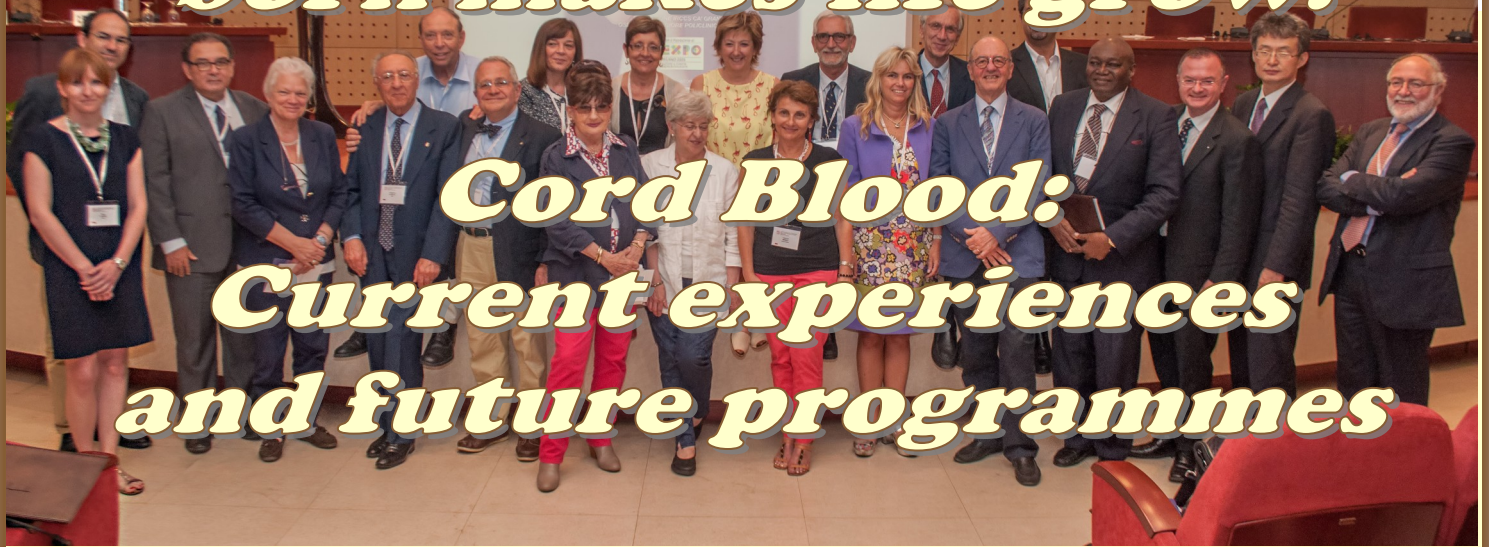


*A life that is
born makes life grow.*



*Cord Blood:
Current experiences
and future programmes*

HIGHLIGHTS



Fondazione
Internazionale
Menarini



*Milan
5-6 june 2015*

HIGHLIGHTS

Current aspects and future developments in cord blood transplant



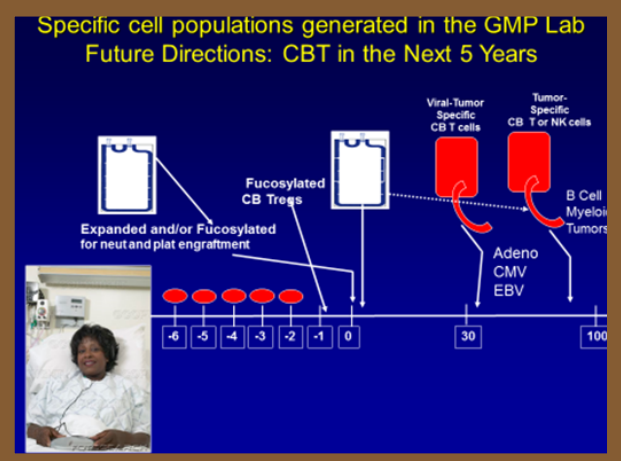
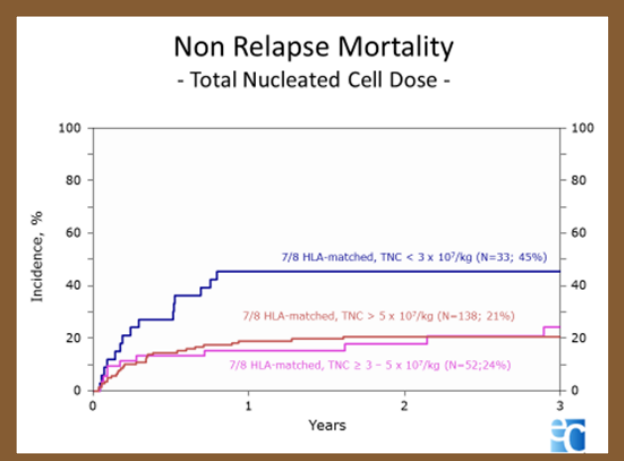
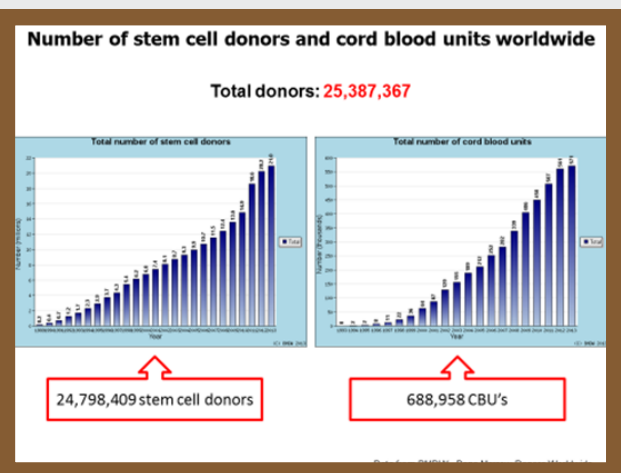
Eliane Gluckman
(Paris, F)

Prof. Gluckman from Paris closely examined this important and innovative issue presenting the lecture “Optimal haemopoietic transplant donor choice”.

Umbilical cord blood transplantation offers great benefits. Over the years, cord blood donors and cord blood transplantation centres have increased exponentially. The phenomenon has acquired a global

