 1979. – V.36. - N10. – P.995-1005
55. Touraine J.L. European experience with fetal tissue transplantation in severe combined immunodeficiency (SCID) // Birth Defects Orig Artic Ser. – 1983. – V.19. – N3. – P.139-142
56. Izzi T., Polchi P., Galimberti M., Delfini C., Moretti L., Porcellini A., Manna A., Sparaventi G., Giardini C., Angelucci E., P.Politi, G.Lucarelli Fetal liver transplant in aplastic anemia and acute leukemia // Prog Clin Biol Res. Fetal Liver Transplant. - Alan R. Liss, Inc. – 1985. – P.237-249

57. Lucarelli G., Izzi T., Delfini C., Grilli G. Fetal liver transplantation in severe aplastic anemia // Haematologica. – 1978. – V.63. - N1. – P.93-4
58. Lucarelli G., Izzi T., Porcellini A., Delfini C., Galimberti M., Moretti L., Polchi P., Agostinelli F., Andreani M., Manna M., Dallapiccola B. Fetal liver transplantation in 2 patients with acute leukaemia after total body irradiation // Scand J Haematol. - 1982. – V.28. - N1. – P.65-71
59. Lucarelli G., Izzi T., Porcellini A., Delfini C. Infusion of fetal liver cells in aplastic anemia // Hamatol Bluttransfus. – 1979. - N24. – P.167-70
60. Jiang N., Jiang C., Tang Z., Zhang F., Li S., Jiang D. Human foetal brain transplant trials in the treatment of Parkinsonism. –-Acta Acad Med Shanghai. - 1987. N14. – P.1
61. Lou F.D., Liu H.C., Wang Y.Z. [Short-term and multiple fetal liver transplantations for the treatment of aplastic anemia: report of 15 cases] // Zhonghua Nei Ke Za Zhi. – 1985. – V.24. -N2. – P.65-67, 124
62. Lou F.D., Liu H.C. [Clinical use of hematopoietic stem cells from fetal livers] // Zhonghua Nei Ke Za Zhi. – 1986. – V.25 – N7. – P.433-435 (Review)
63. Meng P.L, Fei R.G., Gu D.W, Yie W.Z., Liu B.T., Yan F., Yu Y.Y., Mai Z.G., Chen B.Z., Zhu L.X., et al. Allogeneic fetal liver transplantation in acute leukemia // Prog Clin Biol Res. Fetal Liver Transplant. Alan R. Liss, Inc. – 1985. – N.193. – P.281-291
64. Qian F.W. [Transfusion of fetal liver cells in the treatment of hematologic disease] // Zhonghua Yi Xue Za Zhi. – 1986. – V.66. – N.4. – P.237-239
65. Wu C.T. Experimental studies on hemopoietic stem cells of fetal liver origin and its clinical application // Prog Clin Biol Res. Fetal Liver Transplant. - Alan R. Liss, Inc. – 1985. – N.193. – P.95-112
66. Xue L.F., Zhang X.W., Yang L., Liu Y.X. [Fetal liver cell transfusion in chemotherapy of malignant tumors and blood diseases] / Zhonghua Zhong Liu Za Zhi. – 1986. – V.8 - N5. – P.367-369
67. Gorski A. [Transplantation of fetal liver cells] // Pol Arch Med Wewn. – 1977. – V.58. - N3. – P.303-306
68. Ratajczak M.Z. Experimental aspects of transplantation of haemopoietic cells of fetal liver // Arch Immunol Ther Exp. - Warszava. – 1988. – V.36. - N2. – P.235-243
69. Buhrdel P., Rosenkranz M,. Schwenke H., Kuhndel K., Thierbach V. Transplantation of stem cells of embryonic liver in a patient with severe combined immunodeficiency // Acta Paediatr Hung. – 1985. – V.26. - N3. – P.233-240
70. Champlin R.E, Mitsuyasu R.T, Gale R.P. Transplantation of T lymphocyte depleted bone marrow to prevent graft-versus-host disease: its implications for fetal liver transplantation // Prog Clin Biol Res. Fetal Liver Transplant. - Alan R. Liss, Inc. – 1985. - N193. – P.315-25
71. Touraine J.L., Roncarolo M.G., Marseglia G.L., Souillet G., Betend B., Betuel H., Touraine F., Royo C., Philippe N., Francois R. Fetal liver transplantation in immunodeficiencies and inborn errors of metabolism // Prog Clin Biol Res. Fetal Liver Transplant. - Alan R. Liss, Inc. – 1985. -N193. – P.299-313
72. Bhargava M., Karak A.K., Sharma S., Kochupillai V. Bone marrow recovery following fetal liver infusion (FLI) in aplastic anaemia: morphological studies // Thymus. – 1987. – V.10. - N1-2. P.103-108
73. Gale R.P. Development of the immune system in human fetal liver // Thymus. – 1987. – V.10. - N1-2. – P.45-56
74. Gale R.P., Touraine J.L., Kochupillai V. Synopsis and prospectives on fetal liver transplantation // Thymus. – 1987. - V10. - N1-2. – P.1-4
75. Kelemen E., Janossa M., Calvo W., Fliedner T.M., Bofill M., Janossy G. What kind of morphologically recognizable haemopoietic cells do we inject when doing foetal liver infusion in man? // Thymus. – 1987 – V.10. – N.1-2. – P.33-44
76. Wu C.T., Ye G.Y. Advances in experimental studies and clinical application of fetal liver cells // Thymus. – 1987. – V.10. -N1-2. – P.109-116

77. Gale R.P. Fetal liver transplantation in aplastic anemia and leukemia // Thymus. – 1987. – V.10. - N1-2. – P.89-94
78. Baranov A., et al. Bone marrow transplantation after Chernobyl nuclear accident // N.Eng. J.Med. – 1989. – N321. - 205-212.
79. Baranov AE, Gus'kova AK, Protasova TG. [Experience in treating the victims of the accident at the Chernobyl Atomic Electric Power Station and the immediate disease outcomes] // Med Radiol. - Moskow. – 1991. – V.36. – N3. – P.29-32
80. Gale R.P., Reisner Y., The role of bone-marrow transplants after nuclear accidents // Lancet. – 1988. – P.923-926
81. Githens J.H. Editorial: Immunologic reconstitution with fetal tissue // N Engl J Med. – 1976. – V.294. - N20. – P.1116-1167
82. Improving Survival in Acquired Immunodeficiency Syndrome: Is Experience Everything? // Editorial JAMA. - 1989. – V.261. – N20. – P.3016-3017
83. Royo P.C., et all. The Place of Fetal Liver Transplantation in Treatment of Inborn Errors of Metabolism // J. Inher. Metab. Dis. – 1991. - N14. - P.619-626.
84. Buckley R.H., Whisnant K.J., Schiff R.I., Gilbertsen R.B., Huang A.T., Platt M.S. Correction of severe combined immunodeficiency by fetal liver cells // N Engl J Med. – 1976. – V.294. - N20. – P.1076-81
85. Touraine J.L., Laplace S., Rezzoug F., Sanhadji K., Veyron P., Royo C., Maire I., Zabot M.T., Vanier M.T., Rolland M.O., et al. The place of fetal liver transplantation in the treatment of inborn errors of metabolism // J Inherit Metab Dis. - 1991. – V.14. - N4. - 619-626
86. Touraine J.L. In utero fetal liver cell transplantation in the treatment of immunodeficient or thalassemic human fetuses // Transfus Sci. – 1993. – V.14. - N3. – P.299-304
87. Touraine J.L. Rationale and results of in utero transplants of stem cells in humans // Bone Marrow Transplant. – 1992. - N10. – P.121-126
88. Sanberg P.R,. Brundin P. Cell transplantation and neuroscience // Cell Transplant. – 1999. – V.8. - N1. - P.3-6
89. Brundin P., Nilsson P.G., Strecker R.E., Lindvall O., Astedt B., Björklund A. Behavioural effects of human fetal dopamine neurons grafted in a rat model of Parkinson's disease // Exp Brain Res. – 1986. – N.65. – P.235-240
90. Lindvall O., Backlund E.O., Farde L., Sedvall G., Freedman R., Hoffer B., Nobin A., Seiger A., Olson L. Transplantation in Parkinson's disease: two cases of adrenal medullary grafts to the putamen // Ann Neurol. – 1987. –V.22. - N4. – P.457-468
91. Lindvall O., Bjorklund A. Transplantation strategies in the treatment of Parkinson's disease: experimental basis and clinical trials // Acta Neurol Scand Suppl. - 1989. - N126. – P.197-210 (Review)
92. Björklund A., Stenevi U., Schmidt R.H., Dunnett S.B., Gage F.H. Intracerebral grafting of neuronal cell suspensions. I. Introduction and general methods of preparation // Acta Physiol Scand Suppl. – 1983. – V.522. - 1-7
93. Hitchcock E.R., Kenny B.G., Henderson B.T., Clough C.G., Hughes R.C., Detta A. A series of experimental surgery for advanced Parkinson's disease by foetal mesencephalic transplantation // Department of Neurosurgery, University of Birmingham, Midland Centre for Neurosurgery and Neurology, Smethwick, Birmingham, U. K. - Acta Neurochirurgica. - Supplementum. – 1991. - V.52. – P.54-57
94. Freeman T.B., Sanberg P.R. Peer review for fetal tissue transplantation research (editorial) // Cell Transplantation. – 1992. – V.1 – N.4. – P.271-273
95. Freed C.R., Breeze, R.E., Rosenberg N.L., et al. Transplantation of human fetal dopamine cells for Parkonson’s disease. Results at 1 year // Arch. Neurol. – 1990. – V47. – P.505-512
96. Freed Curt R., Paul E. Greene, Robert E. Breeze, Wei-Yann Tsai, William DuMouchel, Richard Kao, Sandra Dillon, Howard Winfield, Sharon Culver, John Q. Trojanowski, David Eidelberg, Stanley Fahn Transplantation of Embryonic Dopamine Neurons for Severe

Parkinson's Disease // The New England Journal of Medicine, - 2001 - V.344. - N.10. – P.710-719.

