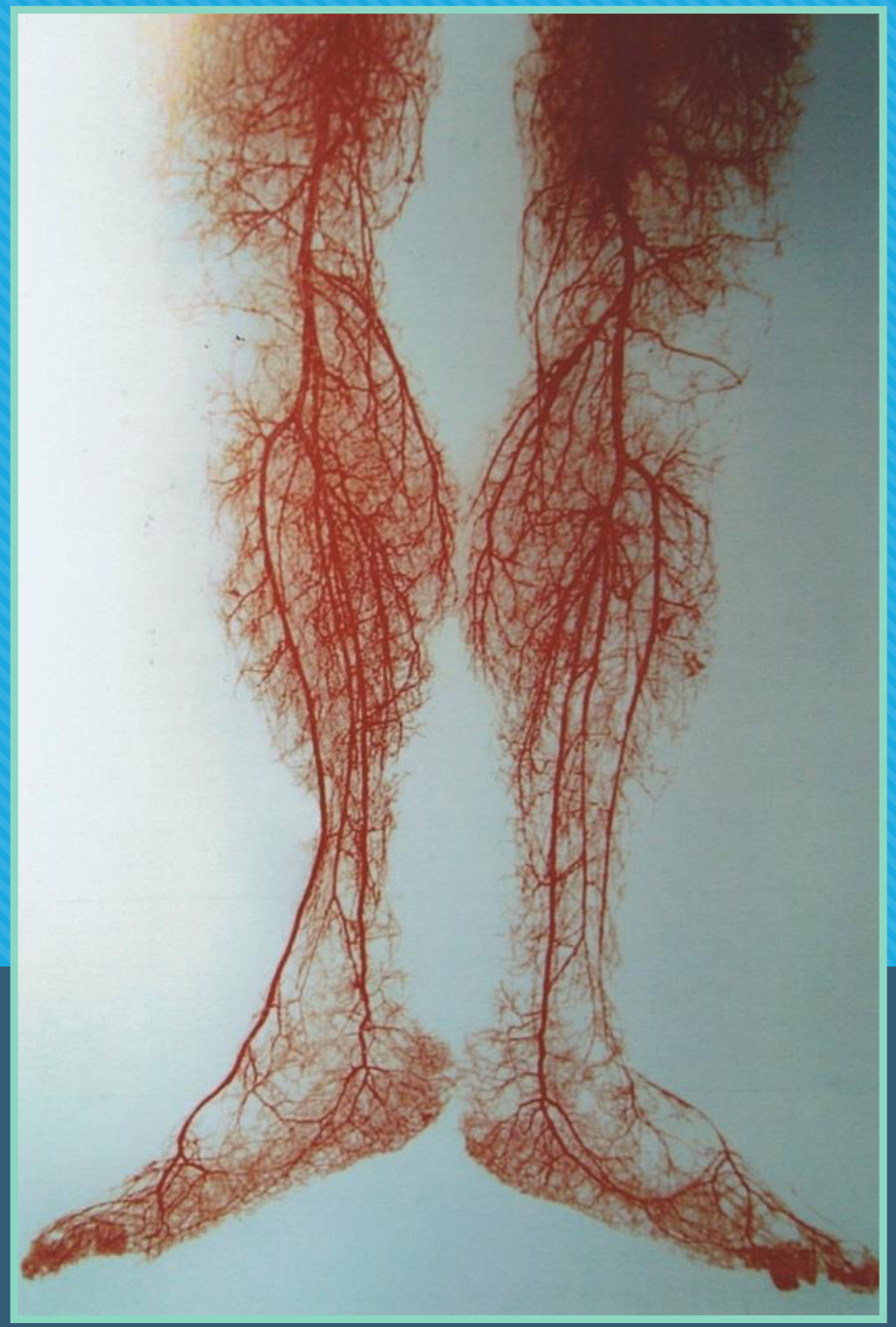
Facultad de Medicina

1992-2020
28 años

TRASPLANTE DE CÉLULAS MONONUCLEARES PROGENITORAS DERIVADAS DE MÉDULA ÓSEA (STEM CELLS) PARA INDUCIR ANGIOGÉNESIS EN PACIENTES CON ISQUEMIA SEVERA EN MIEMBROS INFERIORES



Dr. Luis Padilla [1-2-5]
Dr. Juan Rodríguez –Trejo [3]
Dr. Mauricio Di Silvio FACS[1]
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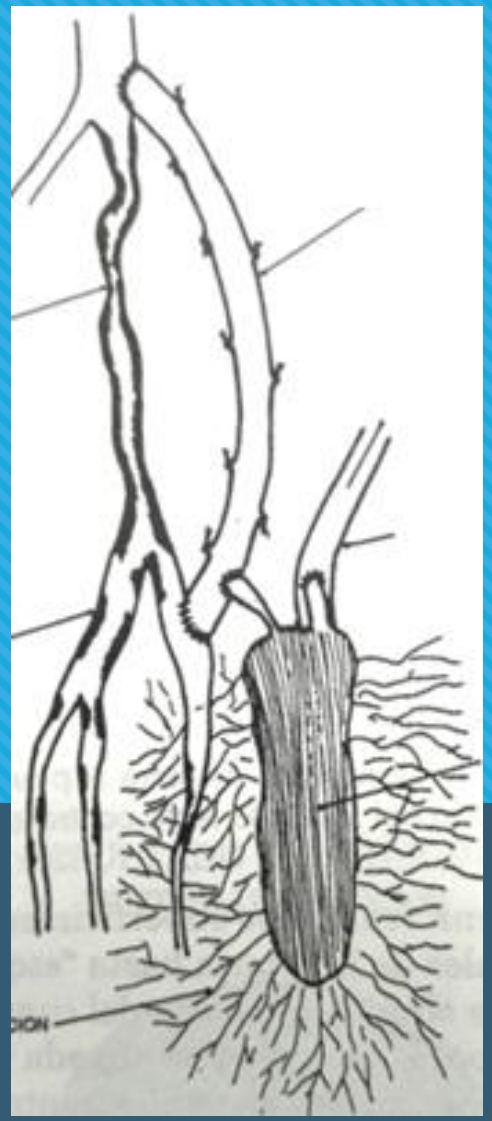
5 Laboratorio de Medicina Regenerativa e Ingeniería de Tejidos

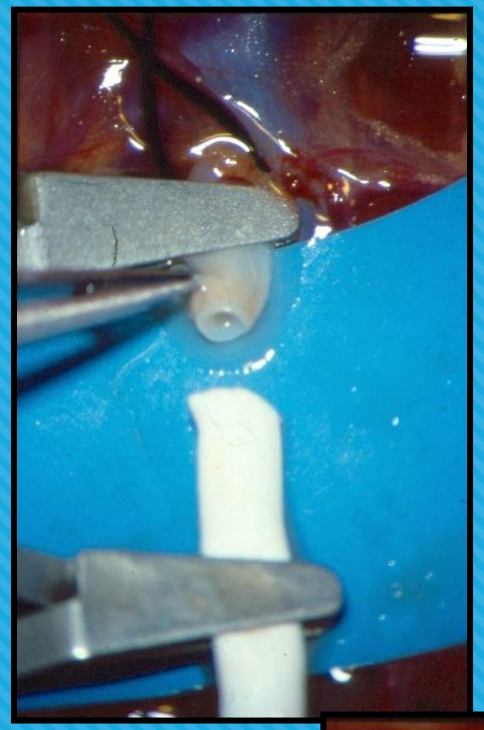
Trasplante de músculo en derivaciones arteriales distales



Dr. Luis Padilla, Dr. Hugo Carrillo, Dr. Juan Rodríguez-Trejo. *et, al.*

El colgajo permite el desahogo del flujo sanguíneo del puente hacia el músculo. Permitiendo el aumento de su velocidad en la derivación arterial. La permeabilidad a largo plazo de estas derivaciones pueden aumentarse gracias a la **angiogénesis** a partir del colgajo.

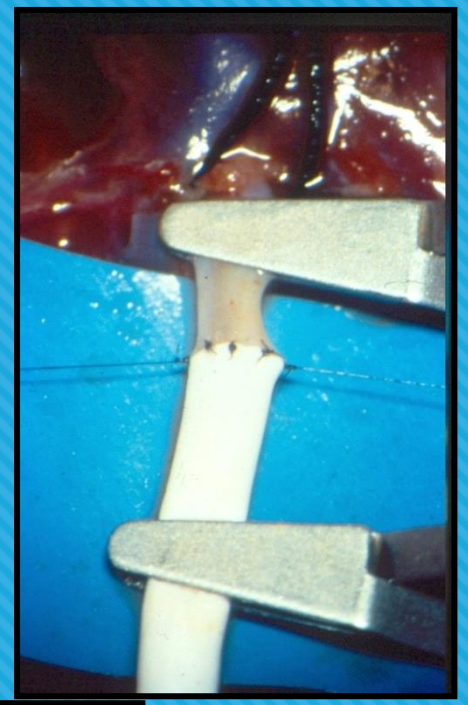
Rev. Mex Angiol **1992**; 20(2):32-36

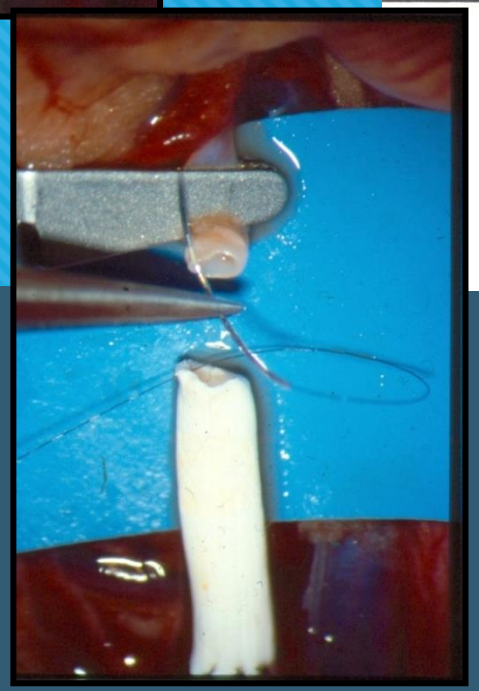


Luis Padilla, Armando Valle,
Hugo Carrillo, Mauricio Di Silvio,
Mauricio Contreras, Fernando Viniegra,
Rodolfo Sanchez, and Javier Fajer