profile and the most involved continents are North America, Europe and Asia. Another important aspect is the absolute safety surgery technique for the donor, whose risk of serious adverse reactions is 1:1379. Prof. Gluckman presented some data regarding the compatibility of cord blood transplantation with A, B, C loci DRB1 of human leukocyte antigen. It has no more than 10% rate of fatal incidence events in three years.

This therapy provides obvious benefits to paediatric patients and to adults; however, it appears to be particularly efficacious in elderly people. These results are undoubtedly encouraging, but they could benefit from further improvements. Finally, prof. Gluckman presented the research areas where to apply this technique and the new clinical indications.

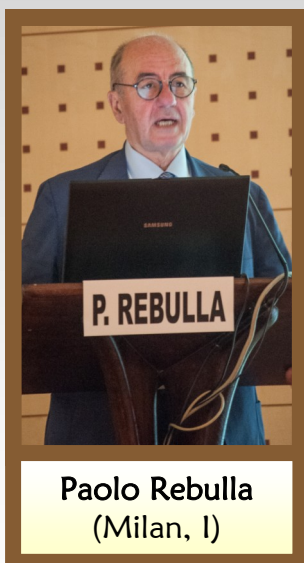


**For which diseases does this technique produce the best results?
How much does the cord blood transplantation cost?
Which are the future developments of this new application?**