97. Ben R., Ji-Chang F., Yao-Dong B., Yie-Jian L., Yi-Fang Z. Transplantation of cultured fetal adrenal medullary tissue into the brain of Parkinsonian. Department of Neurosurgery and Endocrinology, Dalian Municipal Central Hospital, China // Acta Neurochirurgica. – 1991. - Supplementum. – V.52. – P.42-44
98. Savel'ev S.V. [Transplantation of embryonal brain tissue]. (Review) Original Transplantatsiia tkani embrional'nogo golovnogo mozga // Arkhiv Patologii. – 1992. - V.54. - N11. – P.43-6.
99. Blagodatskii M.D. Sufianov A.A. Larionov S.N. Kibort R.V. Seminskii I.Zh. Manokhin P.A. [The transplantation of embryonic nerve tissue in syringomyelia: initial clinical experience]. Original Transplantatsiia embrional'noi nervnoi tkani pri siringomielii: pervyi klinicheskii opyt // Zhurnal Voprosy Neirokhirurgii Imeni N - N - Burdenko. – 1994. - N3. – P.27-29; 1994. – V.85.- N6. – P.1463-1471
100. Цимбалюк В.І., Пічкур Л.Д., В.А. Руденко, Н.О. Пічкур Клініко-імунологічні дослідження впливу нейротрансплантації при спастичних формах дитячого церебрального паралічу // Трансплантологія. – 2000. - т.1. - №1. – С.156-157.
101. Subrt O., Tichy M., Vladyka V., Hurt K. Grafting of fetal dopamine neurons in Parkinson's disease // The Czech experience with severe akinetic patients. Department of Neurosurgery, Charles University Medical School, Prague, Czech. – Wien. - Acta Neurochir Suppl. – 1991. - N52. – P.51-53
102. Zabek M. Mazurowski W. Dymecki J. Stelmachow J. Gawur B. Trautsolt W. Zawada E. [Transplantation of fetal dopaminergic cells in Parkinson disease] [Polish] Original Przeszczepianie plodowych komorek dopaminergicznych w chorobie Parkinsona / Neurologia i Neurochirurgia Polska. – 1992. - Suppl 1. – P.13-19
103. Boer G.J. The Network of European CNS Transplantation and Restoration (NECTAR): an introduction on the occasion of its tenth meeting // Cell Transplant. – 2000. – V.9. - N2. – P.133-137
104. Neural transplantation in neurodegenerative disease // Novartis Found Symp. – 2000. – V. 231 – P. 12-14
105. Lindvall O. Neural transplantation in Parkinson’s disease // Novartis Found Symp. – 2000. – V. 231 – P.110-23; discussion P.123-128, 145-147.
106. Bjorklund A. Cell replacement strategies for neurodegenerative disorders // Novartis Found Symp 2000;231. – P.7-15; discussion 16-20
107. Lindvall O., Widner H., Rehncrona S., Brundin P., Odin P., Gustavii B., Frackowiak R., Leenders K.L., Sawle G., Rothwell J.C., Björklund A., Marsden C.D. Transplantation of fetal dopamine neurons in Parkinson's disease: one-year clinical and neurophysiological observations in two patients with putaminal implants // Ann Neurol. – 1992. - N31. – P.155-165
108. Spencer D.D., Robbins R.J., Naftolin F., Phil D., Marek K.L, Vollmer T., Leranth C., Roth R.H., Price L.H., Gjedde A., Bunney B.S., Sass K.J., Elsworth J.D., Kier E.L., Makuch R., Hoffer P.B., Redmond Jr. D.E. Unilateral transplantation of human fetal mesencephalic tissue into the caudate nucleus of patients with Parkinson's disease // New Engl J Med. – 1992. – V.327. – P.1541-1548
109. Hagell P., Brundin P.. Cell survival and clinical outcome following intrastriatal transplantation in Parkinson disease // J Neuropathol Exp Neurol. - 2001. – V.60. - N8. – P.741-52
110. Piccini P., Lindvall O., Bjorklund A., Brundin P., Hagell P., Ceravolo R., Oertel W., Quinn N., Samuel M., Rehncrona S., Widner H., Brooks D.J.. Delayed recovery of movement-related cortical function in Parkinson's disease after striatal dopaminergic grafts // Ann Neurol. – 2000. – V.48. - N5. – P.689-95
111. Kordower J. H., Freeman Th. B., Barry J. S. at all. Neuropathological Evidence of Graft Survival and Striatal Reinnervation after the Transplantation of Fetal Mesencephalic Tissue

in a Patient with Parkinsons Disease // The New England Journal of Medicine. - 1995. - V.332. N17. - P. 1118-1124.

112. Fine A. Transplantation of fetal cells and tissue: an overview // CMAJ. – 1994. – V.151. - N9. – P.1261-1268. Review
113. Aiuti F., Businco L., Fiorilli M., De Martino M., Vierucci A. Fetal liver transplantation in two infants with severe combined immunodeficiency // Transplant Proc. – 1979. – V.11. - N1. – P.230-234
114. American Medical Association. Medical applications of fetal tissue transplantation // JAMA. – 1990. – V.263. – P.565-570
115. Bakay R.A. Sladek J.R. Jr. Fetal tissue grafting into the central nervous system: yesterday, today, and tomorrow [see comments] // Neurosurgery. – 1993. – V.33. - N4. – P.645-647.
116. Cohen C. B., Jousen A. R. The Future of the Fetal Tissue Bank // Science. – 1993. - V.262. - P.1663-1665.
117. Crombleholme T.M., Langer J.C., Harrison M.R., Zanjani E.D. Transplantation of fetal cells // American Journal of Obstetrics & Gynecology. – 1991 – V.164. - N1. – P.218-230
118. Hollands P. Transplantation of embryonic haemopoietic stem cells without prior recipient X-irradiation // Br J Haematol. – 1988. – V.69. - N4. – P.437-440
119. Jones Deborah. Halifax hospital first in Canada to proceed with controversial fetal-tissue transplant // Can. med. assoc. j. – 1992. – V.146. - N3. – P.389-391.
120. Kohgo Y., Sakamaki S., Hirayama Y., Matsunaga T., Niitsu Y. Hematopoietic stem cell transplantation. Hokkaido Igaku Zasshi // Hokkaido Journal of Medical Science. - 1995 – V.70. – N2. – P.241-245.
121. Kupsch A., Sauer H., Oertel W.H. Transplantation of dopamine producing nerve cells: a new therapy in idiopathic Parkinson syndrome? (Review) (German) // Physiologisches Institut, Ludwig-Maximilians-Universitat // Nervenarzt. - Munchen.- 1991. – V.62. - N2. – P.80-91
122. Lowenberg B., Vossen J.M., Dooren L.J. Transplantation of fetal liver cells in the treatment of severe combined immunodeficiency disease // Blut. – 1977. – V.34. - N3. – P.181-95
123. Nelson R. M. A Policy concerning the therapeutic use of human fetal tissue in transplantation // Western Journal of Medicine. – 1990. – V.152. – N.4. – P.447-448
124. Neural transplantation into the CNS. Selected articles from the 1st American Society for Neural Transplantation meeting. Clearwater, Florida, May 5-7, 1994 // Cell Transplantation. – 1995. – V.4. - N1. – P.1-154
125. Raudrant D., Touraine J.L., Rebaud A. In utero transplantation of stem cells in humans: technical aspects and clinical experience during pregnancy // Bone Marrow Transplant. – 1992. – V.9. - Suppl 1. – P.98-100
126. Touraine J.L., Roncarolo M.G., Bacchetta R., Raudrant D., Rebaud A., Laplace S., Cesbron P., Gebuhrer L., Zabot M.T., Touraine F., et al. Fetal liver transplantation: biology and clinical results // Bone Marrow Transplant. – 1993. – V.11. - Suppl 1. – P.119-122. Review
127. Fact Sheet on Human Pluripotent Stem Cell Research Guidelines // NIH Stem Cell Information Archives, January 23, 2001 // http://www.nih.gov/news/stemcell/stemfactsheet.htm
128. Hajdu K., Tanigawara S., McLean L.K., Cowan M.J., Golbus M.S. In utero allogeneic hematopoietic stem cell transplantation to induce tolerance // Fetal Diagn Ther. – 1996. – V.11. - N4. - P241-248
129. Hollands P. Embryonic stem cell grafting: the therapy of the future? // Hum Reprod. – 1991. – V.6. - N1. – P.79-84. Review
130. Holyoake T. L., Nicolini F. E., Eaves C. J. Functional differences between transplantable human hematopoietic cells from fetal liver, cord blood, and adult marrow // Experimental Hematology. – 1999. - N27. – P.1418-1427