POLYTETRAFLUOROETHYLENE MICROPROSTHESIS IN THE ARTERIAL SYSTEM OF THE RAT

JOURNAL OF RECONSTRUCTIVE MICROSURGERY/VOLUME 4, NUMBER 1 OCTOBER 1987



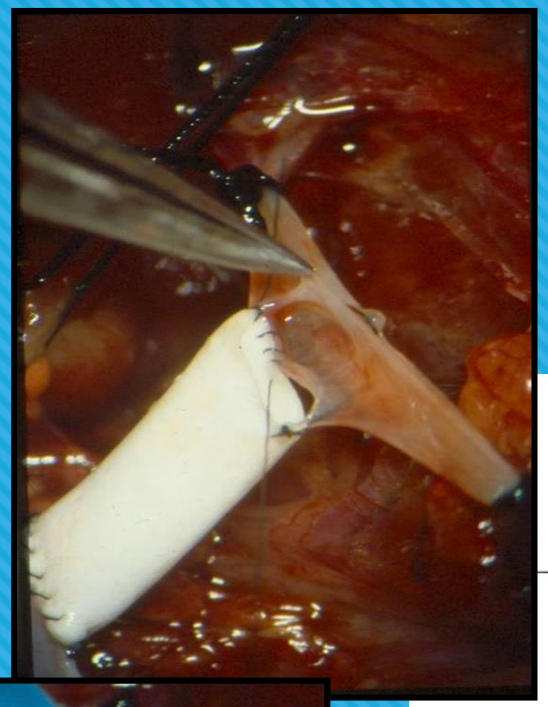


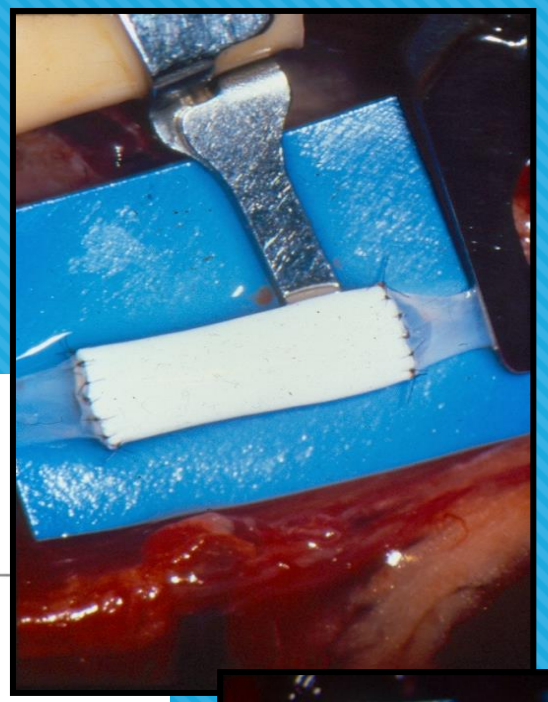
ABSTRACT

The experimental behavior of a 1-mm internal diameter (i.d.) polytetrafluoroethylene (PTFE) microprosthesis, as a substitute for an abdominal aortic segment in the rat, was reviewed. Fifty Wistar rats were divided into four groups: Group I—12 rats with autotransplant of an abdominal aortic segment (AAS); Group II—12 rats with allotransplant of an AAS obtained from Long-Evans rats; Group III—12 rats with xenotransplant of an AAS taken from rabbit femoral arteries; and Group IV—14 rats with substitution of an AAS by a 1-mm i.d. PTFE microprosthesis. The rats were sacrificed at different time intervals ranging from five to 360 days, with previous aortography.

In Group I, there was a 100 percent patency at a mean of 152.41 days; in Group II, a 91.6 percent patency at a mean of 100.08 days; in Group III, an 83.3 percent patency with a 75 percent aneurysmal dilation at a mean of 107.58 days; in Group IV, a 71.42 percent patency with two anastomotic aneurysms at a mean of 105 days ($P < 0.05$, chi square) between Groups I and IV, autotransplant vs. PTFE).

The 1-mm PTFE microprosthesis placed in the arterial system of the rat proved to be a reliable alternative for microvascular substitution.





Luis Padilla, Nicolas Sastre,
Alberto Chousleb, Mauricio Di Silvio,
Mauricio Contreras,
Benjamin Manzano, Nyria Reyes,
Rodolfo Sanchez, and Javier Fajer

POLYTETRAFLUOROETHYLENE MICROPROSTHESIS IN THE VENOUS SYSTEM OF THE RAT

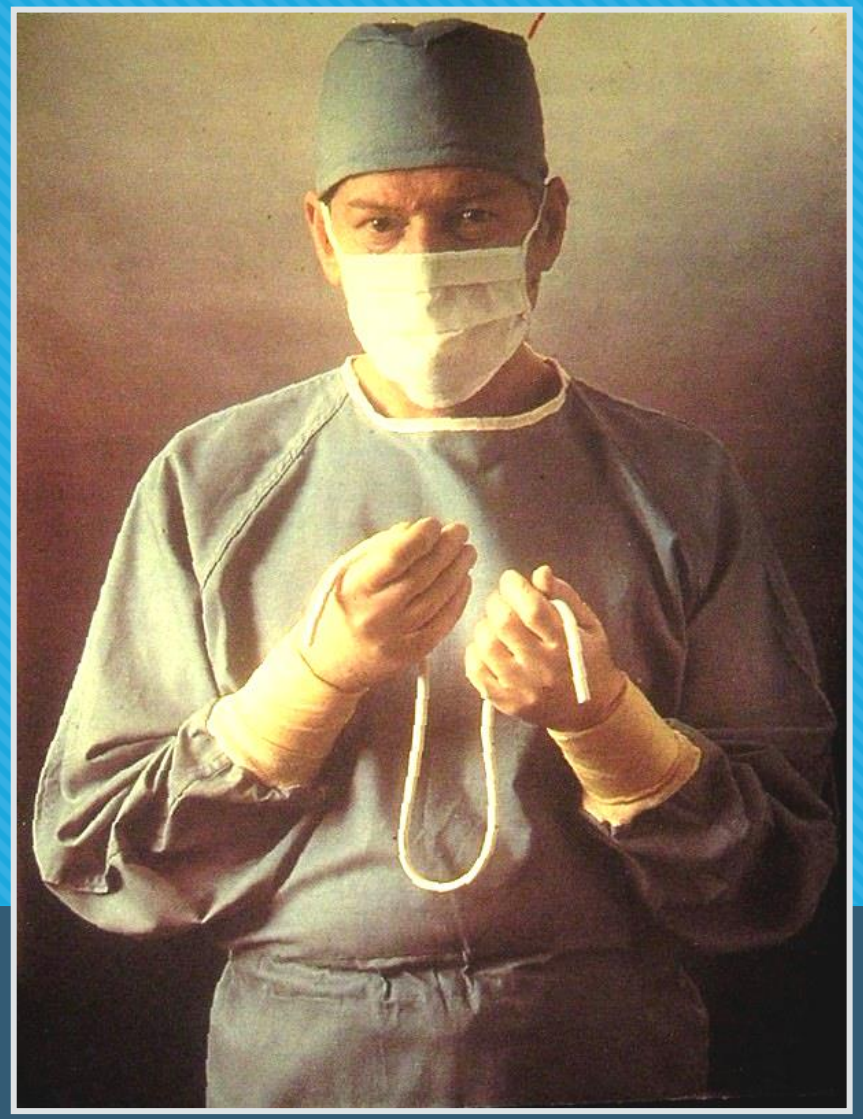
JOURNAL OF RECONSTRUCTIVE MICROSURGERY/VOLUME 3, NUMBER 2 JANUARY 1987

ABSTRACT

In this study, a 2 mm internal diameter (i.d.) polytetrafluoroethylene (PTFE) microprosthesis was used in the venous system of the rat, to determine whether or not it could serve as an acceptable microvenous substitute. Forty Long-Evans rats were divided into four groups: Group 1—10 rats with autotransplant of an inferior vena cava segment; Group 2—10 rats with a segment substitution of the inferior vena cava by a 2 mm i.d. PFTE microprosthesis; Group 3—10 rats with a laterolateral portacaval shunt; and Group 4—10 rats with a portacaval shunt and interposition of a 2 mm i.d. PTFE microprosthesis (new model). The rats were sacrificed at different time intervals up to 100 days, with cavography (femoral access) in Groups 1 and 2 and spleenoportography (direct puncture of the spleen) in Groups 3 and 4, before sacrifice.

In Group 1, a 100 percent patency was observed at a mean of 49 days; in Group 2, a 70 percent patency with a 30 percent stenosis at a mean of 39.4 days ($p < 0.05$); in Group 3, a 100 percent patency at a mean of 42.5 days; and in Group 4, a 30 percent patency at a mean of 38.4 days ($p < 0.01$).

Results showed that the 2 mm i.d. PTFE microprosthesis placed in the venous system of the rat is not an efficacious procedure, and that the search for better microvenous substitutes should focus on those of biologic origin.



Clinical in vitro endothelialization of femoropopliteal bypass grafts: An actuarial follow-up over three years

Peter Zilla, MD, PhD, Manfred Deutsch, MD, Johann Meinhart, PhD,
Rudolf Puschmann, MD, Thomas Eberl, MD, Erich Minar, MD,
Robert Dudczak, MD, Herbert Lugmaier, MD, Peter Schmidt, MD,
Irene Noszian, MD, and Teddy Fischlein, MD, *Wels, Vienna, and Schallerbach, Austria*

Purpose: **The creation of an endothelial coverage on prosthetic vascular surfaces may improve the performance of synthetic small diameter vascular grafts. In vitro lining with cultured autologous endothdial cells offers a confluent endothelium at the time of implantation.**

Methods: **Between June 1989 and December 1991,49 patients who had no saphenous vein available entered the study. Indication for operation was disabling claudication in 37 patients and critical ischemia in 12 patients. With a random 1:2 assignment, 33 patients were admitted to the endothelialized group and 16 control patients received an untreated polytetrafluoroethylene prosthesis. Cultured autologous endothelial cells from the external jugular vein were confluently lined onto polytetrafluoroethylene grafts precoated with fibrinolytically inhibited fibrin glue. The follow - up was based on angiography, platelet labeling studies with indium 111-labeled oxine, assessment of the ankle-brachial index, and duplex sonography.**

Results: **First - passage mass cultures of 16 million endothelial cells - required for the confluent lining of a 70 cm long 6 mm graft - were reached 25.1 ± 11.2 days after vein excision. Growth failure occurred in 27.3%. After 32 months, the actuarial patency was 84.7% for endothelialized grafts and 55.4% for control grafts ($p < 0.041$ by Breslow test; $p < 0.068$ by Mantel-Cox test). The ankle-brachial index was continually diverging, reaching significantly lower values in the control group at 24 months (0.98 ± 0.14 in the endothelialized group versus 0.70 ± 0.12 in the control; $p < 0.0023$). The uptake of indium 111 – labeled platelets – measured at 9 days, 3 months, 6 months, and 12 months-was significantly lower in the endothelialized group during the entire observation period.**

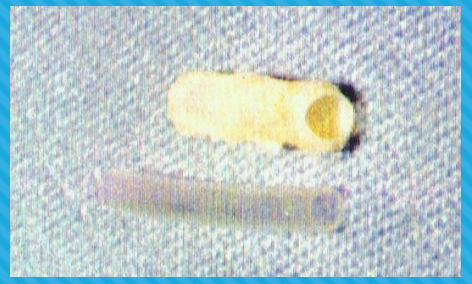
Conclusions**: Our initial 3-year data demonstrate the early superiority of endothelialized synthetic grafts over commonly used untreated expanded polytetrafluoroethylene prostheses. (J VASC SURG 1994;19:540-8.)**

Peter Zilla

(J VASC SURG 1994;19:540-8.)

AORTA DE RATA CON TUBO DE FIBROCOLÁGENA REFORZADO CON POLIÉSTER

a



b

c

e

d

Cirujano General Vol. 18 Núm. 2 - 1996

Angiogénesis inducida por túneles fibrocolágenos

Angiogenesis induced by fibrocolagenous tunnels

Dr. Luis Padilla Sánchez
Dra. Irma Araceli Carrillo-Soto
Dra. Margarita V. García Garduño
Dr. Rafael Valdés González

Resumen

Objetivo: Estudiar, en ratas, la neo-endotelización espontánea de microbioprótesis, utilizándolas como sustitutos de aorta abdominal.

Sede: Departamento de Cirugía, Facultad de Medicina, UNAM. México.

Diseño: Estudio experimental en animales, prospectivo, transversal, sin diseño estadístico.

Material y métodos: Se prepararon tubos fibrolágenos en ratas Wistar, al implantarles tubos de "silastic" grado médico de 1.65 mm de diámetro. El tubo fibrocolágeno se dividió en dos segmentos de 20 mm de longitud. Se practicó a 15 ratas Wistar "autotrasplante" y a 15 ratas "Long-Evans", "alotransplante" en aorta abdominal, con técnica microquirúrgica. Las ratas fueron sacrificadas a diferentes intervalos de tiempo, entre 12 y 120 días, previo estudio angiográfico transfemoral, microfotografía, dibujo de la pieza y microscopía electrónica de barrido, para precisar en detalle la neo-endotelización.