HIGHLIGHTS

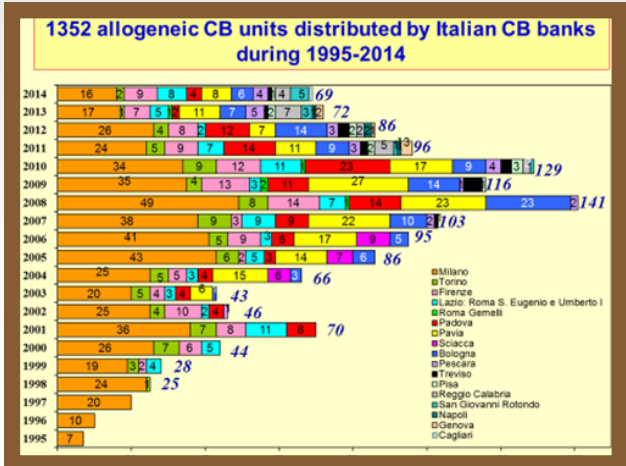
The Italian project on cord blood platelet gel



Paolo Rebulla
(Milan, I)

Professor Rebulla of Cà Granda Foundation in Milano is the co-inventor of platelet gel, a new therapeutic application. He presented the project that brought to Italy one-thousand new cord blood donations useful to treat with platelet gel nearly one hundred patients suffering from diabetic foot ulcers. Platelet gel obtained from cord blood is different from the one obtained from adult blood. Professor Rebulla presented some data regarding costs and benefits of the treatments with this

new product. Platelet gel costs 90% less than the usual advanced medication treatments. To assess clinical effectiveness of platelet gel in treating diabetic foot ulcers a clinical trial has been performed with the main diabetes centres across Italy and nineteen Italian active cord blood banks participated in the project. The clinical trial is still active and evolving in an international study, involving clinical centres and CB banks from different countries.



Platelet Gel obtained by adding thrombin and Ca or batroxobin to a platelet concentrate



**What could be the future application of this technology?
Can we modify the aging phenomena?
What are the costs for the treatments with platelet gel obtained from cord blood?**



HIGHLIGHTS



Noemi Greppi
(Milan, I)

Allogeneic platelet gel for bedsores treatment in elderly patients

Dr. Greppi presented some very interesting data on the use of platelet gel in elderly patients with bedsores.

Of primary importance is the content of a great concentration of growth factors in the allogeneic platelet gel. This is probably a strategic factor in determining the repairing of skin ulcer. The enrolled subjects were eleven elderly

hypo-mobile patients with severe and multiple ulcers.

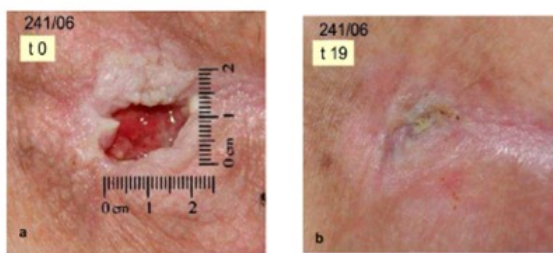
The treatment was carried out, lasting for a minimum of 4 weeks to a maximum of 20 weeks, and it obtained from 80 to 100% ulcer closures.

GROWTH FACTORS CONTENT in BC-PC pools precursors of allogeneic adult platelet gel Biologicals, 2011; 39:73-80

Platelet growth factor concentrations in the supernatants of samples from 40 BC-PC after 3 freeze/thaw cycles (median and range)

	PDGF-AB	PDGF-BB	TGF-β1	TGF-β2	b-FGF	VEGF	EGF	IGF-1
ng/mL	112 (31-157)	20 (3.8-34)	214 (48-289)	0.087 (0.030-0.28)	0.03 (0.006-0.214)	1.15 (0.18-2.46)	4.50 (0.87-6.64)	116 (72-156)
ng per 10 ⁹ platelets	56 (15-84)	11 (2-18)	113 (24-164)	0.046 (0.015-0.15)	0.018 (0.003-0.107)	0.61 (0.09-1.48)	2.28 (0.44-3.65)	61 (35-92)

A REPRESENTATIVE RESULT FROM A MEDIAN SIZE ULCER



IV stage sacrum ulcer from patient no. 7 before treatment (a: t = 0)
and after 19 weeks of treatment (b: t = 19) with 29 PG aliquots

- How was it possible to achieve such results?
- Can we use this therapy for other type of patients?
- Which are the action mechanisms involved in such result?
- What is the overall cost of the treatment with PG?
- What is the cost/benefit relation?



