Privileges of fetal cell / tissue

Why and how the fetus survives in utero, violating the laws of classical transplantation immunology, remains a mystery.

Cont...
It has been further observed that in order to survive the hostile maternal environment, the feto-plancental unit adjusts itself as an allograft and follows the path of the older innate immune system, taking the advantage of its hypo-antigenicity and the tacit support of non-cytopathic blocking antibodies of the mother, as an additional guard.

Cont.…..
To achieve its multiple goals, maturation and non-recognition by the host system Simultaneously, to prepare its own immune system to grow and to differentiate between its self and non-self identities, the fetal cells and tissue acquire many specialized characteristics including immortality.

Cont.....
Cells in our system can be classified under the two basic groups. Mortal cell line (all the cells in our body).
And immortal cells, i.e., cancer cells. And certain specialized fetal cells, viz, stem cells.

Cont.....
With each cell division the telometric end diminishes in size until it reaches an irreducible stage when there is senescence which stimulates apoptosis (programmed cell death).

Stem cells are unique, undifferentiated cells which can respond to demand and change their characteristics according to their milieu.

Cont. . . .
Stems cells can be wandering, as in the case of CD 34 cells, collected from cord blood or fixed to developing or growing organs, viz., fetal liver. These can survive engraft, specialize under regulatory control of the host, and even participate in the repair of damaged cells and restore their function.

In case of embryonic stem cells, they can reach any damaged site through migration, establish intracellular links, liberate specific cytokines under proper and adequate stimulation.
These undifferentiated stem cells have the ability to reproduce rapidly at a rate much higher than that of other cells and can specialize according to the environment into various tissues subtypes.

Cont.....
After the completion of organogenesis, the ability of most tissues to withstand damages due to illness or injury depends on tissue specific stem cells present in various organs. This stem cells are generally seen to be in a quiescent phase and do not normally participate in cellular activities.
BASIC RESEARCH

- Scientists use fetal tissue for numerous purposes, i.e., for basic research in human genetics as well as in the attempted development of new drugs and vaccines.
- Fetal cell cultures have special characteristics – they can allow reproduction of human viruses so that experimentation on the diagnosis of diseases and production of vaccines may be undertaken.
- In 1930, fetal cell cultures were first used in patients suffering from diabetes.
- In 1950, fetal tissue was used to help develop polio vaccine and subsequently, it was also used to develop rubella vaccine, and used for the prenatal diagnosis of genetic diseases.
- Fetal cells, have, moreover, been used to study how smoking affects the fetus by examining the carcinogenicity of tobacco on fetal cells.
There are billions of nerve cells in human brain.

In neuro-degenerative diseases like Parkinson's disease or Huntington's disease, selective loss of some 500,000 cells in critical regions of the brain can have devastating symptoms with varying degrees of rigidity/tremor/dyskinesia, to name a few.

Neuro-degeneration in these patients continues for years to decades, leading to conditions like lack of movement (Parkinsonism) or excessive movement (Huntington's disease).

Cont......
In this way, dopaminergic cells collected from fetal sources (adrenal medulla or substantia nigra) can grow in the Parkinson’s patients’ brain and if even a minute quantity, i.e., one tenth of a million of the total number of nerve cells, grows in the host’s brain, movement disorders show marked improvement. Apart from Parkinson’s disease, other indications of fetal tissue use include Alzheimer’s disease, stroke, spiral cord injury, motor neuron disease to muscular dystrophy, only to mention a few.
In case of congenital immunodeficiency (Di George syndrome) due to congenital thymic hypoplasia – a rare birth defect where the baby is born without a working thymus – only human fetal thymus transplant can provide a cure.

In other cases of acquired immunodeficiency, leucopenia may be corrected with fetal thymus transplantation.

In case of children with severe combined immunodeficiency conditions, fetal liver and thymus transplant can have a positive impact on the overall immune reconstitution.
Fetal tissue has the potentiality to revolutionize the science of transplantation, since it grows more quickly than adult tissue and is far less specialized, which means easy adaptability to foreign tissue.

In the future, transplantation biologists will not be surprised, if fetal cell/tissue transplant gradually replaces adult tissue/organ transplant. This is because of the intrinsic advantages of fetal tissue for better integration, growth and differentiation due to its higher telomer content, and its lack of proper HLA expression and less graft vs. host reaction.

The use of immunosuppressive drugs and the possibility of long-term potential complications of induction of malignancy and other disease conditions, could thus be avoided, leaving aside the present day prohibitive cost of organ transplantation surgery.