131. Roncarolo M.G., Bacchetta R., Bigler M., Touraine J.L., de Vries J.E., Spits H. A SCID patient reconstituted with HLA-incompatible fetal stem cells as a model for studying transplantation tolerance // Blood Cells. – 1991. – V.17. - N2. – P.391-402
132. Roncarolo M.G., Bacchetta R. T cell repertoire and tolerance after fetal stem cell transplantation // Bone Marrow Transplant. – 1992. - N9. - Suppl 1. – P.127-128
133. Touraine J.L., Griscelli C., Betuel H., Durandy A., Betend B., Souillet G. Chimerism following fetal liver transplantation: cell cooperation despite HLA mismatch // Birth Defects Orig Artic Ser. – 1983. - V.19. - N3. – P.143-145
134. Touraine J.L., Bacchetta R., Yssel H. de Vries J., Roncarolo M.G. Transplantation of mismatched human fetal liver cells: tolerance induction via clonal deletion and clonal anergy. INSERM U 80, Hopital Ed. Herriot, Lyon, France // Transplantation Proceedings. - 1995. – V.27. - N1. – P.622-624
135. Yoder M.C., Hiatt K. Engraftment of embryonic hematopoietic cells in conditioned newborn recipients // Blood. – 1997. – V.89. – N6. – P.2176-183
136. Bacchetta R., Vandekerckhove B.A, Touraine J.L., Bigler M., Martino S., Gebuhrer L., de Vries J.E., Spits H., Roncarolo M.G. Chimerism and tolerance to host and donor in severe combined immunodeficiencies transplanted with fetal liver stem cells // J Clin Invest. – 1993. – V.91. – N3. – P.1067-1078
137. Ek S., Westgren M., Pschera H., Seiger A., Sundstrom E., Bui TH., Ringden O. Screening of fetal stem cells for infection and cytogenetic abnormalities // Fetal Diagnosis & Therapy. – 1994 – V.9. – N6. – P.357-361.
138. Rice H.E., Hedrick M.H., Flake A.W., Donegan E., Harrison M.R. Bacterial and funqal contamination of human fetal liver collected transvaginally for hematopoietic stem cell transplantation // Fetal Diagnosis & Therapy. – 1993 – V.8. – N2. – P.74-78
139. Ek S., Ringden O., Markling L., Westgren M. Cryopreservation of fetal stem cells. Department of Obstetrics and Gynecology, Karolinska Institute, Huddinge Hospital, Sweden // Bone Marrow Transplantation. – 1993. – V.11. - Suppl 1. – P.123
140. Meagher R.C., Herzig R.H. Techniques of harvesting and cryoprezervation of stem cellc // Hematology - Oncology Clinics of North America. - 1993– – V.7. – N3. – P.501-533
141. Westgren M. Ek S. Bui T.H. Hagenfeldt L. Markling L. Pschera H. Seiger A. Sundstrom E. Ringden O. Establishment of a tissue bank for fetal stem cell transplantation // Acta Obstetricia et Gynecologica Scandinavica. – 1994. – V.73. - N5. – P.385-388.
142. Белоус А.М., Грищенко В.И. Криобиология. - К.: Наук. Думка, 1994. - 431 с.
143. Грищенко В.И., Лобынцева Г.С., Вотякова И.А. и др. Гемопоэтические клетки эмбриональной печени. - Киев, Наук. Думка, 1988. - 190 с.
144. Федотенков А. Г., Шишкина И. Д., Данилова Л. А., Змиевская К. М., Воронцова Э. И., Герасимова Н. А. Консервирование костного мозга при низких температурах для его клинического применения // Проблемы гематологии и переливания крови. - 1966. – т.11. - N1. - С.45-50
145. Pschera H. Stem cell therapy in utero // J Perinat Med. – 2000. – V.28. - N5. – P.346-354. Review
146. Westgren M. Ringden O. Fetal to fetal transplantation // Acta Obstetricia et Gynecologica Scandinavica. – 1994. – V.73. - N5. – P.371-372
147. Foglia R.P., DiPreta J., Statter M.B., Donahoe P.K. Fetal allograft survival in immunocompetent recipients is age dependent and organ specific // Ann Surg. – 1986. – V.204. - N4. – P.402-140
148. Freeman T.B., Sanberg P.R., Nauert G.M., Boss B.D., Spector D., Olanow C.W., Kordower J.H. The influence of donor age on the survival of solid and suspension intraparenchymal human embryonic nigral grafts. Division of Neurosurgery, University of South Florida, Tampa 33606, USA // Cell Transplantation. – 1995. – V.4. -N1. –P.141-154
149. Lansdorp P.M., Dragowska W., Mayani H. Ontogeny-related changes in proliferative potential of human hematopoietic cells // Journal of Experimental Medicine. – 1993. – V.178. - N3. – P. 787-791

150. Smikodoub A.I, Novitskaya A.V, Yefimov A.S. Experience in treatment of patients suffering from diabetes mellitus with the use of fetal cell suspensions // Cell Transplantation // Abstracts of Fouth International Congress "The Cell Transplantation Society. Montreux / Switzerland, March 21-24, 1999. – 1999. – V.8. - N2. - P.200-121.
151. Smikodoub Alexander, Karpenko Alexey. Psychophysiological changes in patients due to fetal cell transplantations // Cell Transplantation // Abstracts of Fouth International Congress "The Cell Transplantation Society. Montreux / Switzerland, March 21-24, 1999. – 1999. - V.8. - N2. - P.200, 124.
152. Smikodoub A.I., Bushneva V.A. New method of treatment the patients suffering from autoimmune intestinal diseases with the use of embryonic stem cell transplantation cellular therapy // Abstracts of Institute Pasteur Euroconferences. Paris, France, 3-4 February 2000. – Paris. – 2000. - P.20..
153. Embryonic Tissues Center EmCell - http://www.emcell.com.
154. Смикодуб А.И., Новицкая А.В., Дроздовая В.Д., Лифшиц Э.А., Лобынцева Г.С., Вотякова И.А. Клинический случай лечения приобретенной апластической анемии гемопоэтическими клетками эмбриональной печени человека // "Врачебное дело". – 1994. - N3. - С. 104-108.
155. United State patent. Number: 5,811,089. Date of patent: Sep. 22, 1998. Pharmaceutical preparation based on fetal suspension and methods of treating acquired immune deficiency syndrome (HIV infection). Inventors: Smikodub A.I., Markov I.S., Pilipchak E.M.
156. United State patent. Number: 6,184,033 B1. Date of patent: Feb. 6, 2001. Medicinal preparation based on fetal suspension having immune substituting effect for patients with acquired immune deficiency syndrome (HIV infection). Inventor: Smikodub A.I.
157. Smikodub Alexander, Tretyak Natalya, Snigyr Nataliya Treatment of cytostatic agranulocytosis in patients with leukemia by human embryonic liver hemopoietic cells. Abstracts // Society for Minimally Invasive Therapy Ninth Annual International Meeting 14-16 July 1997, Kyoto, Japan // Minimally Invasive Therapy. – 1997. - V.5. – Suppl. 1. - P.67.
158. Smikodub A.I., Yu.A. Grinevich, G.D . Bendyug, L.V. Radziyevskaya, V.V. Snigir, N.N. Kharanovskaya, I.Yu. Gluhovskaya, V.S. Ivankova Transplantation of cryopreserved fetal liver hemopoietic cells in complex treatment of cancer patients // The 25th Anniversary Meeting of the International Society for oncodevelopmental biology and medicine 19-24 september 1997, Montreux, Switzerland // Tumor biology. – 1997. - N18. - Suppl 2. - P.127.
159. Smikodub Alexandr, Pilipchak Elena Treatment of hiv-infection (AIDS) with fetal stem cells. Abstracts // Society for Minimally Invasive Therapy Ninth Annual International Meting 14-16 July 1997, Kyoto, Japan // Minimally Invasive Therapy. – 1997. - V.5. - Suppl 1. - P.67.
160. Smikodoub Alexander, Pilipchak Elena New method of immune substituting therapy with the use of fetal cells in cases of HIV infection (AIDS) // Abstracts of Fouth International Congress of The Cell Transplantation Society. Montreux / Switzerland, March 21-24, 1999 // Cell Transplantation. – 1999. – V.8. - N2. - P.120.
161. Смикодуб О.І. Лікування хворих на вперше виявлений інсулінозалежний цукровий діабет гемопоетичними клітинами ембріональної печінки // Ендокринологія. - Київ, 2001 р. – т.6. - № 1. - С. 80-88.
162. Новицька А. В.Лікування хворих на цукровий діабет з імунними та гематологічними порушеннями гемопоетичними клітинами ембріональної печінки людини // Автореф. канд.дис. Інститут ендокринології та обміну речовин ім.В.П.Комісаренка АМН України. Київ, 2000. - с.21.
163. Снігир Н.В. Застосування гемопоетичних клітин ембріональної печінки людини в лікуванні питостатичної мієлодепресії у онкологічних хворих. Національна Академія Наук України Інститут експериментальної патології, онкології і радіобіології їм. Р.С. Кавецького // Автореферат дисертації на здобуття наукового ступеня кандидата медичних наук. - Київ, 2001. - с.20.

164. Короткий В.Н., Смикодуб А. И., Безродный Б.Г., Мартынович Л.Д., Карташов Б.Т., У. Огадинма, Иванов Н. А. Трансплантация клеток эмбриональной печени человека в комплексном хирургическом лечении больных раком головки поджелудочной железы // Экспериментальная онкология. – 2000. – т.22. – дополнение № 236. Тезисы II съезда онкологов стран СНГ. «Онкология 2000», Украина, Киев, 23-26 мая 2000 г.
165. Pylypchak OM. [Hemopoietic cells from human embryonic liver in the treatment of HIV/AIDS] // Lik Sprava. – 1998. - N8. – P.116-118
166. Smikodoub A.I., Radzievskaya L.V., Snigir N.V. Treatment of cytostatic agranulocytosis by means of transplantation of fetal liver hemopoietic cells // Cell Transplantation. – 1999. - V.8. - N2. – P.200, poster N 123. Abstracts of Fouth International Congress of The Cell Transplantation Society. Montreux / Switzerland, March 21-24, 1999.
167. Гриневич Ю.Я., Смикодуб О.І., Бендюг Г.Д., Радзієвська Л.В., Снігир Н.В., Глуховська І.Ю., Іванкова В.С., Храновська Н.М. Застосування трансплантації кріоконсервованих гемопоетичних клітин ембріональної печінки в комплексному лікуванні хворих на злоякісні новоутворення. Методичні рекомендації. Мінздрав України. - Київ, 1999
168. Смикодуб О.І., Гайдукова С.М., Третяк Н.М., Снігир Н.В. Лікування мієлотоксичного агранулоцитозу у хворих на гострий лейкоз гемопоетичними клітинами ембріональної печінки людини. Методичні рекомендації. Мінздрав України. Академія медичних наук України. - Київ, 2001. - С.13.
169. Єфимов А.С., Смикодуб О.І., Новицька А.В. Лікування хворих з впершевиявленим інсулінозалежним цукровим діабетом гемопоетичними клітинами ембріональної печінки. Методичні рекомендації. Мінздрав України. Академія медичних наук України. - Київ, 2000. - С.16.
170. Smikodub A.I. Embryonic stem cell transplantation in anti-cancer treatment // Supportive Care in Cancer. – 2000. - V.8. N3. – P.256.
171. Smikodub O. Application Of Embryonic Cell Suspensions In Patients With Solid Tumors Before Initiation Of Radical Treatment // Supportive Care in Cancer, 2002. – V.10 – N.4 – P.96.
172. Smikodub O., Snigir N. Febrile neutropenia treatment of patients with acute leucosis by fetal stem cells // Abstracts of the 3rd International Symposyum on Febril Neutropenia. Brussels, Belgium, December 10-13, 1997 // Supportive Care in Cancer. – 1998. – V.6. - N3. - P.326
173. Smith R. T. Cancer and the Immune System // Pediatrics Clinics of North America. – 1994. – V.41. - N4. - P.841-849.
174. Гріневич Ю.А., Смикодуб О.І., Бендюг Г.Д., Храновська Н.М., Іванкова В.С., Снігирь Н.В., Радзієвська Л.В. Можливості коррекції гематологічних порушень в процесі променевої терапії хворих на гінекологічний рак за допомогою трансплантації клітин ембріональної печінки // Променева діагностика, променева терапія. Збірка наукових робіт асоціації радіологів України. Випуск № 6. - Київ, 1999. - С.52-58.
175. Смикодуб А.И., Бушнева В.А. Иммунологические нарушения при неспецифических воспалительных заболеваниях кишечника // Імунологія та алергологія. – 2000. - №4. – С.28-33
176. Смикодуб А.И., Бушнева В.А. Лечение неспецифических воспалительных заболеваний кишечника в терапевтической практике // Сучасна гастроентерологія. – 2001. - № 1. – С.52-57
177. Approval Process for the Documentation of Compliance with NIH Guidelines on the Use of Human Pluripotent Stem Cells in NIH Intramural Research // NIH Stem Cell Information Archives, January 16, 2001 // http://www.nih.gov/news/stemcell/irpnotice_011601.htm
178. Implementation Issues for Human Embryonic Stem Cell Research // National Institutes of Health Stem Sell Information, December 19, 2001 // http://grants.nih.gov/grants/stem_cells.htm
179. Touraine J.L. Stem cell transplantation in primary immunodeficiency, with special reference to the first prenatal, in utero, transplants // Allergologia et Immunopathologia. – 1991. – V.19. - N2. – P.49-51