HIGHLIGHTS



Gianluca Tadini
(Milan, I)

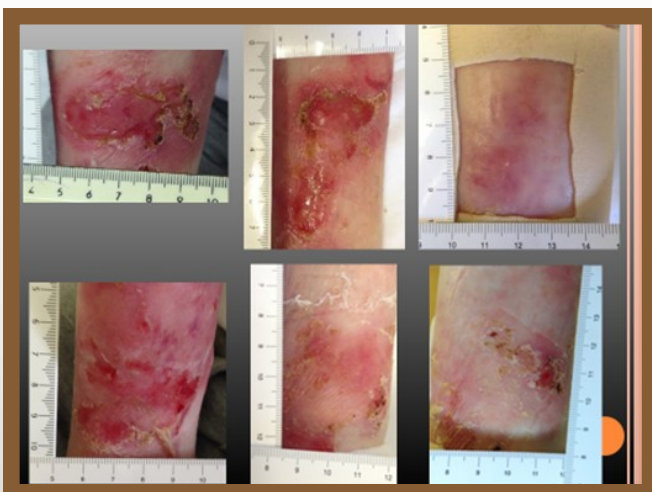
Platelet gel in the treatment of epidermolysis bullosa

Dr. Tadini presented data related to the therapeutic use of platelet gel in paediatric patients affected from epidermolysis bullosa. This disease affects children sharing a common feature: a very fragile epithelium. The disease is due to genetic defects, the mutated genes are all linked to keratin. The most severe forms are the so-called junctional epidermolysis bullosa, particularly when it is autosomal dominant. A further variant is the dermolytic epidermolysis bullosa, which results from mutations in the gene encoding the protein type VII collagen, characterized by recurring scarring with large blisters and sores.



Although considerable progress has been done with the cures for these diseases, we are still very far from achieving an acceptable standard. Attempts have been made applying in vivo and ex vivo gene therapy and other techniques as the recombinant DNA technology and the myeloablative bone marrow transplant but without satisfactory results. The use of platelet gel produced very encouraging results in treating ulcers and more generally in epidermal treatments. Although very interesting, these are now preliminary results based on three patients treatments. The outcomes of their skin healing level was valuated as "normal" by the anatomic-pathologist.

Dr. Tadini finally presented data related to a paediatric patient affected from a dominant autosomal epidermolysis bullosa characterized by large leg skin lesions. Platelet gel treatments technically healed the patient's skin tissues.



Which are the scenarios after these results?
Which is the mechanism of action?
How much does the growth factor effect on these results?



HIGHLIGHTS

Diabetic foot ulcer: what are the most effective therapies-



Mauro Gargiulo
(Bologna, I)

Prof. Gargiulo from Bologna presented a series of extremely innovative data on this important and extremely invalidating disease. Diabetic foot ulcer is a common disease involving different levels of peripheral arteries. Patients with diabetic arterial disease often suffer from unpainful neuropathy. This phenomenon seriously damages the limb causing large trophic lesions and important infections. Trophic lesions are an unfavourable prognostic factor as they are related to a significant increase in

mortality of diabetic patients.