Resultados: En el grupo I se observó permeabilidad del 100% y 66% de aneurismas. En el grupo II, permeabilidad del 80% y 26.6% de aneurismas con 13% de calcificaciones. La neo-endotelización fue irregular y sólo a nivel de las anastomosis; sin embargo, la observación constante de ambos grupos de estudio, demostró la presencia de vasos de neoformación o "angiogénesis", en la periferia del tubo microfibrocolágeno antes de su extirpación.

Abstract

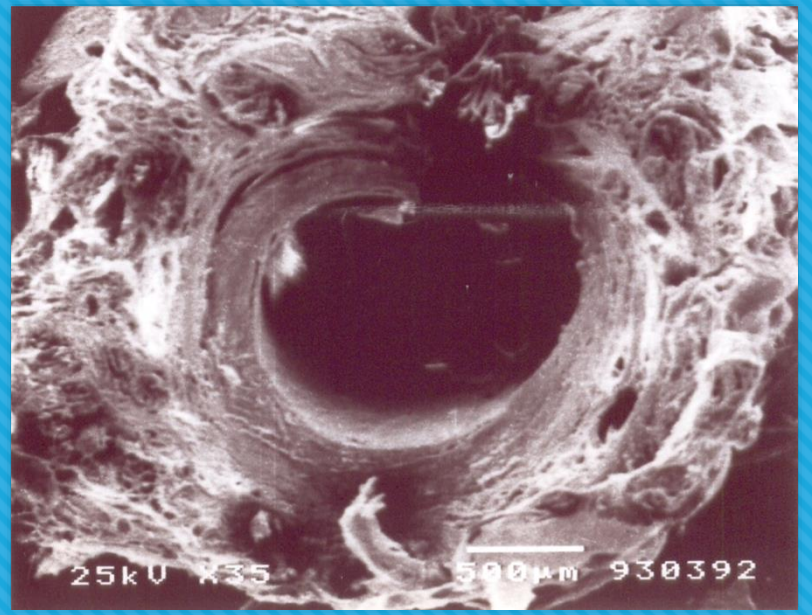
Objective: To study in rats the spontaneous neo-endothelization of microbioprosthesis, using them to substitute the abdominal aorta.

Setting: Departament of Surgery, School of Medicine, National Autonomous University of México (UNAM), Mexico City, Mexico.

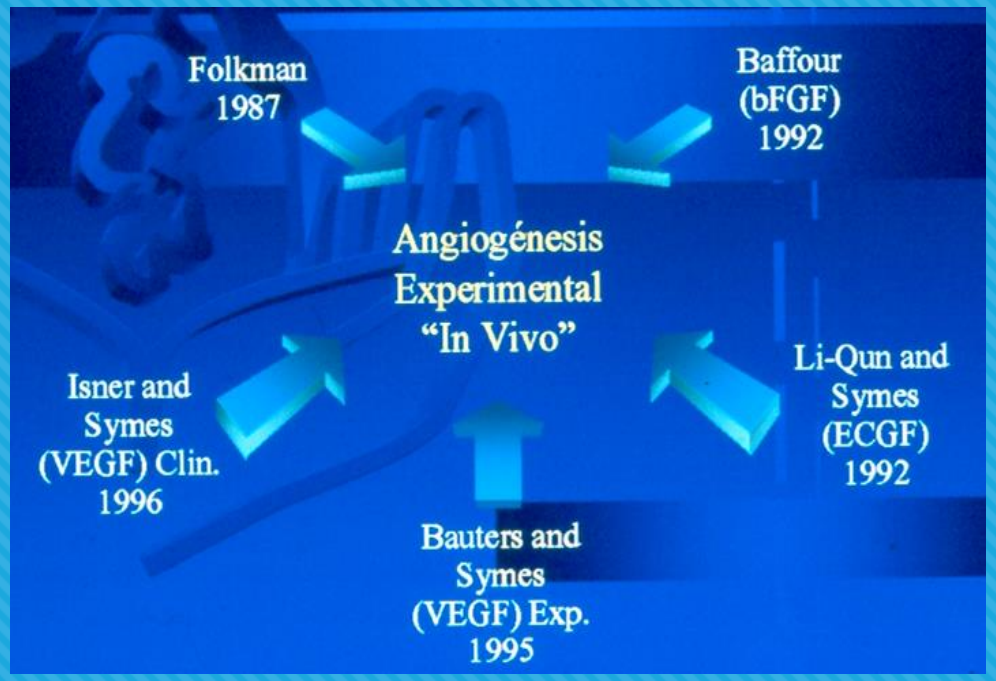
Design: Experimental, prospective, transversal study in animals, without statistical analysis.

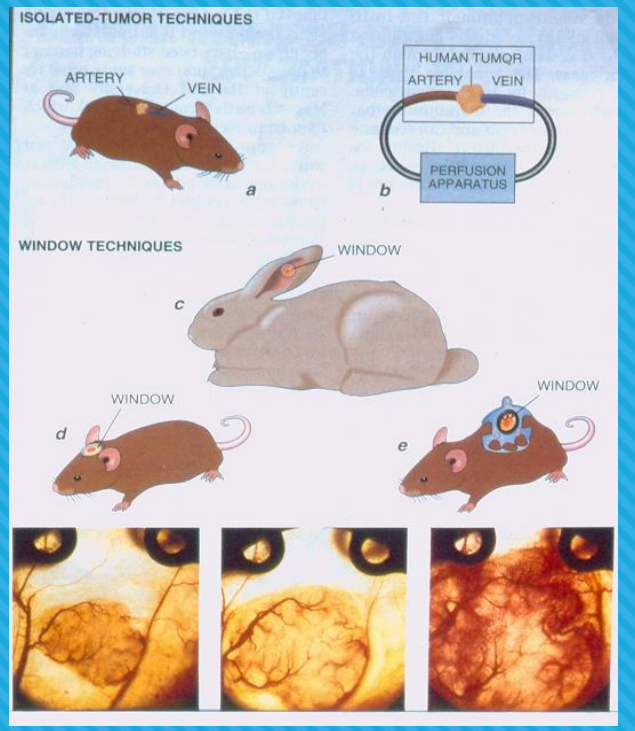
Material and methods: We prepared fibrocolagenous tubes in Wistar rats, by implanting medical grade Silastic tubes of 11.65 mm in diameter. The fibrocolagenous tube was divided in two segments of 20 mm length. Fifteen Wistar rats were submitted to autotransplant (Group I) and 15 Long-Evans rats to an allotransplant (Group II) in the abdominal aorta, using microsurgery techniques. Rats were killed at different time intervals, between 12 and 120 days, after performing transfemoral angiographic studies, microphotographies, drawing of the piece, scanner electronmicroscopy, to identify precisely the neo-endothelialization process.

Results: Group I yielded a 100% permeability and 66% of aneurysms. Group II presented an 80% permeability and 26.6% of aneurysms with 13% calcification. Neo-endothelialization was irregular and occurred only on the site of anastomosis; however, a constant finding in both groups was the presence of neoformed vessels or "angiogenesis"



Red de vasos en neoformación


Folkman
1987
Baffour
(bFGF)
1992
Angiogénesis
Experimental
"In Vivo"
Isner and
Symes
(VEGF) Clin.
1996
Li-Qun and
Symes
(ECGF)
1992
Bauters and
Symes
(VEGF) Exp.
1995


ISOLATED-TUMOR TECHNIQUES
ARTERY
VEIN
a
HUMAN TUMOR
ARTERY
VEIN
PERFUSION
APPARATUS
b
WINDOW TECHNIQUES
WINDOW
c
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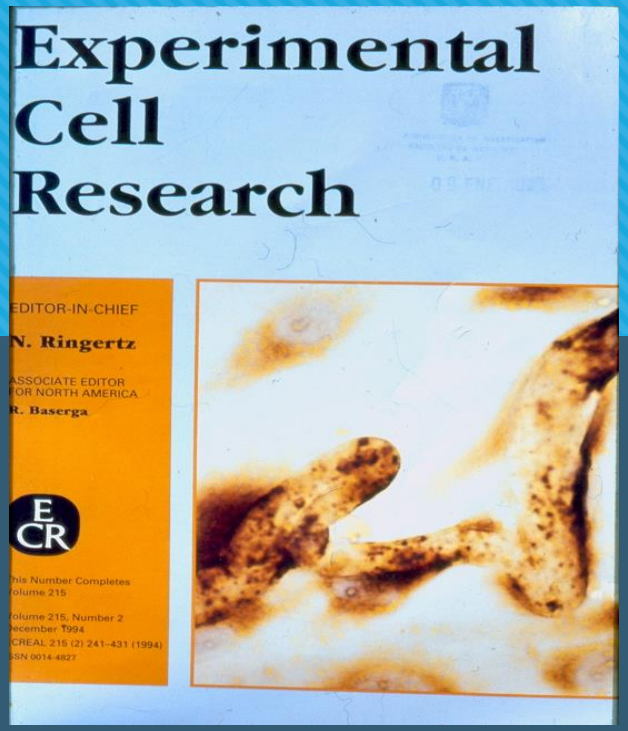
Experimental
Cell
Research
EDITOR-IN-CHIEF
N. Ringertz
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FOR NORTH AMERICA
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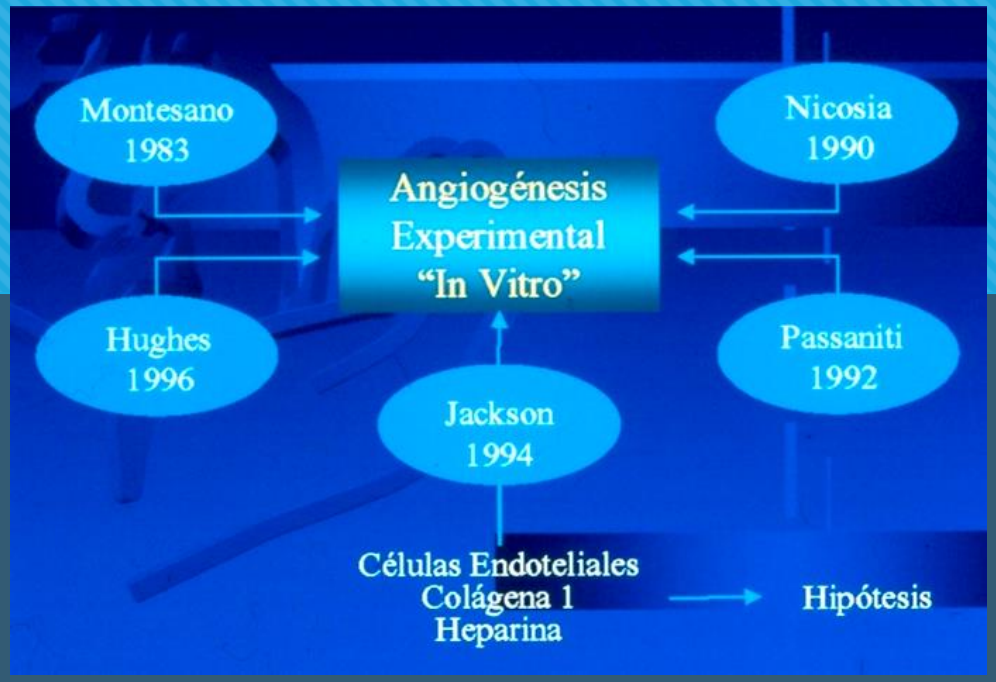

Montesano
1983
Nicosia
1990
Angiogénesis
Experimental
"In Vitro"
Hughes
1996
Passaniti
1992
Jackson
1994
Células Endoteliales
Colágena 1
Heparina
Hipótesis

Túnel fibrocolágeno

Cir Ciruj 1999; 67: 59-65

Angiogénesis inducida por colágena polivinilpirrolidona y heparina en el músculo isquémico