Cont…..
According to one report from the United States there is a progressive and increased disparity between the demand and supply of the organs needed for patients awaiting organ transplantation. While the number of patients awaiting transplant increase at approximately 15% per year the number of cadaver donors increases only by 1 to 3%.
This research actually started after the first description of stem cell by Leroy Stevens, Gail Martin and Martin Evans. The existence of the concept of some form of stem cells began with a suspicion among scientists working on the problem of bone marrow repopulation, after ionizing radiation.

Cont....
Stem cells (CD 34) could be obtained from embryonal sources (inner cell mass stage of development), fetal sources (fetal organs like liver, etc.), neonatal sources (placenta after the birth of the baby) or from mature adult sources.

Cont.....
Fetal tissue is the richest source of primordial stem cells. A discarded human placenta, after the birth of a baby, contains enough placental cord blood stem cells, which can supply the total stem cell demand of a 40 kg individual.
Recent stem cell researches have suggested that diabetes in mouse could be reversed, blood cells may be made from muscle cells, bone marrow stem cell can be converted to brain cells, or in case of liver failure, stem cells can help in the formation of new liver tissue.

In case of muscular dystrophy or in acute leukemia or even in atherosclerosis, stem cell technologies can extend life and relieve the sufferings of our patients and can even reverse replicate senescence, which has immediate implications for geriatric patients with multiple organ failure dysfunction.
The principle of cell transplantation in bio-ionic devices as a replacement of diseased or failing tissue function, may have many potential fields of application.

The hypoantigenic fetal tissue has the potentialities to make a perfect non-irritant, i.e., biofriendly interphase in case of different synthetic/metallic grafts used in medicine and surgery.

Cont.......
For example, any stent in the body, be it in the prostate, pancreas, common bile duct or coronary artery, can be made much more biofriendly through a fetal endothelial cell lining and this can also lead to a minimization of progressive platelet and other cellular interaction/vis a vis erosion; and it can help extend the life/patency of these stents.
In case of orthopaedic surgery, total hip replacement /knee/shoulder replacement, if allowed to be covered with fetal cells, they too can help extend the life of the implant by the biofriendly interphase formation which can minimize the lining tissue and inert tissue interphase interactions and thus prevent TH2 cellular responses by fibroblast proliferation and other tissue specific degranulation/ degradation attempts by the host tissue.
The use of fetal tissue will raise certain value-loaded questions in society about life, death, parenthood. It is undoubtedly a very complicated issue, but if simple rationality prevails, one will fail to understand why the discarded fetus going to a pink box/incinerator, should not be used in a worthy potential life saving endeavor, thoroughly screened and in front of the eagle eye of the Ethical Committee and senior medical experts, who will justify the procedure with objectivity, provided the woman having the abortion gives her proper informed consent.
HUMAN FETAL TISSUE TRANSPLANT

Umbilical cord whole blood transplant as an emergency alternative to adult whole blood, taking advantage of nature’s finest biological sieve, i.e., the placenta.
Brain transplant in Parkinsonism

Parkinsonism is a neurodegenerative condition and the treatment is symptomatic

Fetal dopaminergic neuronal transplant has been attempted at centres of excellence
HUMAN FETAL TISSUE TRANSPLANT
HUMAN FETAL TISSUE TRANSPLANT
HUMAN FETAL TISSUE TRANSPLANT
HUMAN FETAL TISSUE TRANSPLANT
HUMAN FETAL TISSUE TRANSPLANT

- Fetal adrenal tissue transplant
- The medullary component of fetal adrenal releases endorphin and other pain relieving substances
- The cortical component of the fetal adrenal may contribute in relieving inflammation
HUMAN FETAL TISSUE TRANSPLANT
HUMAN FETAL TISSUE TRANSPLANT
HUMAN FETAL TISSUE TRANSPLANT

- Fetal thymus transplant in immunodeficiency conditions
- A patient with non-Hodgkins lymphoma with leucopaenia improved after treatment with fetal thymus
HUMAN FETAL TISSUE TRANSPLANT
HUMAN FETAL TISSUE TRANSPLANT
HUMAN FETAL TISSUE TRANSPLANT
Fetal liver transplant to improve hepatic function in cirrhosis liver.
Fetal pancreas transplant in diabetic gangrene
HUMAN FETAL TISSUE TRANSPLANT

✓ Fetal lung transplant in adeno-carcinoma lung
HUMAN FETAL TISSUE TRANSPLANT
HUMAN FETAL TISSUE TRANSPLANT
HUMAN FETAL TISSUE TRANSPLANT
HUMAN FETAL TISSUE TRANSPLANT
FUTURISTIC IMPLICATIONS
HUMAN FETAL TISSUE/STEM CELLS’ TRANSPLANT
Fetal Tissue Transplant in Adult Disease