180. Balashova VA, Abdulkadyrov KM. [Cellular composition of hemopoietic tissue of the liver and spleen in the human fetus] // Arkh Anat Gistol Embriol. – 1984. –V.86. - N4. – P.80-83
181. Абдулкадыров К.М., А. А. Ганакиев, Э. Р. Шилова, Т. И. Попова, Розанова О. Э., Кацадзе Ю. Л. Результаты лечения больных апластической анемией различными дозами антилимфоцитарного глобулина // Терапевтический архив. - 1995. - т. 67. - N 8. - с. 51-54.
182. Gale RP. Henon P. Juttner C. Blood stem cell transplants come of age // Bone Marrow Transplantation. – 1992. – V.9. – N3. – P.151-155.
183. Lindvall O, Björklund A, Widner H (eds) Intracerebral transplantation in movement disorders. – Amsterdam. – Elsevier. - 1991
184. Lindvall O, Bjorklund A. First step towards cell therapy for Huntington's disease // Lancet. – 2000. - V356. - N9246. – P.1945-1946
185. Lindvall O., Brundin P., Widner H., Rehncrona S., Gustavii B., Frackowiak R., Leenders K.L., Sawle G., Rothwell J.C., Marsden C.D., Björklund A. Grafts of fetal dopamine neurons survive and improve motor function on Parkinson's disease // Science. – 1990. - N247. – P.574-577
186. Lindvall O. Parkinson disease. Stem cell transplantation // Lancet. – 2001. –V.358. - Suppl:S48
187. Lindvall O. Cell transplantation: a future therapy for Parkinson's disease?. [Review] // Neurologia. – 1994. – V.9. - N3. – P.101-107
188. Lindvall O. Cerebral implantation in movement disorders: state of the art // Mov Disord. 1999. - V.14. - N2. – P.201-205. Review
189. Lindvall O. Transplants in Parkinson's disease // Eur Neurol. – 1991. – V.31. - Suppl 1. – P.17-27. Review.
190. Sramka M. Rattaj M. [The legal and ethical aspects of nerve tissue transplantation]. [RUSSIAN] Original Pravovye i eticheskie aspekty neirotransplantatsii // Zhurnal Voprosy Neirokhirurgii Imeni N - N - Burdenko. – 1992. - N6. – P.12-13
191. Wolff H.P. [Medical use of fetal cells and tissue: ethical aspects]. [German] Original Die medizinische Nutzung fetaler Zellen und Gewebe: ethische Aspekte // Diskussionsforum Medizinische Ethik. – 1992. - N1. – P.I-IV.

Reference (alphabetic)


1. Adams B. Restoring hope: lifting the ban on fetal tissue transplantation research // Academic Medicine. – 1992. – V.67. - N4. – P.246-247
2. Aiuti F., Businco L., Fiorilli M., De Martino M., Vierucci A. Fetal liver transplantation in two infants with severe combined immunodeficiency // Transplant Proc. – 1979. – V.11. - N1. – P.230-234
3. American Medical Association. Medical applications of fetal tissue transplantation // JAMA. – 1990. – V.263. – P.565-570
4. Approval Process for the Documentation of Compliance with NIH Guidelines on the Use of Human Pluripotent Stem Cells in NIH Intramural Research // NIH Stem Cell Information Archives, January 16, 2001 // http://www.nih.gov/news/stemcell/irpnotice_011601.htm
5. Bacchetta R., Vandekerckhove B.A, Touraine J.L., Bigler M., Martino S., Gebuhrer L., de Vries J.E., Spits H., Roncarolo M.G. Chimerism and tolerance to host and donor in severe combined immunodeficiencies transplanted with fetal liver stem cells // J Clin Invest. – 1993. – V.91. – N3. – P.1067-1078
6. Bakay R.A. Sladek J.R. Jr. Fetal tissue grafting into the central nervous system: yesterday, today, and tomorrow [see comments] // Neurosurgery. – 1993. – V.33. - N4. – P.645-647.
7. Balashova VA, Abdulkadyrov KM. [Cellular composition of hemopoietic tissue of the liver and spleen in the human fetus] // Arkh Anat Gistol Embriol. – 1984. –V.86. - N4. – P.80-83
8. Baranov A., et al. Bone marrow transplantation after Chernobyl nuclear accident // N.Eng. J.Med. – 1989. – N321. - 205-212.
9. Baranov AE, Gus'kova AK, Protasova TG. [Experience in treating the victims of the accident at the Chernobyl Atomic Electric Power Station and the immediate disease outcomes] // Med Radiol. - Moskow. – 1991. – V.36. – N3. – P.29-32
10. Bauer A.R. Fetal tissue transplantation: legal and ethical implications of a "magic bullet" [Review] // Legal Medicine. – 1991. - P.245-267
11. Bell N.M. Regulating transfer and use of fetal tissue in transplantation procedures: the ethical dimensions // American Journal of Law & Medicine. – 1994. – V.20. - N3. – P.277-294
12. Ben R., Ji-Chang F., Yao-Dong B., Yie-Jian L., Yi-Fang Z. Transplantation of cultured fetal adrenal medullary tissue into the brain of Parkinsonian. Department of Neurosurgery and Endocrinology, Dalian Municipal Central Hospital, China // Acta Neurochirurgica. – 1991. - Supplementum. – V.52. – P.42-44
13. Betend B., Touraine J.L., Hermier M., Francois R. Restoration of mixed and severe immunologic deficiency, by fetal liver and thymus graft // Arch Fr Pediatr. – 1979. – V.36. - N10. – P.995-1005
14. Bhargava M., Karak A.K., Sharma S., Kochupillai V. Bone marrow recovery following fetal liver infusion (FLI) in aplastic anaemia: morphological studies // Thymus. – 1987. – V.10. - N1-2. P.103-108
15. Bjorklund A, Lindvall O. Self-repair in the brain //Nature. – 2000. – V.22. - N405(6789). – P.892-893, 895
16. Bjorklund A. Cell replacement strategies for neurodegenerative disorders // Novartis Found Symp 2000;231. – P.7-15; discussion 16-20

17. Björklund A., Stenevi U., Schmidt R.H., Dunnett S.B., Gage F.H. Intracerebral grafting of neuronal cell suspensions. I. Introduction and general methods of preparation // Acta Physiol Scand Suppl. – 1983. – V.522. - 1-7

18. Blagodatskii M.D. Sufianov A.A. Larionov S.N. Kibort R.V. Seminskii I.Zh. Manokhin P.A. [The transplantation of embryonic nerve tissue in syringomyelia: initial clinical experience]. Original Transplantatsiia embrional'noi nervnoi tkani pri siringomielii: pervyi klinicheskii opyt // Zhurnal Voprosy Neirokhirurgii Imeni N - N - Burdenko. – 1994. - N3. – P.27-29; 1994. – V.85.- N6. – P.1463-1471

19. Bodley Scott R., Matthias J.Q., Constandoulakis M., Kay H.E.M. Lucas P.F., Whiteside J.D. Hypoplastic anemia treated be transfusion of foetal haemopoietic cells // Lancet. – 1961. - N2. – P.1385-1388 (Цит. по Fine A., 1994)

20. Boer G.J. Ethical guidelines for the use of human embryonic or fetal tissue for experimental and clinical neurotransplantation and research // Network of European CNS Transplantation and Restoration (NECTAR). - J Neurol. – 1994. – V.242. – N.1. – P.1-13

21. Boer G.J. Notes for the discussion on the ethical issue of clinical neurotransplantation // Report at Founding meeting Network for European CNS Transplantation and Regeneration (NECTAR). - Le Vésinet. - 1991

22. Boer G.J. The Network of European CNS Transplantation and Restoration (NECTAR): an introduction on the occasion of its tenth meeting // Cell Transplant. – 2000. – V.9. - N2. – P.133-137

23. Boer GJ. Ethical issues in neurografting of human embryonic cells // Theor Med Bioeth. – 1999. – V.20. – N.5

24. Brundin P., Nilsson P.G., Strecker R.E., Lindvall O., Astedt B., Björklund A. Behavioural effects of human fetal dopamine neurons grafted in a rat model of Parkinson's disease // Exp Brain Res. – 1986. – N.65. – P.235-240

25. Buckley R.H., Whisnant K.J., Schiff R.I., Gilbertsen R.B., Huang A.T., Platt M.S. Correction of severe combined immunodeficiency by fetal liver cells // N Engl J Med. – 1976. – V.294. - N20. – P.1076-81

26. Buhrdel P., Rosenkranz M,. Schwenke H., Kuhndel K., Thierbach V. Transplantation of stem cells of embryonic liver in a patient with severe combined immunodeficiency // Acta Paediatr Hung. – 1985. – V.26. - N3. – P.233-240

27. Champlin R.E, Mitsuyasu R.T, Gale R.P. Transplantation of T lymphocyte depleted bone marrow to prevent graft-versus-host disease: its implications for fetal liver transplantation // Prog Clin Biol Res. Fetal Liver Transplant. - Alan R. Liss, Inc. – 1985. - N193. – P.315-25

28. Cohen C. B., Jousen A. R. The Future of the Fetal Tissue Bank // Science. – 1993. - V.262. - P.1663-1665.

29. Crombleholme T.M., Langer J.C., Harrison M.R., Zanjani E.D. Transplantation of fetal cells // American Journal of Obstetrics & Gynecology. – 1991 – V.164. - N1. – P.218-230

30. Ek S., Ringden O., Markling L., Westgren M. Cryopreservation of fetal stem cells. Department of Obstetrics and Gynecology, Karolinska Institute, Huddinge Hospital, Sweden // Bone Marrow Transplantation. – 1993. – V.11. - Suppl 1. – P.123

31. Ek S., Westgren M., Pschera H., Seiger A., Sundstrom E., Bui TH., Ringden O. Screening of fetal stem cells for infection and cytogenetic abnormalities // Fetal Diagnosis & Therapy. – 1994 – V.9. – N6. – P.357-361.