Acad. Dr. Luis Padilla S,* Dr. Siegfried Figueroa B,* Dr. David de León,* Dra. Irma Carrillo S,*
Dra. Ana Cristina King M,** Dr. Paul Schalch L,** Dr. Horacio Mollinedo R,**
Dr. Horacio Olguín J,** Dr. Fernando Viniegra R,** Dr. Gerardo Mercado L**

Resumen

Estudio de investigación experimental, prospectivo y comparativo, con el objeto de evaluar los efectos de la aplicación exógena de colágena tipo I, Polivinilpirrolidona (PVP) y heparina, en túneles musculares fibrocolágenos, en la extremidad isquémica de la rata, para inducir neovascularización o angiogénesis. Se usó un modelo de isquemia en la extremidad posterior derecha de 40 ratas Wistar en dos tiempos. 1º Ligadura de la arteria iliaca común vía abdominal y colocación de una prótesis de silasticpoliéster en el músculo gracilis para la generación de un túnel fibrocolágeno. 2º Ocho semanas después, exposición del paquete vascular femoral, ligadura de esta arteria, localización y extracción de la prótesis, perforación y lavado del túnel fibrocolágeno y aplicación de sustancias. En el grupo I se aplicó solución fisiológica, en el grupo II colágena tipo I con PVP, en el grupo III heparina sódica y grupo IV colágena tipo I con (PVP) y heparina sódica. Para la valoración se llevó a cabo angiografía de las extremidades tratadas, cuantificando el número de intersecciones en una superficie milimétrica de 50 x 50 mm. El mayor número de intersecciones se obtuvo en el grupo IV con una media de 20.22 contra una media de 13.5 intersecciones en el grupo I (control con sol. fisiológica) = p de 0.14 mediante el análisis de varianza para comparar dos grupos (ANOVA). El estudio demuestra mayor angiogénesis en el músculo isquémico de la rata, si se aplica colágena tipo I con (PVP) y heparina.

Palabras clave: angiogénesis, neovascularización, colágena tipo I, túnel fibrocolágeno.

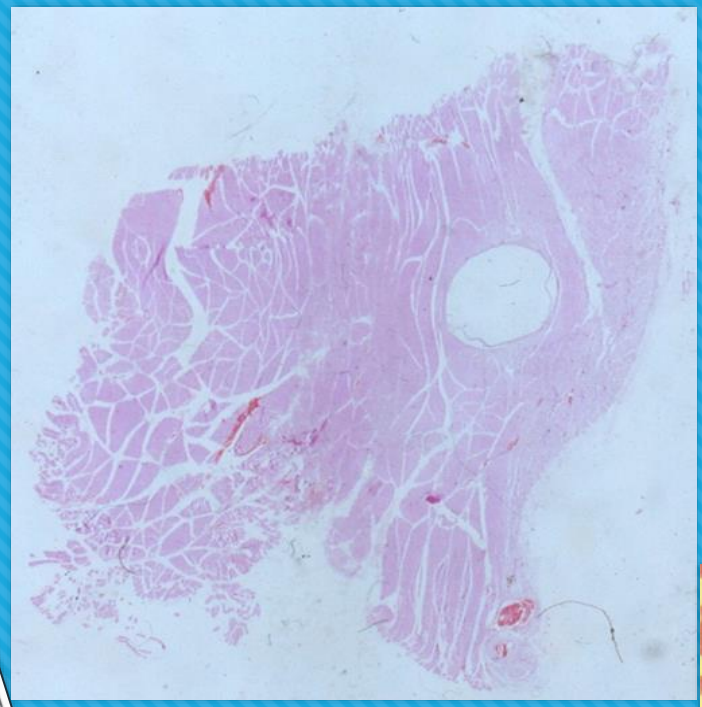
Summary

Experimental, prospective and comparative research to evaluate the effects of exogenous application of the type I collagen, polyvinylpirrolidon (PVP) and heparin into fibrocollagenous muscle tunnel of an ischemic lower limb of the rat, in search of new blood vessel formation or angiogenesis. We used a two-stage ischemia model in the right hindlimb of 40 Wistar rat's. 1°, by abdominal ligature of the common iliac artery and colocation of a silastic-polyester prosthesis into the gracilis muscle to create a fibrocollagen tunnel. 2°, weeks later, exposition and ligature of the femoral artery, localization and extraction of the prosthesis, perforating and washing the tunnel and application of different substances in four different groups.

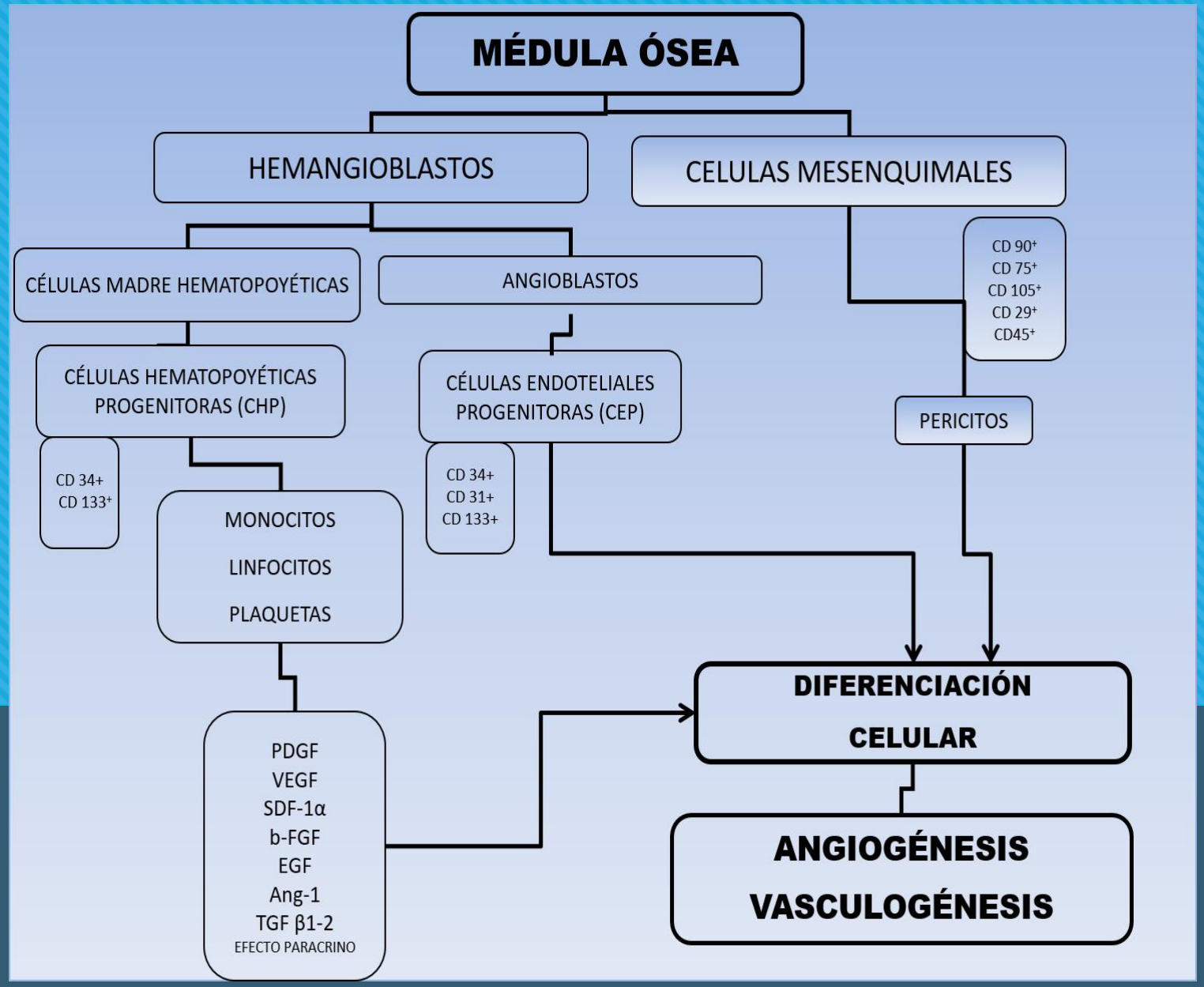
We used saline solution for the pilot-group (I) where angiogenesis appeared as a response to ischemia; Group II type I collagen with (PVP); Group III heparin, and Group IV type I collagen with PVP and heparin. For the evaluation we practiced angiography of the treated limbs and quantified the number of intersection on a 50 x 50 mm milimetric surface. We obtained a p = 0.14 by comparing group IV (mean, 20.22 intersections) with group I (mean 13.5 intersections) using the analysis of variance (ANOVA) to compare two the groups.

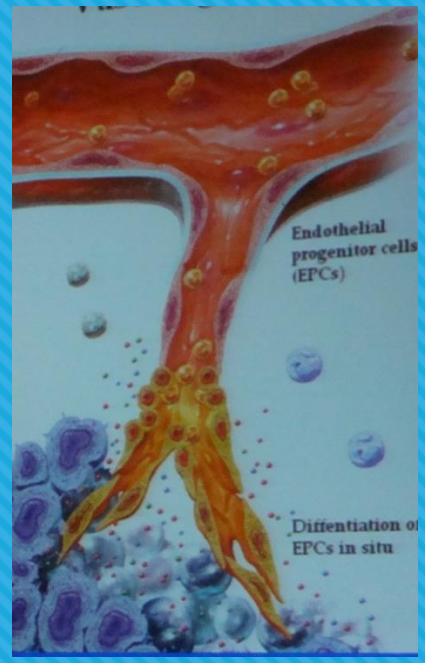
It is proved that there is a larger neoformation of vessels in an ischemia model in the rat muscle if there is applied type I collagen with PVP and heparin in a muscular fibrocollagen tunnel.

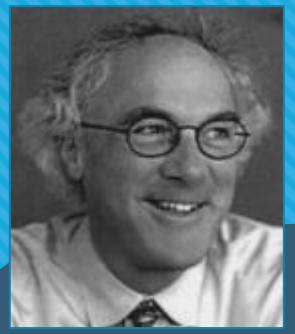
Key words: Angiogenesis, Neovascularization, Type I collagen, Muscular fibrocollagen tunnel.