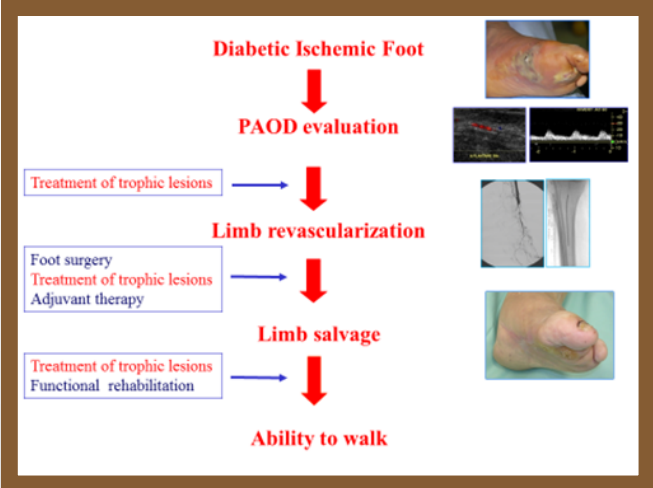
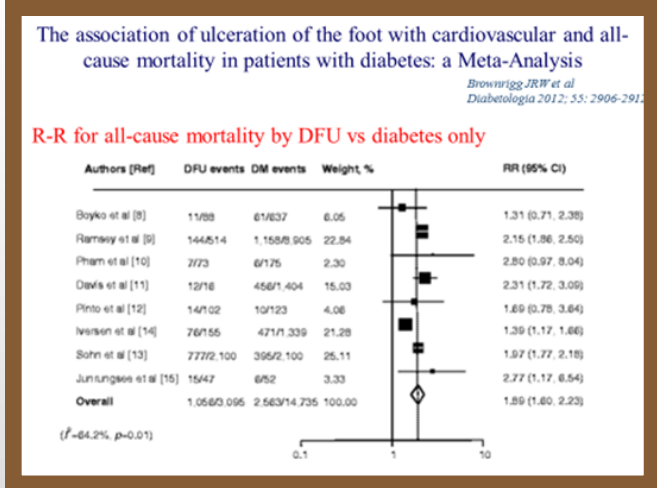
How to treat these patients? Why is the percentage of amputations in Italy still extremely high?

The optimal management of diabetic foot patients is the

result of a teamwork. The primary end-point consists in an effective revascularisation for the success of subsequent treatments. There are different revascularization techniques for diabetic patients, no one is the best one; there are rather several methods for different types of patients. After revascularization it is important to heal the ulcers. In this case, there are various techniques for different types of ulcers. Both have in common long healing times. In order to ensure shorter healing times it is fundamental to combine these methods to other strategies, one of them is the platelet gel.

Diabetic Foot

1. Arterial Disease
2. Arterial Disease + Neuropathy
3. Neuropathy



Diabetic foot: which are the most effective therapeutic strategies? - - - Which are the main revascularization techniques? - - - Which are the strategies to treat the trophic lesions? - - - How to reduce the healing times of trophic lesions?



HIGHLIGHTS



Caterina Minniti
(New York, USA)

Complex Wounds: lower extremities ulcers in patients with blood disorders

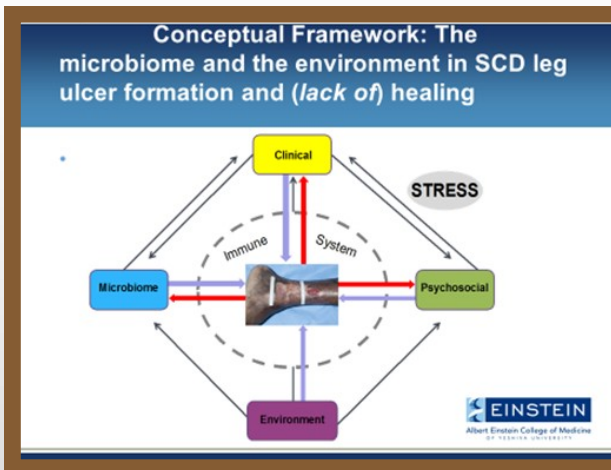
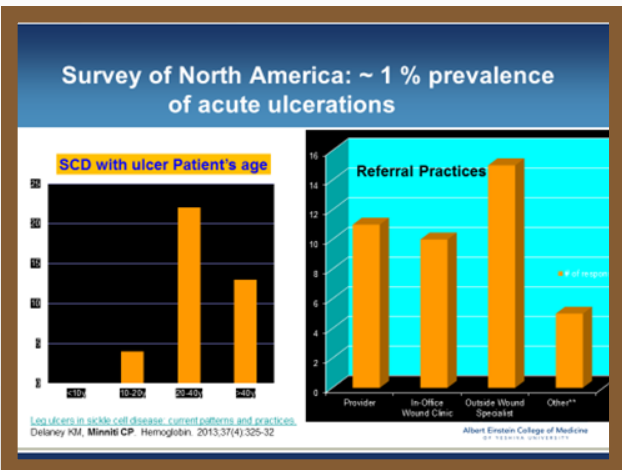
Prof. Minniti from New York presented innovative data on ulcers in patients with blood disorders, particularly on patients with sickle cell anaemia. This is the most common complication of sickle cell anaemia and it is often underestimated. Its incidence varies apparently according to the countries involved. The aetiology is still unknown. Endothelial dysfunction seems to play an important role. Another important factor seems to be chronic inflammation, thrombosis and prostatic hyperplasia. The ulcer formation often precedes painful symptoms in the absence of other factors and skin symptoms. The symptomatology is probably an early indicator of an alteration of peripheral microcirculation, vascular diseases and chronic inflammation.