32. Embryonic Tissues Center EmCell - http://www.emcell.com.

33. Fact Sheet on Human Pluripotent Stem Cell Research Guidelines // NIH Stem Cell Information Archives, January 23, 2001 // http://www.nih.gov/news/stemcell/stemfactsheet.htm

34. Fine A. Human fetal tissue research: practice, prospects, and policy. [Review] // Cell Transplantation. – 1994. - N3. – V.2. – P.113-145

35. Fine A. Transplantation of fetal cells and tissue: an overview // CMAJ. – 1994. – V.151. - N9. – P.1261-1268. Review

36. Foglia R.P., DiPreta J., Statter M.B., Donahoe P.K. Fetal allograft survival in immunocompetent recipients is age dependent and organ specific // Ann Surg. – 1986. – V.204. - N4. – P.402-140

37. Freed C.R., Breeze, R.E., Rosenberg N.L., et al. Transplantation of human fetal dopamine cells for Parkonson's disease. Results at 1 year // Arch. Neurol. – 1990. – V47. – P.505-512

38. Freed Curt R., Paul E. Greene, Robert E. Breeze, Wei-Yann Tsai, William DuMouchel, Richard Kao, Sandra Dillon, Howard Winfield, Sharon Culver, John Q. Trojanowski, David Eidelberg, Stanley Fahn Transplantation of Embryonic Dopamine Neurons for Severe Parkinson's Disease // The New England Journal of Medicine, - 2001 - V.344. - N.10. – P.710-719.

39. Freeman T.B., Sanberg P.R. Peer review for fetal tissue transplantation research (editorial) // Cell Transplantation. – 1992. – V.1 – N.4. – P.271-273

40. Freeman T.B., Sanberg P.R., Nauert G.M., Boss B.D., Spector D., Olanow C.W., Kordower J.H. The influence of donor age on the survival of solid and suspension intraparenchymal human embryonic nigral grafts. Division of Neurosurgery, University of South Florida, Tampa 33606, USA // Cell Transplantation. – 1995. – V.4. -N1. –P.141-154

41. Gale R.P. Development of the immune system in human fetal liver // Thymus. – 1987. – V.10. - N1-2. – P.45-56

42. Gale R.P. Fetal liver transplantation in aplastic anemia and leukemia // Thymus. – 1987. – V.10. - N1-2. – P.89-94

43. Gale R.P. Fetal liver transplantation in hematologic disorders // Prog Clin Biol Res. Fetal Liver Transplant. - Alan R. Liss, Inc. – 1985. – N.193. – P.293-297

44. Gale R.P. Fetal liver transplants // Bone Marrow Transplant. – 1992. - N9. – P.118-20 (Review)

45. Gale R.P., Reisner Y., The role of bone-marrow transplants after nuclear accidents // Lancet. – 1988. – P.923-926

46. Gale R.P., Touraine J.L., Kochupillai V. Synopsis and prospectives on fetal liver transplantation // Thymus. – 1987. - V10. - N1-2. – P.1-4

47. Gale RP. Henon P. Juttner C. Blood stem cell transplants come of age // Bone Marrow Transplantation. – 1992. – V.9. – N3. – P.151-155.

48. Gearhart J. New Potential for Human Embryonic Stem Cells // Science. – 1998. – V.282. – N5391. - P.1061-1062.

49. Githens J.H. Editorial: Immunologic reconstitution with fetal tissue // N Engl J Med. – 1976. – V.294. - N20. – P.1116-1167

50. Gorski A. [Transplantation of fetal liver cells] // Pol Arch Med Wewn. – 1977. – V.58. - N3. – P.303-306

51. Hagell P., Brundin P.. Cell survival and clinical outcome following intrastriatal transplantation in Parkinson disease // J Neuropathol Exp Neurol. - 2001. – V.60. - N8. – P.741-52

52. Hajdu K., Tanigawara S., McLean L.K., Cowan M.J., Golbus M.S. In utero allogeneic hematopoietic stem cell transplantation to induce tolerance // Fetal Diagn Ther. – 1996. – V.11. - N4. - P241-248

53. Hematopoietic Cell Transplantation. Edited by E.D.Thomas, K.G.Blume, S.J.Forman. – Blackwell Science, Inc., 1999, II edition. – 1260 p.

54. Hitchcock E.R., Kenny B.G., Henderson B.T., Clough C.G., Hughes R.C., Detta A. A series of experimental surgery for advanced Parkinson's disease by foetal mesencephalic

transplantation // Department of Neurosurgery, University of Birmingham, Midland Centre for Neurosurgery and Neurology, Smethwick, Birmingham, U. K. - Acta Neurochirurgica. - Supplementum. – 1991. - V.52. – P.54-57

55. Hollands P. Transplantation of embryonic haemopoietic stem cells without prior recipient X-irradiation // Br J Haematol. – 1988. – V.69. - N4. – P.437-440

56. Hollands P. Embryonic stem cell grafting: the therapy of the future? // Hum Reprod. – 1991. – V.6. - N1. – P.79-84. Review

57. Holyoake T. L., Nicolini F. E., Eaves C. J. Functional differences between transplantable human hematopoietic cells from fetal liver, cord blood, and adult marrow // Experimental Hematology. – 1999. - N27. – P.1418-1427

58. Hovatta O, Ahrlund-Richter L. [Ethical aspects of stem cell research. Legislation and guidelines in Europe] // Lakartidningen. – 2001. - V.98. - N34. – P.3515-3519

59. Hurd R.E. Ethical issues surrounding the transplantation of human fetal tissues [Review] // Clinical Research. – 1992. – V.40. - N4. – P.661-666

60. Implementation Issues for Human Embryonic Stem Cell Research // National Institutes of Health Stem Sell Information, December 19, 2001 // http://grants.nih.gov/grants/stem_cells.htm

61. Improving Survival in Acquired Immunodeficiency Syndrome: Is Experience Everything? // Editorial JAMA. - 1989. – V.261. – N20. – P.3016-3017

62. Izzi T., Polchi P., Galimberti M., Delfini C., Moretti L., Porcellini A., Manna A., Sparaventi G., Giardini C., Angelucci E., P.Politi, G.Lucarelli Fetal liver transplant in aplastic anemia and acute leukemia // Prog Clin Biol Res. Fetal Liver Transplant. - Alan R. Liss, Inc. – 1985. – P.237-249

63. Jiang N., Jiang C., Tang Z., Zhang F., Li S., Jiang D. Human foetal brain transplant trials in the treatment of Parkinsonism. –-Acta Acad Med Shanghai. - 1987. N14. – P.1

64. Jones Deborah. Halifax hospital first in Canada to proceed with controversial fetal-tissue transplant // Can. med. assoc. j. – 1992. – V.146. - N3. – P.389-391.

65. Kansal V., Sood S.K, Batra A.K, Adhar G., Malviya A.K., Kucheria K., Balakrishnan K. Fetal liver transplantation in aplastic anemia // Acta Haematol. – 1979. – V.62. - N3. – P.128-136

66. Keightley R.G., Lawton A.R., Cooper M.D., Yunis E.J. Successful fetal liver transplantation in a child with severe combined immunodeficiency // Lancet. – 1975. – V.2. - N7940. – P.850-853

67. Kelemen E. Recovery from chronic idiopathic bone marrow aplasia of a young mother after intravenous injection of unprocessed cells from the liver (and yolk sac) of her 22 mm CR-length embryo // A preliminary report. Scand J Haematol. – 1973. – V.10. - N4. – P.305-8

68. Kelemen E., Janossa M., Calvo W., Fliedner T.M., Bofill M., Janossy G. What kind of morphologically recognizable haemopoietic cells do we inject when doing foetal liver infusion in man? // Thymus. – 1987 – V.10. – N.1-2. – P.33-44

69. King P, Areen J Legal regulation of fetal tissue transplantation // Clin Res. – 1998. – N36. – P.205-208

70. Kochupillai V., Sharma S., Francis S., Mehra N.K., Nanu A., Kalra V., Menon P.S., Bhargava M. Bone marrow reconstitution following human fetal liver infusion (FLI) in sixteen severe aplastic anemia patients // Prog Clin Biol Res. Fetal Liver Transplant. - Alan R. Liss, Inc. – 1985. – N.193. – P.251-265

71. Kochupillai V., Sharma S., Francis S., Mehra N.K., Nanu A., Verma I.C., Takkar D., Kumar S., Gokhale U. Fetal liver infusion: an adjuvant in the therapy of acute myeloid leukemia (AML) // Prog Clin Biol Res. Fetal Liver Transplant. - Alan R. Liss, Inc. – 1985. - N193. – P.267-279

72. Kochupillai V., Sharma S., Francis S., Nanu A., Mathew S., Bhatia P., Dua H., Kumar L., Aggarwal S., Singh S., et al. Fetal liver infusion in aplastic anaemia // Thymus. – 1987. – V.10. - N1-2. – P.95-102

73. Kochupillai V., Sharma S., Francis S., Nanu A., Verma I.C., Dua H., Kumar L., Aggarwal S., Singh S. Fetal liver infusion in acute myelogenous leukaemia // Thymus. – 1987. – V10. - N1-2. – P.117-124

74. Kohgo Y., Sakamaki S., Hirayama Y., Matsunaga T., Niitsu Y. Hematopoietic stem cell transplantation. Hokkaido Igaku Zasshi // Hokkaido Journal of Medical Science. - 1995 – V.70. – N2. – P.241-245.