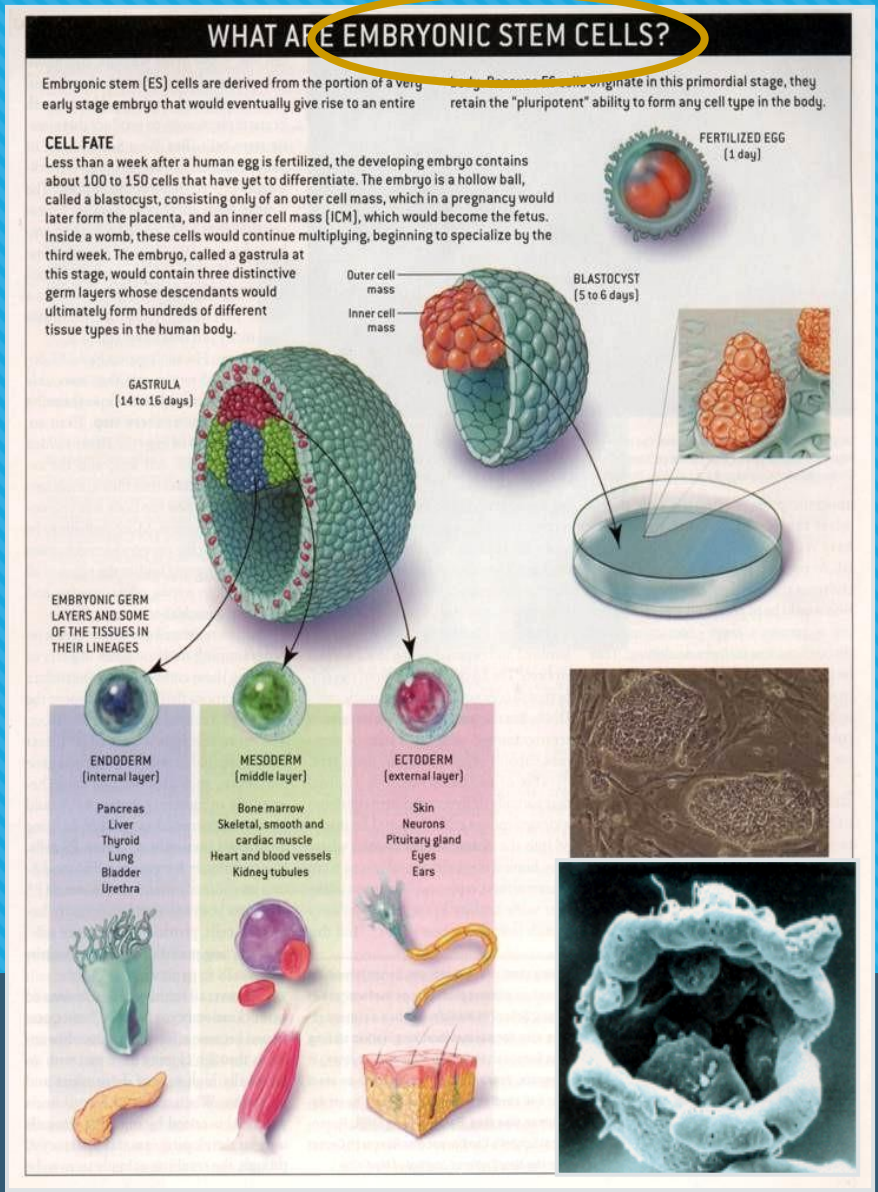
Células CD34⁺ se diferencian en células endoteliales.



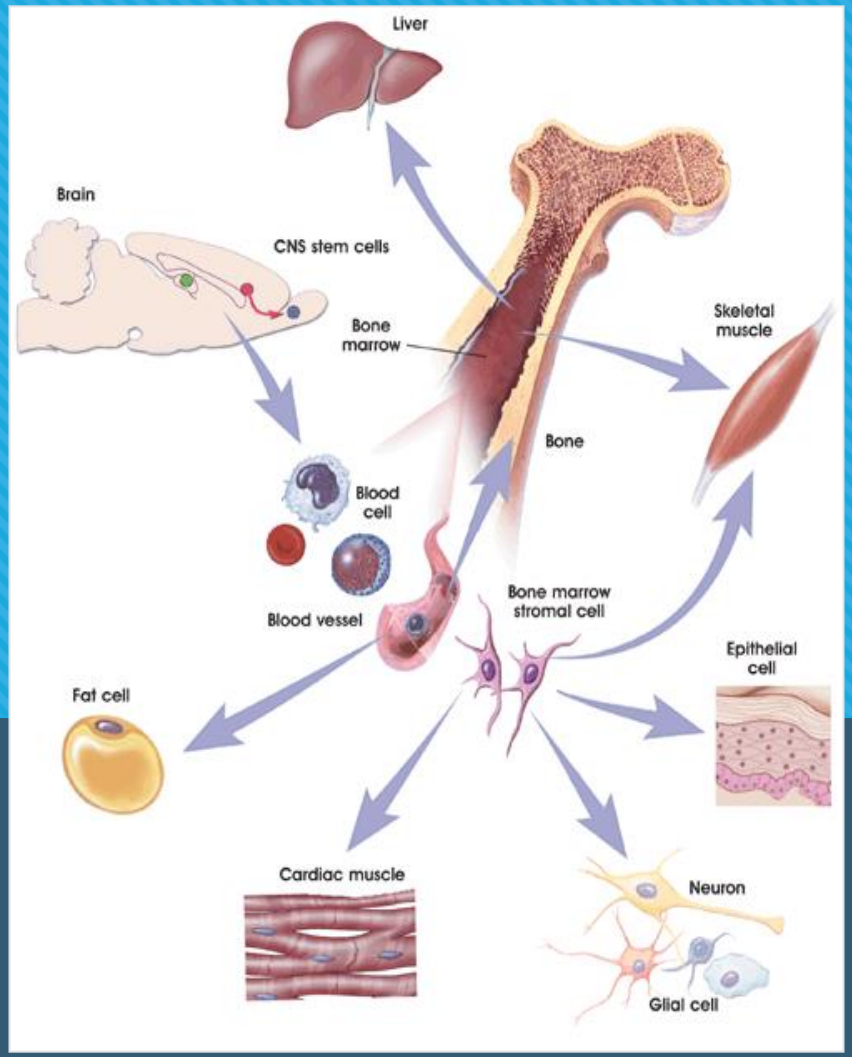




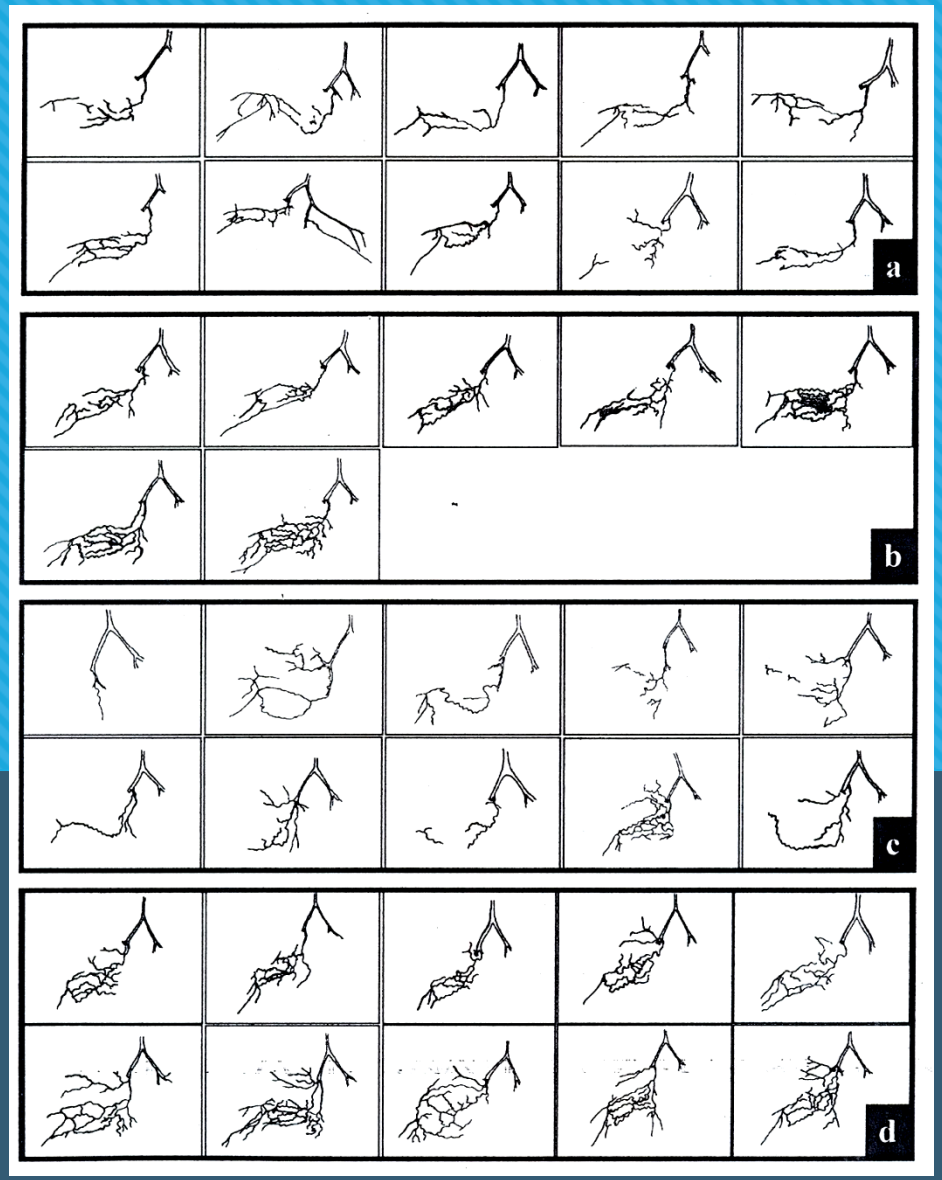
Asahara T. , Isner F.M. *et al.,*
Insolation of Putative Progenior Endothelial Cells for Angiogenesis
Science 275:964-967., **1997**

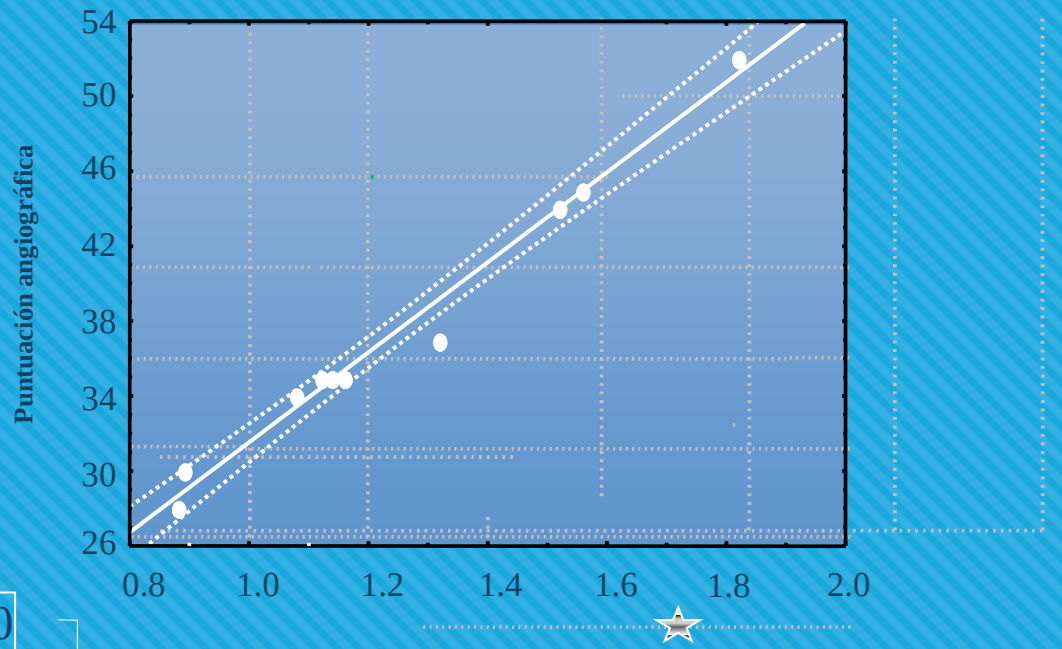


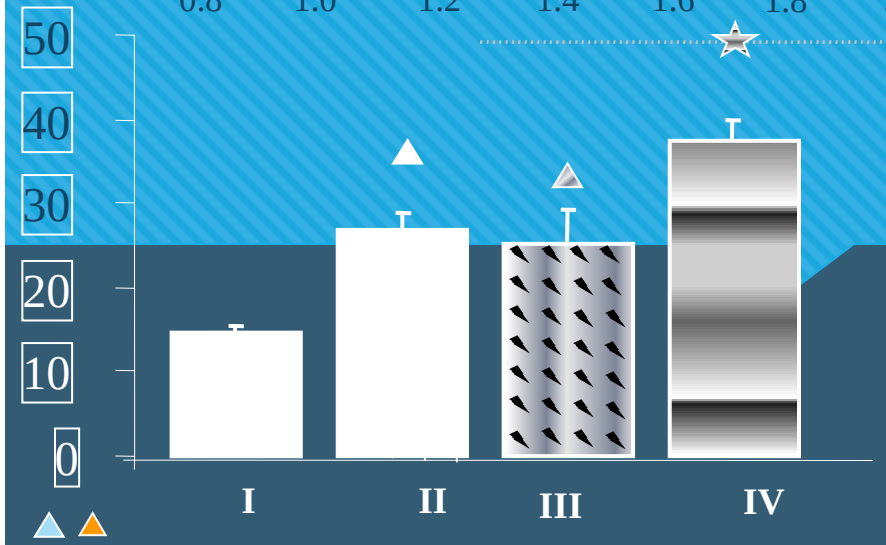
Stem cells Adults



Administration of bone marrow cells in to surgically induced fibrocollagenous tunnels induces angiogénesis in ischemic rat hindlimb model.