What are the most appropriate therapeutic strategies to adopt? There is a variety of approaches but no one is the solution.

An important aspect seems to be the genetic typing of those patients suffering from sickle cell anaemia, to identify specific skin microbiome for leg ulcers.

Professor Minniti pointed out that we are still at “ground zero” in treating this disease.



**What is the impact of leg ulcers on these patients?
How to value the treatment and the monitoring applying the genetic typing?
Which are the most effective therapeutic strategies?**



HIGHLIGHTS



Alejandra Vivas
(Miami, USA)

Patient's training and role on prevention and management of diabetic foot ulcers, USA perspective.

Dr. Vivas from Miami presented very recent data on the effects of diabetes and its complications, particularly regarding diabetic foot ulcers. She said we are facing a problem of epidemic proportions: in 2013 USA spent 17 billion to care these patients. The real problem is the diabetic patient's noncompliance to medical advices. Studies have been carried out to assess the impact of education on healthy lifestyles and to take the main appropriate measures to slow down the disease progression towards its complications, particularly for the diabetic foot ulcers (DFU). These educational interventions improved the patient's knowledge on the health risks of diabetes and, as a result, most of them changed radically their lifestyles. Unfortunately, there are insufficient evidence to prove that a new lifestyle regime reduces the incidence of complications.

This data show the importance of a correct patient's education particularly at an early stage of the disease. In case of complications, it is fundamental to intervene with specific therapeutic controls.

At this point of her report, Dr. Vivas presented some data related to clinical studies with new drugs based on growth factor. The pharmacological treatment with Becaplermin platelet gel has provided evidence in increasing healing rates of DFUs, although extreme caution is required in patients with neoplastic pathologies. These

results could be further confirmed by the use of new platelet-enriched plasma drugs.

Diabetic foot ulcers (DFU)

- 1.5 million individuals with DM (6%) have a DFU
- DFU are the most costly and preventable complication of DM
- Significant health risk: increased morbidity and mortality
- Up to 25% of individuals with DM develop a DFU during their lifetime

Singh N. JAMA. 2009
Luhmann N. Diabetic Care. 2011

Goal

Successful primary prevention

Platelet Rich Plasma

- There is scientific evidence that PRP favors the healing process and has favorable outcomes on the treatment of DFUs
- RCT, n=72 DFUs
Ulcers treated with PRP gel healed significantly more (81.3% vs 42.1%) than their control gel matching group (P = 0.036)
- RCT= application of PRP led to a statistically significant shorter mean healing time compared to platelet poor plasma.

Driver VR. Ostomy Wound Manage. 2009
Saad Setta HE. Int Wound J. 2011

Which is the incidence of diabetes in USA? Which are the main health risk due to diabetic foot? - - - How to educate patients to manage the diabetic foot disease? Which is the role of PDGR in treating diabetic foot ulcers? Which is the role of platelet-enriched plasma for such diseases?