Dr. NIRANJAN BHATTACHARYYA, D.Sc., M.D., M.S., FACS, FICS, FSOG, FAIS, FICOG,

&

Prof. Subrata Pal,
Umbilical cord whole blood transplant as an emergency alternative to adult whole blood, taking advantage of nature’s finest biological sieve, i.e., the placenta.
HUMAN FETAL TISSUE TRANSPLANT

✔ Brain transplant in Parkinsonism

✔ Parkinsonism is a neuro-degenerative condition and the treatment is symptomatic

✔ Fetal dopaminergic neuronal transplant has been attempted at centres of excellence
HUMAN FETAL TISSUE TRANSPLANT

- **Fetal adrenal tissue transplant**

- The medullary component of fetal adrenal releases endorphin and other pain relieving substances.

- The cortical component of the fetal adrenal may contribute in relieving inflammation.
Fetal thymus transplant in immunodeficiency conditions

A patient with non-Hodgkins lymphoma with leucopaenia improved after treatment with fetal thymus
HUMAN FETAL TISSUE TRANSPLANT

- Fetal liver transplant to improve hepatic function in cirrhosis liver
- Fetal pancreas transplant in diabetic gangrene
- Fetal lung transplant in adeno-carcinoma lung
- Fetal cardiac transplant to combat cardiomyopathy
HUMAN FETAL TISSUE TRANSPLANT

- Fetal skin transplant in burn cases
- Fetal amniotic fluid as a substitute for costly antibiotic dressing in burn injury to expedite healing
- Fetal kidney transplant in early renal failure
HUMAN FETAL TISSUE TRANSPLANT

- Placenta and aborted fetuses are normally considered to be biological waste to be discarded.
- In the West, incinerators are used to burn this biological waste.
- In government hospitals, in spite of increasing consciousness, scavengers like cats and dogs do this job.
A study report of 174 units of placental umbilical cord whole blood transfusion in 62 patients as a rich source of fetal hemoglobin supply in different indications of blood transfusion

N. Bhattacharya, M.D. MS, FACS; K. Mukherjee, MBBD, Ph.D. (Cal); Ph.D. (Wisconsin);
S. Bhattacharya, Ph.D.

Principal Investigator of the Project, Surgeon, Superintendent, Rajendra State Hospital, Saharanpur,
Executive Professor, Department of Medical Sciences, Banaras Hindu University;
Former Director of Medical Services, Govt. of West Bengal and of the Institute of Post Graduate Medical Education and Research (IPGME & R),
Director Professor, Dept. of Medicine, IGMR, Calcutta;
Principal Scientific Officer, Dept. of Science & Technology, Govt. of West Bengal, Salt Lake, Calcutta;
Research Associate in the project "Extravillous Trophoblast", University of California, Berkeley.
Fetal tissue/organ transplant in HLA-randomized adult vascular subcutaneous axillary folds: preliminary report of 14 patients

N. Bhattacharya, M.B.B.S., M.D., M.S., F.A.C.S.

Principal investigator of the Project on Fetal Tissue Transplant at Kochi Orthopaedic Division, and Surgeon-Superintendent, Shyamak Trust Hospital, Kolkata (India)
Human fetal adrenal transplant: a possible role in relieving intractable pain in advanced rheumatoid arthritis

K. L. Mukherjee³, M.B.B.S., Ph.D.; S. Prasad Das⁴, M.B.B.S., M.S.; A. Mukherjee⁵, M.B.B.S., M.D.;
M. Bhattacharya¹, M.B.B.S., D.A., D.G.C.; S. Bhattacharya¹, Ph.D.

¹Principal Investigator of the prospective magnesium and experiment of Alcganathare Hospital, Calcutta,
²Former Director of Health Service, Dept. of West Bengal and currently Emeritus Professor,
³Dept. of Medicine, Institute of Postgraduate Medical Education and Research, Calcutta,
⁴Executive Professor, Dept. of Biochemistry, Postgraduate Institute of Post-Graduate Med. Educ. and Res., Calcutta,
⁵Res. Associate, in Alcganathare, Medical Jodpur University, Calcutta (India)
Can human fetal cortical brain tissue transplant (up to 20 weeks) sustain its metabolic and oxygen requirements in a heterotopic site outside the brain? A study of 12 volunteers with Parkinson’s disease