p < 0.05 del grupo VEGF y Col/PVP vs SS Col/PVP

p < 0.05 del grupo MO vs SS, VEGF y Col/PVP

ADMINISTRATION OF BONE MARROW CELLS INTO SURGICALLY INDUCED FIBROCOLLAGENOUS TUNNELS INDUCES ANGIOGENESIS IN ISCHEMIC RAT HINDLIMB MODEL

LUIS PADILLA, M.D.,[1–3]* EDGAR KRÖTZSCH, Ph.D.,[2]
PAUL SCHALCH, M.D.,[1] SIEGFRIED FIGUEROA, M.D.,[1]
ADRIANA MIRANDA, M.D.,[2] ENRIQUE ROJAS, M.D., Ph.D.,[2]
SANDRO ESPERANTE, M.D.,[1] FERNANDO VILLEGAS, M.D.,[3]
ANABEL S. DE LA GARZA, M.D.,[3] AND
MAURICIO DI SILVIO, M.D.[1]

We established a comparative model of angiogenic induction in previously formed fibrocollagenous tunnels in rat inner thigh muscles. A unilateral hindlimb chronic ischemia model was performed in male Sprague-Dawley rats. A device was then inserted in the central portion of the inner thigh muscles. Vascularity in the ischemic limb was determined by means of an angiographic score, capillary/fiber ratio, and endothelial proliferation by histochemistry and immunohistochemistry. Autologous transplant of bone marrow, vascular endothelial growth factor (VEGF), or collagen-polyvinylpyrrolidone plus heparin induced significant vascularization of the ischemic hindlimb when compared to saline solution. However, the bone marrow group presented a higher angiographic score than the other two. No differences among groups were observed in capillary/fiber ratio or proliferation, except for the VEGF group, where capillary proliferating cells were significantly higher than in controls. Based on these results, bone marrow-derived progenitor cells may constitute a safe and viable alternative for the induction of therapeutic angiogenesis.

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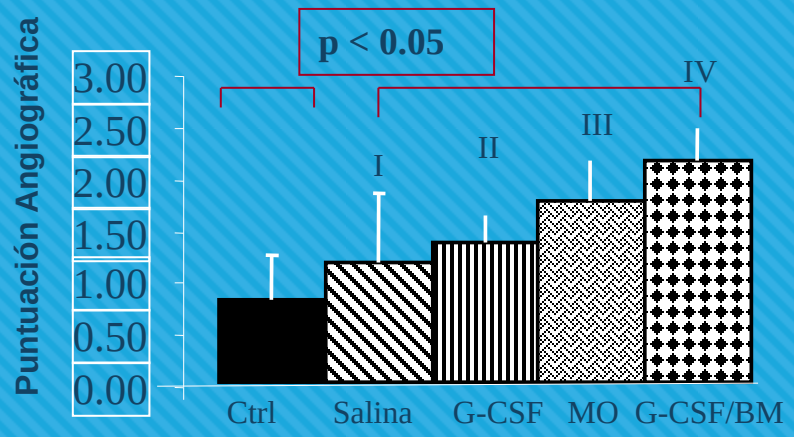
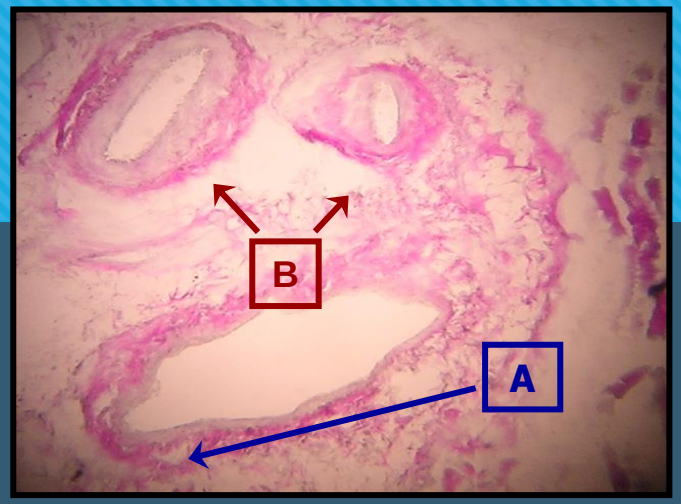
MICROSURGERY 23:568–574 2003

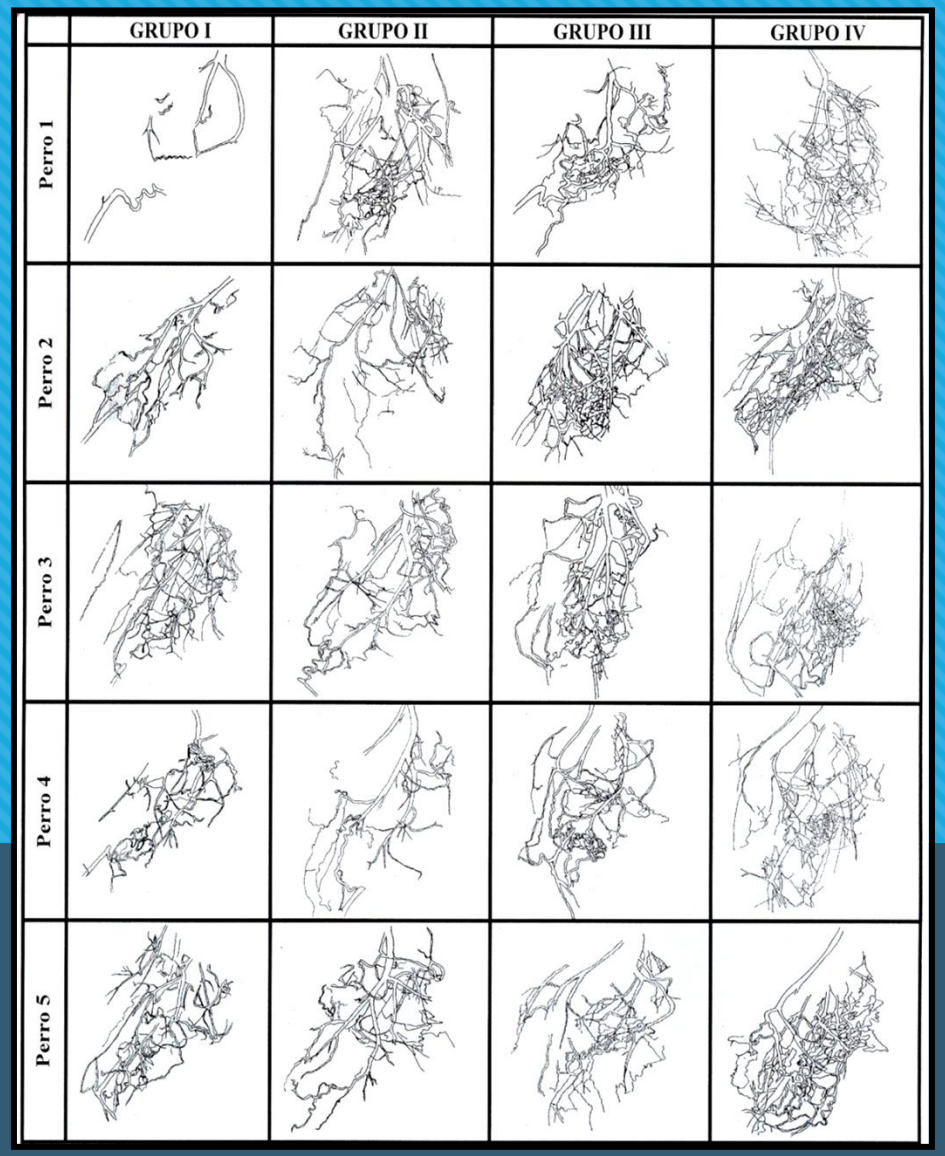
Administración de Médula Ósea en Túneles de Fibrocolágena en un Modelo de Isquemia Canino



Diferencias significativas entre el grupo control y los grupos experimentales (I,II,III,IV); con una $p<0.05$



Tinción de Herovici. Colagena tipo I y III



BONE MARROW MONONUCLEAR CELLS STIMULATE ANGIOGENESIS WHEN TRANSPLANTED INTO SURGICALLY INDUCED FIBROCOLLAGENOUS TUNNELS: RESULTS FROM A CANINE ISCHEMIC HINDLIMB MODEL

LUIS PADILLA, M.D.,[1,2,3*] EDGAR KRÖTZSCH, Ph.D.,[4] ANABEL S. DE LA GARZA, M.D.,[1] SIEGFRIED FIGUEROA, M.D.,[1] JUAN RODRIGUEZ-TREJO, M.D.,[5] GERARDO ÁVILA, M.D.,[1] PAUL SCHALCH, M.D.,[1] IGNACIO ESCOTTO, M.D.,[5] GERMÁN GLENNIE, D.V.M.,[6] FERNANDO VILLEGAS, M.D.,[3] and MAURICIO DI SILVIO, M.D., F.A.C.S.[1]

Progenitor cell transplantation has been considered as a potential angiogenesis therapy for the ischemic hindlimb. In this work we performed an ischemic hindlimb model in dogs. We ligated the middle sacra and the external right iliac arteries. After 7 days, the femoral artery was ligated and removed, and three Silastic® tubes were inserted into the gracilis muscle to create fibrocollagenous tunnels. After Silastic® implantation, we administered saline or granulocyte colony stimulating factor (G-CSF) subcutaneously daily during 5 days. Fourteen days after device positioning we transplanted bone marrow mononuclear cells (BMMC) into the tunnels previously formed by Silastic® tube reaction. Twenty-eight days later, contrasted angiographies were performed and angiographic scores were calculated. Also, vessels and endothelial cells and proliferating cells were identified by immunochemistry of muscle sections. Results demonstrated that BMMC transplantation enriched by G-CSF administration significantly stimulates angiogenesis in the ischemic hindlimb, and more than BMMC transplantation alone. Transplantation of progenitor cells in an appropriate extracellular matrix is a potential therapy for hindlimb ischemia. © 2006 Wiley-Liss, Inc. Microsurgery 27:91–97, 2007.

CENTRO MEDICO NACIONAL 20 DE NOVIEMBRE
Subdirección de Enseñanza e Investigación
Coordinación de Investigación

No. de Registro _____

PROTOCOLO

Unidad Médica:	SERVICIO DE ANGIOLOGIA Y CIRUGÍA VASCULAR. LABORATORIO DE TRASPLANTE CELULAR y LABORATORIO DE TEJIDO CONJUNTIVO DE LA UNIDAD DE ENSEÑANZA E INVESTIGACION
Telefono /ext	14276
Título:	**"Angiogénesis Terapéutica en pacientes con Isquemia Crítica de los miembros inferiores mediante trasplante Autólogo de células mononucleares en túneles de fibrocolágeno "**

	NOMBRES	FIRMAS
Investigadores responsables:	Dr. Luis Padilla Sánchez Dr. Juan Miguel Rodríguez Trejo	
Investigadores asociados:	Dr. José de Diego Dr. Ignacio Escotto Sánchez Dr. José Antonio Morales Dr. Neftalí Rodríguez Ra mírez Dr. Edgar Krötzsch Trejo. Dr. Siegfried Figueroa Barkow Dra. Anabel S. de la Garza Rodea Dr. Mauricio Di Silvio López	

Instituto de Seguridad y Servicios Sociales para los Trabajadores del Estado
ISSSTE

CENTRO MEDICO NACIONAL
"20 DE NOVIEMBRE"

COMISION DE ETICA

ASUNTO: *El que se indica.*
OFICIO: *295/2003*
México D.F., Noviembre 18 del 2003.