HIGHLIGHTS

Biological eye drops



Marina Buzzi
(Bologna, I)

Professor Marina Buzzi from Bologna introduced this important subject. One of the most prevalent ocular surface disorders is the so-called dry eye disease. These patients are characterized by damages of the ocular surface epithelium with a decrease of the tears film. The main implications include bleedings, ulcerations and consequent perforations in untreated severe cases. Currently conventional treatment for ocular surface disorders based on the use of artificial teardrops, topical anti-inflammatory agents,

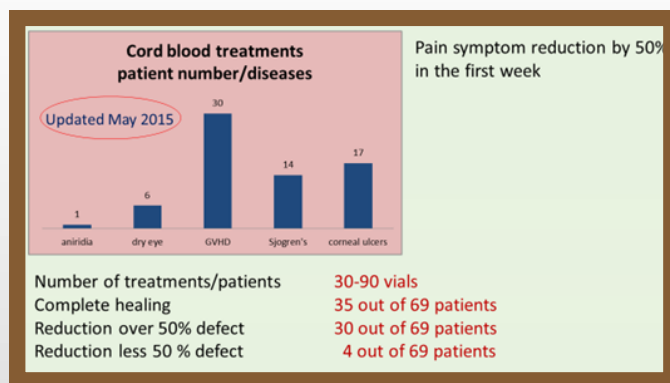
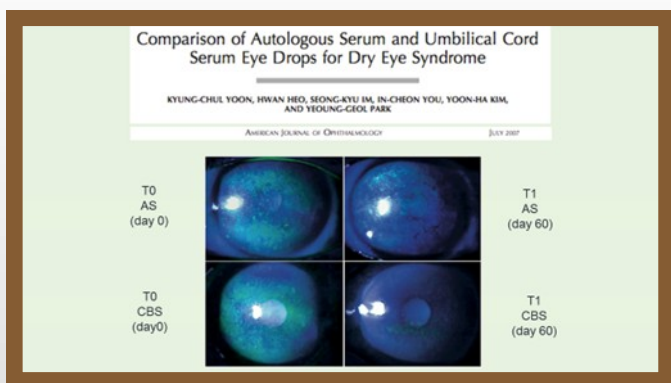
	Cord Blood Serum	Autologous Serum	Tear Substitutes	NSAID Steroids	Cyclosporin A
pH/Osmolarity	natural	natural	chemically buffered controlled	chemically buffered controlled	chemically buffered controlled
Preservatives	free	free	present	present	present
Patients compliance	optimal	optimal	good depending upon type	products burn	products burn
Chemical components	absent	absent	present	present	present
Ocular nutrients	present	present	present only in the last generations of products	absent	absent
Growth factors	present	present	absent	absent	absent
Anti-inflammatory properties	present, natural substances (direct)	absent (presence of pro-inflammatory)	absent (only diluting, indirect effects)	present, chemical compounds	present, chemical compounds

therapeutic contact lenses, without, however, tackling and resolving the main problem of the lack of biologically active components usually present in normal tears.

It is high time to make a change in the therapy of dry eye disease introducing the new therapy of biological eye drops. Dr. Buzzi presented different eye drops types and formulations.

The therapeutic benefit consists mainly in the high concentration of growth factors and other biological active components. Among them, homologous platelet-rich plasma derivate products, from adult blood donors and cord blood donors, seem to be the most effective.

Clinical data regarding the use of these products, especially umbilical cord blood serum eye drops (blood derived biological eye drops), show an intensive clinical activity and high healing efficacy.



Which is the procedure to product biological eye drops?
Which are the main components determining the clinical efficacy?
Why homologous products have a better performance than autologous products?



**A life that is born makes life grow.
Cord Blood: current experiences and future programmes
Milan, 5-6 june 2015**

HIGHLIGHTS

These are just some of the topics tackled during the congress. Additional in-depth information and complete talks are available on Fondazione Menarini website.

Visit this link: <http://www.fondazione-menarini.it/> and subscribe Fondazione Internazionale Menarini website and enter the Multimedia Contents.



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