S. Bhattacharya Ph.D.; T. Bandopadhyaya Ph.D.

1. Principal Investigator of the project and surgeon and a professor of the Department of Neurosurgery, Calcutta University. Former Director of Health Services, Govt. of West Bengal and currently Executive Professor, Dept. of Medicine, Institute of Post-Graduate Medical Education and Research, Calcutta.
2. Associate Professor, Dept. of Neurosurgery, Kolkata Medical College and Lady, and Red Cross, Calcutta. Was Active in the project.
3. Reader, Jadavpur University, Calcutta. Principal Scientific Officer, Dept. of Science and Technology, Govt. of West Bengal, Calcutta (India)
A unique experience with human pre-immune (12 weeks) and hypo-immune (16 weeks) fetal thymus transplant in a vascular subcutaneous axillary fold in patients with advanced cancer: A report of two cases

N. Bhattacharya, MBBS, MD, MS, FACS; K. L. Mukherjee, MBBS, MD;
M.K. Chettri, MD, MBBS, FRCP; T. Banerjee, PhD;
S. Bhattacharya, PhD; A. Ghosh, MD, MBBS; M. Bhattacharya, MBBS, DGO, DA
Lastly, one important question may be raised, i.e., the ethical issue of fetal tissue transplant. There is of course a fine line that is chalked between being ethical and being corrupt. State/country regulations must be effective must in order to ensure that a woman is never coerced into having an abortion, so that the medical scientist can have an extra tissue that he needs for a procedure. Fortunately, technology today has enable the storage and preservation of fetal tissue for a significant period of time and supply and demand can thus, coincide.
Dear Sir,

In the 19th January issue of BMJ.com (2002;324:134), Doug Payne from Dublin reported in the 'News Extra' section that elective operations in Ireland had to be postponed due to the non-availability of blood. The author tried to explain the situation in terms of a less altruistic attitude and also a seasonal variation in collection, leading to a 46% increase in the price of blood bags ($199.32).

CONT.....
Do not discard 99.99% of the human placental umbilical cord blood for the sake of stem cells only

Niranjan Bhattacharya, Surgeon and Superintendant Bijoygarh State Hospital, Calcutta, India

To The Editor, BMJ, Dear Sir, Thank you very much for publishing a very interesting editorial by Drs. SJ Proctor, AM Dickinson, T Parekh and C Chapman in BMJ, 2001; 323: 60-1 (14 July). While the emphasis in this article is on stem cells, which constitute only 0.01% of the nucleated cells in the umbilical cord blood, the use of other cells which constitute 99.9% of the umbilical cord whole blood has not been mentioned. Our group of clinicians and researchers have been working in Calcutta on freshly collected placental cord whole blood transfusion, which is a rich source of fetal haemoglobin, growth factor and cytokine rich plasma as well as other nucleated cells, of which stem cells are an important constituent.

CONT.....
Dear Sir,

Thank you for publishing a thought provoking news piece by Scott Gottlieb (BMJ 2001;323:1025(b)) on drug related deaths among geriatric patients in hospitals.

CONT....
Function of thymus; An immune kaleidoscope?
Niranjan Bhattacharya (6 June 2003)

Thanks for publishing a very interesting review on the thymus (G. Werlen et al., Science 299, 1859, 2003). Although there is an abundance of fascinating literature on the immunological and molecular biological aspects of the thymus's growth and differentiation, there is a paucity of reports on its role in pathology vis a vis clinical implications.
Sally Hargreaves' news article is of great contemporary interest (BMJ 2003;326:675, 29 Mar). Like all other rational people, we are extremely distressed by the loss of innocent human lives in war. A large number of war casualties die because of haemorrhagic shock. Bellany (1) has projected that the percentage of wounded soldiers who die in battle fields will increase from 20 to 26% unless they are evacuated within two hours, and 32% if not evacuated within 24 hours. The majority of soldiers and civilians killed in action, crossfire or bombings die due to blood loss from compressible wounds and these deaths thus have the potential to be preventable if there can be timely blood, or a blood substitute, transfusion.
Pre-Immune and hypoimmune human fetal whole thymus transplant in a surgically prepared vascular subcutaneous axillary space of patent with varying degree of immuno-deficiency and its implications.
I) Dr. Niranjan Bhattacharya, (2) Dr. M.K. Chettri. (3) Dr. Kanai Lal Mukherjee. (4) Dr. Tara Shankar Bandopadhyay.(5) The Dept

Human Placental Umbilical Cord
CONCLUSIONS

- FETAL TISSUE IS THE RICHEST SOURCE OF TISSUE SPECIFIC AND NON-SPECIFIC STEM CELLS, WHOSE ENORMOUS REGENERATION CAPACITY AND ITS POSSIBLE ROLE IN THE REVERSAL OF HAYFLICKS LIMIT OF REPLICATIVE SENESCENCE HAS NOT BEEN EVALUATED PROPERLY SO FAR IN MEDICINE AND BIOLOGY.
THANK YOU FOR A PATIENT HEARING.