C.DR. RENE BEAUROYRE HIJAR,
COORDINADOR DE INVESTIGACION.
P R E S E N T E.

En relacion al protocolo enviado por usted, con fecha 19 de agosto del año en curso y con No. de Oficio: **SEI/CI/294/03:**

3 COPIAS DEL PROTOCOLO:

"Angiogenésis Terapéutica en pacientes con Isquemia Crítica de los miembros inferiores mediante trasplante Autólogo de células mononucleares en túneles de fibrocolágeno"

Conclusiones:

Cumple con todos los lineamientos éticos de transplante de nuestro país. Como se señala en el protocolo en las páginas 15 y 16.
En la Hoja de Consentimiento Informado es recomendable poner en ella un numero telefónico del investigador principal o de los asociados, para que se realice alguna consulta, duda o inquietud de los pacientes sometidos a la investigación.

A T E N T A M E N T E

DR.EDUARDO AUGUSTO ORDOÑEZ GUTIERREZ.
PRESIDENTE DE LA COMISION DE ETICA.

c.c.p.-Minuta.
AOG/nrch.

C. M. N.
"20 DE NOVIEMBRE"
DIC 19 2003
COORDINACION DE INVESTIGACION

Enfermedad Arterial en Miembros Inferiores

Amputaciones al año

USA: 100.000

MEXICO: 30.000

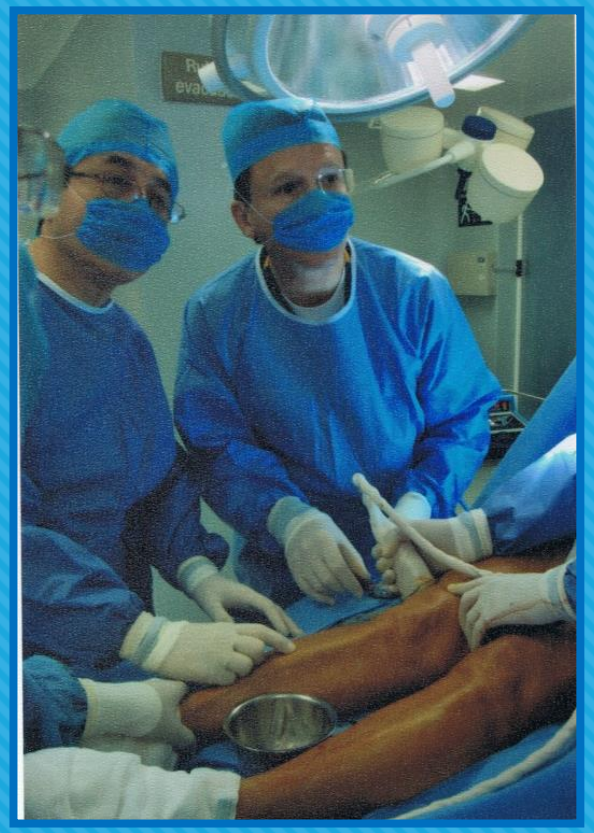
Clasificación de Rutherford

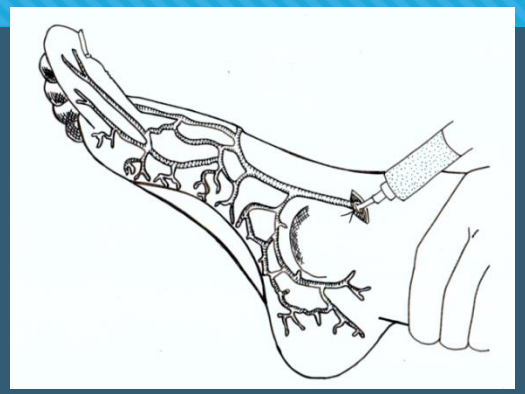
Categoría 1	Claudicación > 200m
Categoría 2	Claudicación < 200m (moderada)
Categoría 3	Claudicación < 100m (severa)
Categoría 4	**Dolor Isquémico en reposo**
Categoría 5	**Pérdida de tejido menor (úlcera)**
Categoría 6	Pérdida de tejido mayor (gangrena)

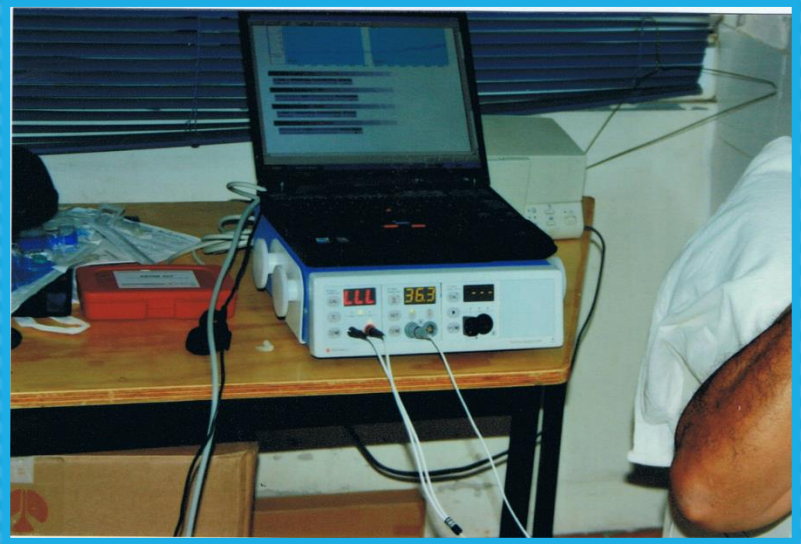
Norgen L. (TASC II) J. Vasc. Surg. 2007; 45:55-67

20 Extremidades

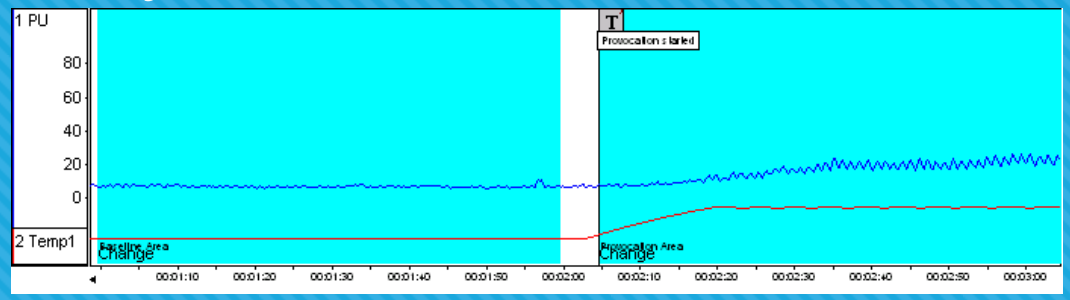
- **10 Trasplante intramuscular**
- **10 Trasplante intramuscular e intravenoso retrogrado distal (vena safena)**





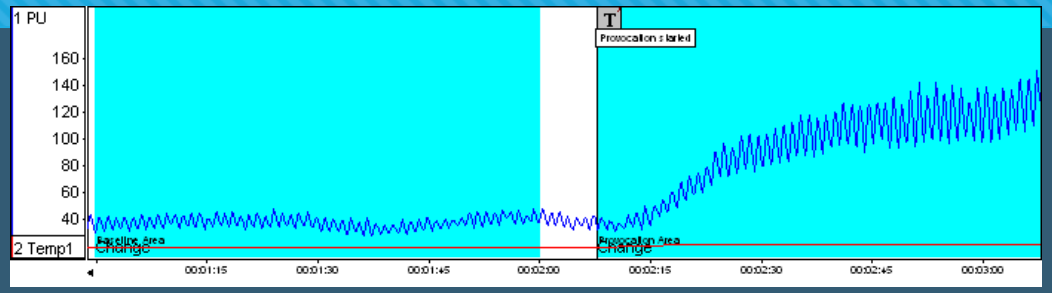


MDJ 14-11-2007



MDJ 18-09-2009

Item	Baseline Area	Provocation Area	All areas
Mean value	6.64	16.09	11.37

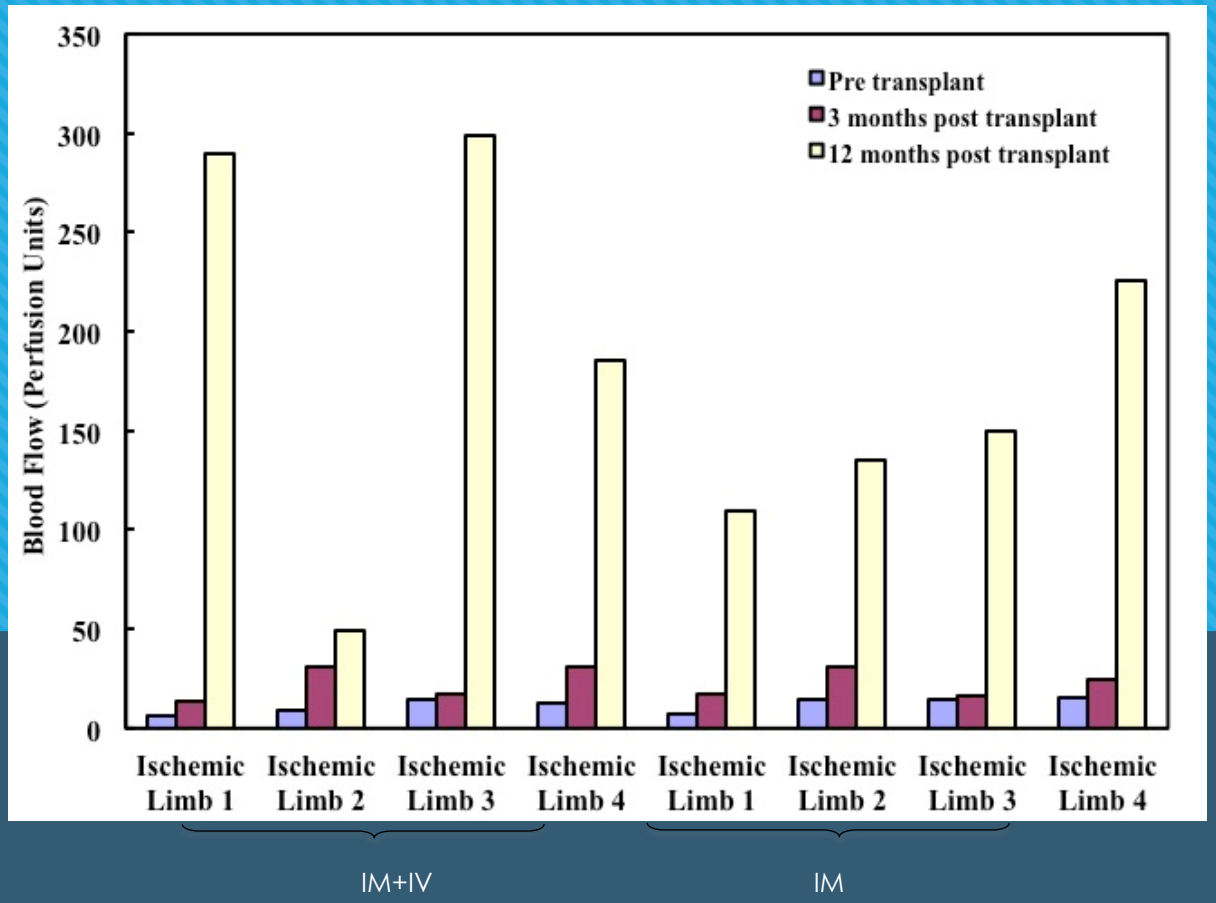


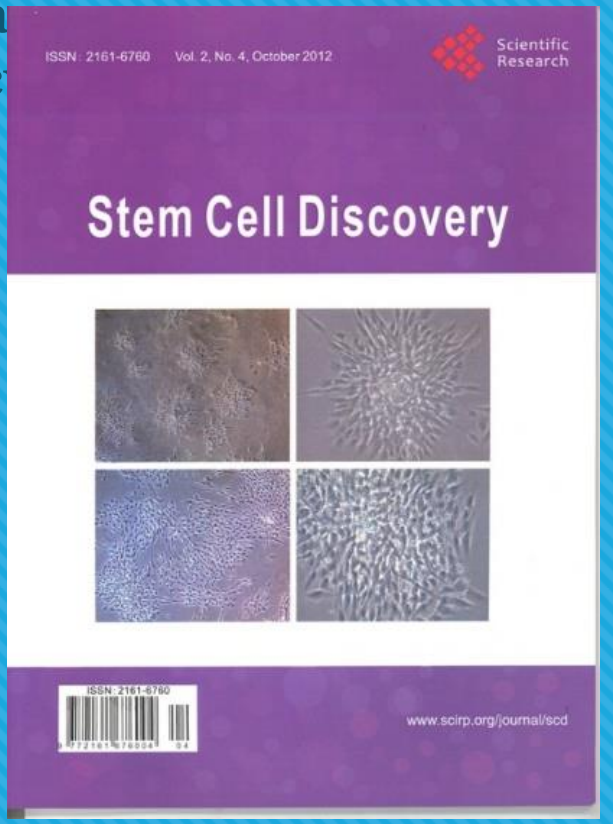
Item	Baseline Area	Provocation Area	All areas
Mean value	38.38	93.60	65.99