75. Kordower J. H., Freeman Th. B., Barry J. S. at all. Neuropathological Evidence of Graft Survival and Striatal Reinnervation after the Transplantation of Fetal Mesencephalic Tissue in a Patient with Parkinsons Disease // The New England Journal of Medicine. - 1995. - V.332. N17. - P. 1118-1124.

76. Kupsch A., Sauer H., Oertel W.H. Transplantation of dopamine producing nerve cells: a new therapy in idiopathic Parkinson syndrome? (Review) (German) // Physiologisches Institut, Ludwig-Maximilians-Universitat // Nervenarzt. - Munchen.- 1991. – V.62. - N2. – P.80-91

77. Lane H. C., Masur H., Longo L., Klein H. G., et all. Partial immune reconstitution in a patient with the acquired immunodeficiency syndrome // N. Engl. J. Med. - 1984. - V. 311. - N17. - P.1099-1103.

78. Lansdorp P.M., Dragowska W., Mayani H. Ontogeny-related changes in proliferative potential of human hematopoietic cells // Journal of Experimental Medicine. – 1993. – V.178. - N3. – P. 787-791

79. Lindvall O, Björklund A, Widner H (eds) Intracerebral transplantation in movement disorders. – Amsterdam. – Elsevier. - 1991

80. Lindvall O, Bjorklund A. First step towards cell therapy for Huntington's disease // Lancet. – 2000. - V356. - N9246. – P.1945-1946

81. Lindvall O. Parkinson disease. Stem cell transplantation // Lancet. – 2001. –V.358. - Suppl:S48

82. Lindvall O. Cell transplantation: a future therapy for Parkinson's disease?. [Review] // Neurologia. – 1994. – V.9. - N3. – P.101-107

83. Lindvall O. Cerebral implantation in movement disorders: state of the art // Mov Disord. 1999. - V.14. - N2. – P.201-205. Review

84. Lindvall O. Neural transplantation in Parkinson’s disease // Novartis Found Symp. – 2000. – V. 231 – P.110-23; discussion P.123-128, 145-147.

85. Lindvall O. Transplants in Parkinson's disease // Eur Neurol. – 1991. – V.31. - Suppl 1. – P.17-27. Review.

86. Lindvall O., Backlund E.O., Farde L., Sedvall G., Freedman R., Hoffer B., Nobin A., Seiger A., Olson L. Transplantation in Parkinson's disease: two cases of adrenal medullary grafts to the putamen // Ann Neurol. – 1987. –V.22. - N4. – P.457-468

87. Lindvall O., Bjorklund A. Transplantation strategies in the treatment of Parkinson's disease: experimental basis and clinical trials // Acta Neurol Scand Suppl. - 1989. - N126. – P.197-210 (Review)

88. Lindvall O., Brundin P., Widner H., Rehncrona S., Gustavii B., Frackowiak R., Leenders K.L., Sawle G., Rothwell J.C., Marsden C.D., Björklund A. Grafts of fetal dopamine neurons survive and improve motor function on Parkinson's disease // Science. – 1990. - N247. – P.574-577

89. Lindvall O., Widner H., Rehncrona S., Brundin P., Odin P., Gustavii B., Frackowiak R., Leenders K.L., Sawle G., Rothwell J.C., Björklund A., Marsden C.D. Transplantation of fetal dopamine neurons in Parkinson's disease: one-year clinical and neurophysiological

observations in two patients with putaminal implants // Ann Neurol. – 1992. - N31. – P.155-165

90. Lou F.D., Liu H.C. [Clinical use of hematopoietic stem cells from fetal livers] // Zhonghua Nei Ke Za Zhi. – 1986. – V.25 – N7. – P.433-435 (Review)

91. Lou F.D., Liu H.C., Wang Y.Z. [Short-term and multiple fetal liver transplantations for the treatment of aplastic anemia: report of 15 cases] // Zhonghua Nei Ke Za Zhi. – 1985. – V.24. -N2. – P.65-67, 124

92. Lowenberg B., Vossen J.M., Dooren L.J. Transplantation of fetal liver cells in the treatment of severe combined immunodeficiency disease // Blut. – 1977. – V.34. - N3. – P.181-95

93. Lucarelli G., Izzi T., Delfini C., Grilli G. Fetal liver transplantation in severe aplastic anemia // Haematologica. – 1978. – V.63. - N1. – P.93-4

94. Lucarelli G., Izzi T., Porcellini A., Delfini C. Infusion of fetal liver cells in aplastic anemia // Hamatol Bluttransfus. – 1979. - N24. – P.167-70

95. Lucarelli G., Izzi T., Porcellini A., Delfini C., Galimberti M., Moretti L., Polchi P., Agostinelli F., Andreani M., Manna M., Dallapiccola B. Fetal liver transplantation in 2 patients with acute leukaemia after total body irradiation // Scand J Haematol. - 1982. – V.28. - N1. – P.65-71

96. Meagher R.C., Herzig R.H. Techniques of harvesting and cryoprezervation of stem cellc // Hematology - Oncology Clinics of North America. - 1993– – V.7. – N3. – P.501-533

97. Meng P.L, Fei R.G., Gu D.W, Yie W.Z., Liu B.T., Yan F., Yu Y.Y., Mai Z.G., Chen B.Z., Zhu L.X., et al. Allogeneic fetal liver transplantation in acute leukemia // Prog Clin Biol Res. Fetal Liver Transplant. Alan R. Liss, Inc. – 1985. – N.193. – P.281-291

98. Metcalf D. Stem Cells, Pre-Progenitor Cells and Lineage-Committed Cells: Are Our Dogmas Correct? // Annals of the New York Academy of Sciences. – 1999. - N872. – P.289-304

99. Metcalf D., Moore, M.A.S. Embryonic aspects of hemopoiesis // Frontiers of biology: Hematopoietic cells (Neuberger, A., Tatum E.L. eds). – Amsterdam. – 1971. - North Holland Publising Co. – P.172-271 (Цит. по Fine A., 1994).

100. National Consultative Ethics Committee for Life Sciences and Health (CNESVS) (1984) Recommendation on the use of embryo tissue as well as tissue of dead foetuses for therapeutic, diagnostic and scientific purposes

101. National Consultative Ethics Committee for Life Sciences and Health (CNESVS) (1990) Statement on intracerebral graft of mesencephalic tissue of human embryo origin in patients with Parkinsonism for therapeutic experimentation

102. National Institutes of Health Guidelines for Research Using Human Pluripotent Stem Cells // NIH Stem Cell Information Archives, August 25, 2000 (corrected November 21, 2000) // http://www.nih.gov/news/stemcell/stemcellguidelines.htm

103. Nelson R. M. A Policy concerning the therapeutic use of human fetal tissue in transplantation // Western Journal of Medicine. – 1990. – V.152. – N.4. – P.447-448

104. Neural transplantation in neurodegenerative disease // Novartis Found Symp. – 2000. – V. 231 – P. 12-14

105. Neural transplantation into the CNS. Selected articles from the 1st American Society for Neural Transplantation meeting. Clearwater, Florida, May 5-7, 1994 // Cell Transplantation. – 1995. – V.4. - N1. – P.1-154

106. NIH: What would you hope to achieve from human pluripotent stem cell research? // NIH Stem Cell Information Archives, April 26, 2000 // http://www.nih.gov/news/stemcell/achieve.htm

107. NINDS and NIDDK Directors' Congressional Testimony on Stem Cells // NIH Stem Cell Information Archives, April 26, 2000 // http://www.nih.gov/news/stemcell/State.htm

108. Pahwa R., Pahwa S., Good R.A., Incefy G.S., O'Reilly R.J. Rationale for combined use of fetal liver and thymus for immunological reconstitution in patients with variants of severe combined immunodeficiency // Proc Natl Acad Sci U S A. – 1977. – V.74. - N7. – P.3002-3005

109. Parliamentary Assembly of the Council of Europe (1986) On the use of human embryos and foetuses for diagnostic, therapeutic, scientific, industrial and commerical purposes // Council of Europe. – Strasbourg. –1986. - Recommendation 1046

110. Parliamentary Assembly of the Council of Europe (1989) On the use of human embryos and foetuses for scientific research // Council of Europe. – Strasbourg. – 1989. - Recommendation 1100

111. Piccini P., Lindvall O., Bjorklund A., Brundin P., Hagell P., Ceravolo R., Oertel W., Quinn N., Samuel M., Rehncrona S., Widner H., Brooks D.J.. Delayed recovery of movement-related cortical function in Parkinson's disease after striatal dopaminergic grafts // Ann Neurol. – 2000. – V.48. - N5. – P.689-95

112. Pschera H. Stem cell therapy in utero // J Perinat Med. – 2000. – V.28. - N5. – P.346-354. Review

113. Pylypchak OM. [Hemopoietic cells from human embryonic liver in the treatment of HIV/AIDS] // Lik Sprava. – 1998. - N8. – P.116-118

114. Qian F.W. [Transfusion of fetal liver cells in the treatment of hematologic disease] // Zhonghua Yi Xue Za Zhi. – 1986. – V.66. – N.4. – P.237-239

115. Ratajczak M.Z. Experimental aspects of transplantation of haemopoietic cells of fetal liver // Arch Immunol Ther Exp. - Warszava. – 1988. – V.36. - N2. – P.235-243

116. Raudrant D., Touraine J.L., Rebaud A. In utero transplantation of stem cells in humans: technical aspects and clinical experience during pregnancy // Bone Marrow Transplant. – 1992. – V.9. - Suppl 1. – P.98-100

117. Rice H.E., Hedrick M.H., Flake A.W., Donegan E., Harrison M.R. Bacterial and funqal contamination of human fetal liver collected transvaginally for hematopoietic stem cell transplantation // Fetal Diagnosis & Therapy. – 1993 – V.8. – N2. – P.74-78

118. Roncarolo M.G., Bacchetta R. T cell repertoire and tolerance after fetal stem cell transplantation // Bone Marrow Transplant. – 1992. - N9. - Suppl 1. – P.127-128

119. Roncarolo M.G., Bacchetta R., Bigler M., Touraine J.L., de Vries J.E., Spits H. A SCID patient reconstituted with HLA-incompatible fetal stem cells as a model for studying transplantation tolerance // Blood Cells. – 1991. – V.17. - N2. – P.391-402

120. Royo P.C., et all. The Place of Fetal Liver Transplantation in Treatment of Inborn Errors of Metabolism // J. Inher. Metab. Dis. – 1991. - N14. - P.619-626.