Láser Doppler

Long-term effect of autologus progenitor cell therapy to induce neo angiogénesis in patients with critical limb ischemia transplanted via intarmuscular vs combined intramusc and distal retrograde intra venous

Dr. Luis Padilla, Dr. Juan Rodriguez-Trejo, Biol. Pilar Carranza, Dr. Paul Mondragón-Terán, *et al.*





- 20 extremidades
- 2 amputaciones
- 18 salvamentos

Seguimiento a tres años

Stem Cell Discovery, 2012; 2:155-162

Benoit., O´Donnell T.F., Patel A. N.
Safety and Efficacy of Autologous Cell Therapy in Critical Limb Ischemia:
A Systematic Review
Cell Trasnplant. 2013;22(3):545-62

45 Ensayos Clínicos (Clinical Trials) **1518 Pacientes**

7 ENSAYOS CLÍNICOS «ALEATORIZADOS» (NIH-FDA)

(2009-2012)

365 Pacientes
195 Terapia Celular
170 Placebo

Eficacia (Índice de Amputación)

14.4% Terapia Celular
27.0% Placebo
p=0.0019

La Terapia Celular reduce significativamente las tasas de amputación en pacientes con isquemia crítica de miembros inferiores

Meta-Análisis
OR= 0.36 p=0.0004

Jueves 11 de julio:

Panorama Mundial Actual de la Terapia Angiogénica.

State of Art of Angiotherapy

Acad. Dr. Luis Padilla

CELA SMACV 2013 Cancún, México

Viernes 12 de julio:

Eficacia y Seguridad de la Terapia Celular Autóloga para Isquemia Crítica. Una Década de Experiencia.

Safety & Efficacy Of Autologous Cell Therapy In Critical Limb Ischemia: A Decade Of Experience

Eric Benoit

SALUD
SECRETARÍA DE SALUD

Cofepris
Comisión Federal para la Protección contra Riesgos Sanitarios

2013, Año de la Lealtad Institucional y Centenario del Ejército Mexicano"

OFICIO No. CAS/01/OR/1934/2013

México D.F. a 12 Noviembre de 2013

Dr. Luis Padilla Sánchez
San Lorenzo No. 502
Edificio "D" 3er piso
Col. Del Valle
Del. Benito Juárez
C.P.03229
México D.F.
Presente

Doy respuesta a su escrito de fecha 11 de septiembre del presente año, en donde solicita se emita un criterio, en el que se puntualice que el "trasplante de células mononucleares progenitoras derivadas de medula ósea induce la angiogénesis en pacientes con isquemia severa de miembros inferiores" y que los establecimientos en los cuales se puedan realizar este tipo de procedimiento deben de contar con una autorización que debe me permito informar a usted lo siguiente:

Que derivado de la reunión, realizada el 15 de julio de 2013 en estas oficinas de la Comisión Federal para la Protección contra Riesgos Sanitarios, en la que se hizo el señalamiento que la COFEPRIS no autoriza procedimientos médicos, que estos son responsabilidad del médico tratante y que la autoridad sanitaria vigila que dichos tratamientos se den dentro de lo que establece la buena "Praxis médica", es decir bajo los principios éticos y científicos que señala la Ley General de Salud y sus Reglamentos, así como que los procedimientos se realicen en establecimientos autorizados, que garanticen el riesgo sanitario mínimo o debidamente controlado en el cual el bienestar del paciente sea el objetivo principal.

Una vez enterados de los buenos resultados del ensayo clínico referido, consideramos que los establecimientos en donde se realicen este tipo de tratamiento con células progenitoras, deberán de contar con una licencia de disposición de órganos, tejidos o células progenitoras o troncales con fines de trasplante, emitida por la autoridad sanitaria competente, con un Comité Hospitalario de Bioética que avale los casos y un grupo de especialistas que consideren los beneficios para el paciente con dicho tratamiento.

Sin otro particular le mando un cordial saludo.

SUFRAGIO EFECTIVO. NO REELECCION
EL COMISIONADO DE AUTORIZACION SANITARIA

DR. JUAN CARLOS GALLAGA SOLORZANO

ahh

REQUISITOS

Cofepris

Comisión Federal para la Protección contra Riesgos Sanitarios

1. Hospital con **licencia** de disposición de órganos, tejidos o células progenitoras o troncales con fines de trasplante.

2. Aval de los casos por un **«Comité Hospitalario de Bioética»**.

3. Presentación del caso en **sesión clínica** con un **grupo de especialistas** que consideren los beneficios para el paciente.

Primer caso de trasplante de células progenitoras derivadas de la médula ósea en isquemia crítica de miembros inferiores como terapéutica consolidada

Dr. Juan Rodriguez-Trejo, Dr. Luis Padilla, Biol. Pilar Carranza, Dr. Paul Mondragón-Terán, *et al.*

Rev. Mex Angiol 2014; 42(4):163-169

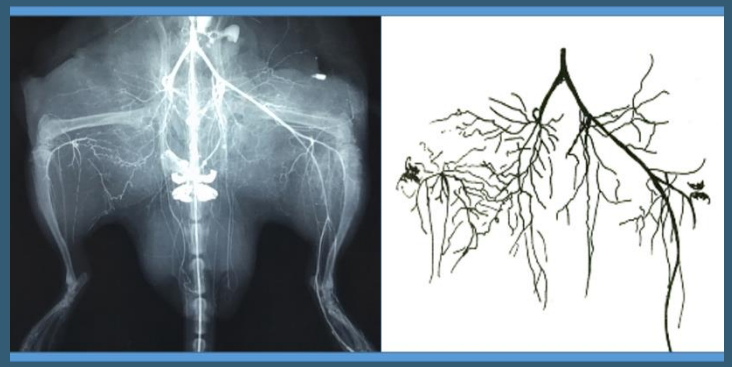
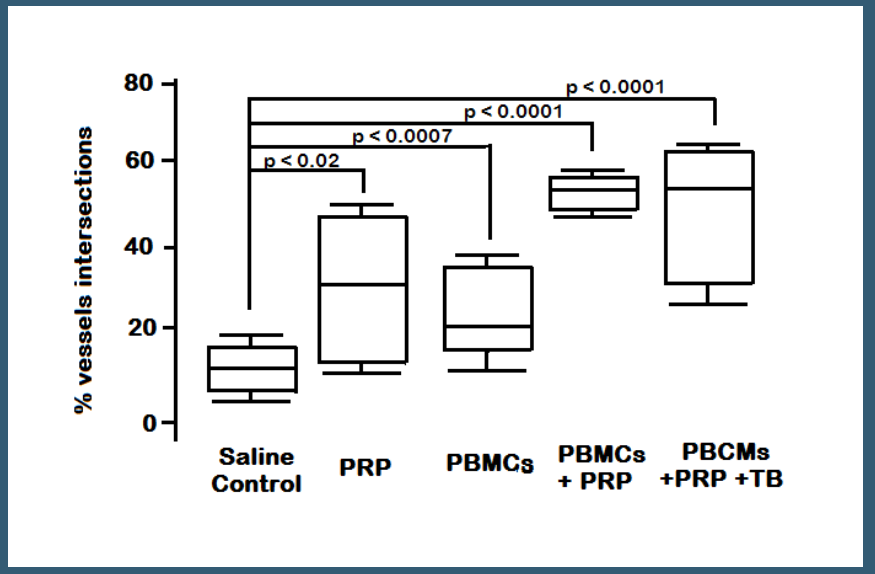
J Tissue Eng Regen Med. 2020 Feb 18. doi: 10.1002/term.3024. [Epub ahead of print]

Effect of autologous transplant of peripheral blood mononuclear cells in combination with proangiogenic factors during experimental revascularization of lower limb ischemia.

Padilla L[1,2], Argüero-Sánchez R[2], Rodríguez-Trejo JM[3], Carranza-Castro PH[1], Suárez-Cuenca JA[4], Polaco-Castillo J[2], DiSilvio-López M[1], López-Gutiérrez J[1], Olguín-Juárez H[1], Hernández-Patricio A[4], Vera-Gómez E[4], Gómez-Calderón AJ[5], Téllez-González MA[5], Mondragón-Terán P[5].

Abstract

Peripheral blood mononuclear cells (PBMCs) contain a cell fraction of mononuclear progenitor cells (MPCs), which own significant angiogenic potential. Autologous transplant of PBMC and/or platelet-rich plasma (PRP) promotes endothelial cells differentiation in experimental lower limb ischemia, which is considered a safe and effective strategy to support revascularization, either in animal models or clinical trials. In addition, thrombin has been proposed to enrich biological scaffolds, hence increasing MPC viability after intramuscular administration, whereas proangiogenic mediators such as vascular endothelial growth factor (VEGF), tumor necrosis factor alpha (TNF-α), inhibitor of the plasminogen activator-1 (PAI-1), and chemokine (CXCL1; GRO-α) participate in the endothelial response to ischemia, through their proangiogenic effects over endothelial cells proliferation, survival, migration, endothelial integrity maintenance, and physiologic vascular response to injury. In the present study, we describe the effect of autologous PBMCs transplant and PRP, either with or without thrombin, over proangiogenic mediators (measured by enzyme-linked immunosorbent assay) and revascularization response (angiographic vascular pattern at 30 days after vascular occlusion) in a rat model of lower limb ischemia. The group treated with PBMC + PRP significantly induced PAI-1, an effect that was prevented by the addition of thrombin. Furthermore, treatment with PBMC + PRP + thrombin resulted in the induction of VEGF. GRO-α showed a sensitive induction of all proangiogenic mediators. All treatments significantly stimulated revascularization, according to angiographic assessment, whereas higher effect was observed with PBMC + PRP treatment ($p < .0001$). In conclusion, autologous PBMC transplant stimulates revascularization during experimental ischemia of the lower limb, whereas particular effects over proangiogenic and fibrinolytic mediators may be attributed to PBMCs and its combination with PRP and thrombin.

© 2020 The Authors. Journal of Tissue Engineering and Regenerative Medicine published by John Wiley & Sons Ltd.

KEYWORDS: PBMC; angiogenesis; lower limb ischemia; proangiogenic factors; revascularization