121. Sanberg P.R,. Brundin P. Cell transplantation and neuroscience // Cell Transplant. – 1999. – V.8. - N1. - P.3-6

122. Savel'ev S.V. [Transplantation of embryonal brain tissue]. (Review) Original Transplantatsiia tkani embrional'nogo golovnogo mozga // Arkhiv Patologii. – 1992. - V.54. - N11. – P.43-6.

123. Seto S., Miyake T., Hirao T. Reconstitution of cell-mediated immunity in severe combined immunodeficiency following fetal liver transplantation // Tokai J Exp Clin Med. – 1985. – V.10. - N2-3. – P.233-238

124. Simonova L.I., Shantyr' V.I., Morozov I.A., Lakiza B.S., Trunov N.P. [Processing and transplantation of preserved (-196 degrees) fetal hemopoietic tissue]// Probl Gematol Pereliv Krovi. – 1976. – V.21. - N12. – P.20-23

125. Smikodoub A.I, Novitskaya A.V, Yefimov A.S. Experience in treatment of patients suffering from diabetes mellitus with the use of fetal cell suspensions // Cell Transplantation // Abstracts of Fouth International Congress "The Cell Transplantation Society. Montreux / Switzerland, March 21-24, 1999. – 1999. – V.8. - N2. - P.200-121.

126. Smikodoub A.I., Bushneva V.A. New method of treatment the patients suffering from autoimmune intestinal diseases with the use of embryonic stem cell transplantation cellular therapy // Abstracts of Institute Pasteur Euroconferences. Paris, France, 3-4 February 2000. – Paris. – 2000. - P.20..

127. Smikodoub A.I., Radzievskaya L.V., Snigir N.V. Treatment of cytostatic agranulocytosis by means of transplantation of fetal liver hemopoietic cells // Cell Transplantation. – 1999. - V.8. - N2. – P.200, poster N 123. Abstracts of Fouth International Congress of The Cell Transplantation Society. Montreux / Switzerland, March 21-24, 1999.

128. Smikodoub Alexander, Karpenko Alexey. Psychophysiological changes in patients due to fetal cell transplantations // Cell Transplantation // Abstracts of Fouth International Congress "The Cell Transplantation Society. Montreux / Switzerland, March 21-24, 1999. – 1999. - V.8. - N2. - P.200, 124.

129. Smikodoub Alexander, Pilipchak Elena New method of immune substituting therapy with the use of fetal cells in cases of HIV infection (AIDS) // Abstracts of Fouth International Congress of The Cell Transplantation Society. Montreux / Switzerland, March 21-24, 1999 // Cell Transplantation. – 1999. – V.8. - N2. - P.120.

130. Smikodub A.I. Embryonic stem cell transplantation in anti-cancer treatment // Supportive Care in Cancer. – 2000. - V.8. N3. – P.256.

131. Smikodub A.I., Yu.A. Grinevich, G.D . Bendyug, L.V. Radziyevskaya, V.V. Snigir, N.N. Kharanovskaya, I.Yu. Gluhovskaya, V.S. Ivankova Transplantation of cryopreserved fetal liver hemopoietic cells in complex treatment of cancer patients // The 25th Anniversary Meeting of the International Society for oncodevelopmental biology and medicine 19-24 september 1997, Montreux, Switzerland // Tumor biology. – 1997. - N18. - Suppl 2. - P.127.

132. Smikodub Alexander, Tretyak Natalya, Snigyr Nataliya Treatment of cytostatic agranulocytosis in patients with leukemia by human embryonic liver hemopoietic cells. Abstracts // Society for Minimally Invasive Therapy Ninth Annual International Meeting 14-16 July 1997, Kyoto, Japan // Minimally Invasive Therapy. – 1997. - V.5. – Suppl. 1. - P.67.

133. Smikodub Alexandr, Pilipchak Elena Treatment of hiv-infection (AIDS) with fetal stem cells. Abstracts // Society for Minimally Invasive Therapy Ninth Annual International Meting 14-16 July 1997, Kyoto, Japan // Minimally Invasive Therapy. – 1997. - V.5. - Suppl 1. - P.67.

134. Smikodub O. Application Of Embryonic Cell Suspensions In Patients With Solid Tumors Before Initiation Of Radical Treatment // Supportive Care in Cancer, 2002. – V.10 – N.4 – P.96.

135. Smikodub O., Snigir N. Febrile neutropenia treatment of patients with acute leucosis by fetal stem cells // Abstracts of the 3rd International Symposyum on Febril Neutropenia. Brussels, Belgium, December 10-13, 1997 // Supportive Care in Cancer. – 1998. – V.6. - N3. - P.326

136. Smith R. T. Cancer and the Immune System // Pediatrics Clinics of North America. – 1994. – V.41. - N4. - P.841-849.

137. Spencer D.D., Robbins R.J., Naftolin F., Phil D., Marek K.L, Vollmer T., Leranth C., Roth R.H., Price L.H., Gjedde A., Bunney B.S., Sass K.J., Elsworth J.D., Kier E.L., Makuch R., Hoffer P.B., Redmond Jr. D.E. Unilateral transplantation of human fetal mesencephalic tissue into the caudate nucleus of patients with Parkinson's disease // New Engl J Med. – 1992. – V.327. – P.1541-1548

138. Sramka M. Rattaj M. [The legal and ethical aspects of nerve tissue transplantation]. [RUSSIAN] Original Pravovye i eticheskie aspekty neirotransplantatsii // Zhurnal Voprosy Neirokhirurgii Imeni N - N - Burdenko. – 1992. - N6. – P.12-13

139. Stem Cells: Scientific Progress and Future Research Directions // National Institutes of Health Stem Sell Information. - July 2001 // http://www.nih.gov/news/stemcell/scireport.htm

140. Subrt O., Tichy M., Vladyka V., Hurt K. Grafting of fetal dopamine neurons in Parkinson's disease // The Czech experience with severe akinetic patients. Department of Neurosurgery, Charles University Medical School, Prague, Czech. – Wien. - Acta Neurochir Suppl. – 1991. - N52. – P.51-53

141. The Director's Congressional Testimony on Stem Cell Research // NIH Stem Cell Information Archives, December 2, 1998 // http://www.nih.gov/about/director/120298.htm

142. The Director's Congressional Testimony on Stem Cell Research // NIH Stem Cell Information Archives, January 26, 1999 // http://www.nih.gov/news/stemcell/statement.htm

143. The President's Address to the Nation // NIH Stem Sell Information, August 9, 2001 // http://www.whitehouse.gov/news/releases/2001/08/20010809-2.html

144. Thomson J.A., Joseph Itskovitz-Eldor, Sander S. Shapiro, Michelle A. Waknitz, Jennifer J. Swiergiel, Vivienne S. Marshall, and Jeffrey M. Jones Embryonic Stem Cell Lines Derived from Human Blastocysts // Science. – 1998. - V.282. N5391. – P.1145-1147.

145. Touraine J.L. European experience with fetal tissue transplantation in severe combined immunodeficiency (SCID) // Birth Defects Orig Artic Ser. – 1983. – V.19. – N3. – P.139-142

146. Touraine J.L. In utero fetal liver cell transplantation in the treatment of immunodeficient or thalassemic human fetuses // Transfus Sci. – 1993. – V.14. - N3. – P.299-304

147. Touraine J.L. Rationale and results of in utero transplants of stem cells in humans // Bone Marrow Transplant. – 1992. - N10. – P.121-126

148. Touraine J.L. Stem cell transplantation in primary immunodeficiency, with special reference to the first prenatal, in utero, transplants // Allergologia et Immunopathologia. – 1991. – V.19. - N2. – P.49-51

149. Touraine J.L. The fetal liver as a source of stem cells for transplantation into fetuses in utero // Curr Top Microbiol Immunol. – 1992. N177. - P.187-193 (Review)

150. Touraine J.L., Bacchetta R., Yssel H. de Vries J., Roncarolo M.G. Transplantation of mismatched human fetal liver cells: tolerance induction via clonal deletion and clonal anergy. INSERM U 80, Hopital Ed. Herriot, Lyon, France // Transplantation Proceedings. - 1995. – V.27. - N1. – P.622-624

151. Touraine J.L., Griscelli C., Betuel H., Durandy A., Betend B., Souillet G. Chimerism following fetal liver transplantation: cell cooperation despite HLA mismatch // Birth Defects Orig Artic Ser. – 1983. - V.19. - N3. – P.143-145

152. Touraine J.L., Laplace S., Rezzoug F., Sanhadji K., Veyron P., Royo C., Maire I., Zabot M.T., Vanier M.T., Rolland M.O., et al. The place of fetal liver transplantation in the treatment of inborn errors of metabolism // J Inherit Metab Dis. - 1991. – V.14. - N4. - 619-626

153. Touraine J.L., Roncarolo M.G., Bacchetta R., Raudrant D., Rebaud A., Laplace S., Cesbron P., Gebuhrer L., Zabot M.T., Touraine F., et al. Fetal liver transplantation: biology and clinical results // Bone Marrow Transplant. – 1993. – V.11. - Suppl 1. – P.119-122. Review

154. Touraine J.L., Roncarolo M.G., Marseglia G.L., Souillet G., Betend B., Betuel H., Touraine F., Royo C., Philippe N., Francois R. Fetal liver transplantation in immunodeficiencies and inborn errors of metabolism // Prog Clin Biol Res. Fetal Liver Transplant. - Alan R. Liss, Inc. – 1985. -N193. – P.299-313

155. Transplantation of stem cells from fetal liver. - Lancet. – 1981. – V.1. - N8231. – P.1193-1194

156. United State patent. Number: 5,811,089. Date of patent: Sep. 22, 1998. Pharmaceutical preparation based on fetal suspension and methods of treating acquired immune deficiency syndrome (HIV infection). Inventors: Smikodub A.I., Markov I.S., Pilipchak E.M.

157. United State patent. Number: 6,184,033 B1. Date of patent: Feb. 6, 2001. Medicinal preparation based on fetal suspension having immune substituting effect for patients with acquired immune deficiency syndrome (HIV infection). Inventor: Smikodub A.I.

158. Uphoff D.E. Preclusion of secondary phase of irradiation syndrome by inoculation of fetal hematopoietic tissue following lethal total body X-irradiation // J.Natl. Cancer Inst. – 1958. – N.20. – P.625-632 (Цит. по Fine A., 1994)

159. Westgren M. Ek S. Bui T.H. Hagenfeldt L. Markling L. Pschera H. Seiger A. Sundstrom E. Ringden O. Establishment of a tissue bank for fetal stem cell transplantation // Acta Obstetricia et Gynecologica Scandinavica. – 1994. – V.73. - N5. – P.385-388.

160. Westgren M. Ringden O. Fetal to fetal transplantation // Acta Obstetricia et Gynecologica Scandinavica. – 1994. – V.73. - N5. – P.371-372

161. Wolff H.P. [Medical use of fetal cells and tissue: ethical aspects]. [German] Original Die medizinische Nutzung fetaler Zellen und Gewebe: ethische Aspekte // Diskussionsforum Medizinische Ethik. – 1992. - N1. – P.I-IV.

162. Wu C.T. Experimental studies on hemopoietic stem cells of fetal liver origin and its clinical application // Prog Clin Biol Res. Fetal Liver Transplant. - Alan R. Liss, Inc. – 1985. – N.193. – P.95-112

163. Wu C.T., Ye G.Y. Advances in experimental studies and clinical application of fetal liver cells // Thymus. – 1987. – V.10. -N1-2. – P.109-116

164. Xue L.F., Zhang X.W., Yang L., Liu Y.X. [Fetal liver cell transfusion in chemotherapy of malignant tumors and blood diseases] / Zhonghua Zhong Liu Za Zhi. – 1986. – V.8 - N5. – P.367-369

165. Ye GY. [Fetal liver transfusion (FLT) in the treatment of aplastic anemia] // Zhonghua Nei Ke Za Zhi. – 1983. – V.22. - N2. – P.71-73

166. Yoder M.C., Hiatt K. Engraftment of embryonic hematopoietic cells in conditioned newborn recipients // Blood. – 1997. – V.89. – N6. – P.2176-183

167. Zabek M. Mazurowski W. Dymecki J. Stelmachow J. Gawur B. Trautsolt W. Zawada E. [Transplantation of fetal dopaminergic cells in Parkinson disease] [Polish] Original Przeszczepianie plodowych komorek dopaminergicznych w chorobie Parkinsona / Neurologia i Neurochirurgia Polska. – 1992. - Suppl 1. – P.13-19

168. Абдулкадыров К.М., А. А. Ганакиев, Э. Р. Шилова, Т. И. Попова, Розанова О. Э., Кацадзе Ю. Л. Результаты лечения больных апластической анемией различными дозами антилимфоцитарного глобулина // Терапевтический архив. - 1995. - т. 67. - N 8. - с. 51-54.

169. Баранов А. Э., Гуськова А. К., Селидовкин Г. Д. и соавт. Опыт трансплантации костного мозга, лейкомассы и клеток эмбриональной печени человека больным гемобластозами (Ин-т биофизики МЗ СССР, Москва) // Терапевтический архив. – 1986. - т.58, N9, С.9-18.

170. Белоус А.М., Грищенко В.И. Криобиология. - К.: Наук. Думка, 1994. - 431 с.

171. Бубнов А. Н., Абдулкадыров К. М., Балашова В. А. и др. Методика получения и некоторые морфофункциональные характеристики гемопоэтических клеток фетальных органов // Проблемы гематологии – 1982. – т. 27. - N5. - С.12-16

172. Гриневич Ю.Я., Смикодуб О.І., Бендюг Г.Д., Радзієвська Л.В., Снігир Н.В., Глуховська І.Ю., Іванкова В.С., Храновська Н.М. Застосування трансплантації кріоконсервованих гемопоетичних клітин ембріональної печінки в комплексному лікуванні хворих на злоякісні новоутворення. Методичні рекомендації. Мінздрав України. - Київ, 1999

173. Грищенко В.И., Лобынцева Г.С., Вотякова И.А. и др. Гемопоэтические клетки эмбриональной печени. - Киев, Наук. Думка, 1988. - 190 с.

174. Гріневич Ю.А., Смикодуб О.І., Бендюг Г.Д., Храновська Н.М., Іванкова В.С., Снігирь Н.В., Радзієвська Л.В. Можливості коррекції гематологічних порушень в процесі

променевої терапії хворих на гінекологічний рак за допомогою трансплантації клітин ембріональної печінки // Променева діагностика, променева терапія. Збірка наукових робіт асоціації радіологів України. Випуск № 6. - Київ, 1999. - С.52-58.

175. Єфимов А.С., Смикодуб О.І., Новицька А.В. Лікування хворих з впершевиявленим інсулінозалежним цукровим діабетом гемопоетичними клітинами ембріональної печінки. Методичні рекомендації. Мінздрав України. Академія медичних наук України. - Київ, 2000. - С.16.

176. Каргин В. Д., Абдулкадыров К. М. Применение трансплантаций эмбриональных гемопоэтических и лимфоидных органов и клеток при лечении заболеваний системы крови // Гематология и трансфузиология. – 1983. - N7. - С.16-22.

177. Короткий В.Н., Смикодуб А. И., Безродный Б.Г., Мартынович Л.Д., Карташов Б.Т., У. Огадинма, Иванов Н. А. Трансплантация клеток эмбриональной печени человека в комплексном хирургическом лечении больных раком головки поджелудочной железы // Экспериментальная онкология. – 2000. – т.22. – дополнение № 236. Тезисы II съезда онкологов стран СНГ. «Онкология 2000», Украина, Киев, 23-26 мая 2000 г.

178. Кулаков В.И., Сухих Г.Т., Молнар Э.М. Иммунноцитотерапия. Новое направление в трансплантации фетальных тканей .. Бюлл. эксп. биол. и мед. – 1994. - т.117. - N4. - С.412-417

179. Кулаков В.И., Сухих Г.Т., Молнар Э.М. Трансплантация фетальных тканей человека; анализ состояния проблемы и перспективы развития // Трансплантация фетальных тканей и клеток человека. – 1996. - С.5-10.

180. Новицька А. В.Лікування хворих на цукровий діабет з імунними та гематологічними порушеннями гемопоетичними клітинами ембріональної печінки людини // Автореф. канд.дис. Інститут ендокринології та обміну речовин ім.В.П.Комісаренка АМН України. Київ, 2000. - с.21.

181. Пяткин Э. К., Баранов А. Э., Гордеева А. А. и др. Цитогенетический контроль трансплантации клеток эмбриональной печени больным гемобластозами после лечения цитостатиками в больших дозах и тотального гамма-облучения // Мед. Радиология. – 1982. - т.27. - N11. -С.19-24.

182. Смикодуб А.И., Бушнева В.А. Иммунологические нарушения при неспецифических воспалительных заболеваниях кишечника // Імунологія та алергологія. – 2000. - №4. – С.28-33

183. Смикодуб А.И., Бушнева В.А. Лечение неспецифических воспалительных заболеваний кишечника в терапевтической практике // Сучасна гастроентерологія. – 2001. - № 1. – С.52-57

184. Смикодуб А.И., Новицкая А.В., Дроздовская В.Д., Лифшиц Э.А., Лобынцева Г.С., Вотякова И.А. Клинический случай лечения приобретенной апластической анемии гемопоэтическими клетками эмбриональной печени человека // "Врачебное дело". – 1994. - N3. - С. 104-108.

185. Смикодуб О.І. Лікування хворих на вперше виявлений інсулінозалежний цукровий діабет гемопоетичними клітинами ембріональної печінки // Ендокринологія. - Київ, 2001 р. – т.6. - № 1. - С. 80-88.

186. Смикодуб О.І., Гайдукова С.М., Третяк Н.М., Снігир Н.В. Лікування мієлотоксичного агранулоцитозу у хворих на гострий лейкоз гемопоетичними клітинами ембріональної печінки людини. Методичні рекомендації. Мінздрав України. Академія медичних наук України. - Київ, 2001. - С.13.

187. Снігир Н.В. Застосування гемопоетичних клітин ембріональної печінки людини в лікуванні питостатичної мієлодепресії у онкологічних хворих. Національна Академія Наук України Інститут експериментальної патології, онкології і радіобіології їм. Р.С. Кавецького // Автореферат дисертації на здобуття наукового ступеня кандидата медичних наук. - Київ, 2001. - с.20.

188. Федотенков А. Г., Шишкина И. Д., Данилова Л. А., Змиевская К. М., Воронцова Э. И., Герасимова Н. А. Консервирование костного мозга при низких температурах для его клинического применения // Проблемы гематологии и переливания крови. - 1966. – т.11. - N1. - С.45-50

189. Цимбалюк В.І., Пічкур Л.Д., В.А. Руденко, Н.О. Пічкур Клініко-імунологічні дослідження впливу нейротрансплантації при спастичних формах дитячого церебрального паралічу // Трансплантологія. – 2000. - т.1. - №1. – С.156-157.

190. Шерешков С. И., Алексеев Л. П., Ярцев М. Н. Трансплантация эмбриональной печени при тяжелой комбинированной иммунной недостаточности (Обзор) // Терапевтический архив. – 1988. - N5. - С. 36-42

191. Шерешков С. И., Бугаидзе Л. И., Баранов А. Э. Трансплантация клеток фетальной печени от многих эмбрионов больным гемобластозами, кондиционированным общим облучением и химиопрепаратами // Гематология и трансфузиология. – 1984. – т.29, N4. - С.9-15.

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