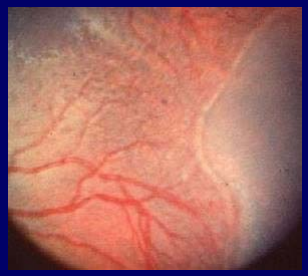
Sociedad Argentina de Pediatría

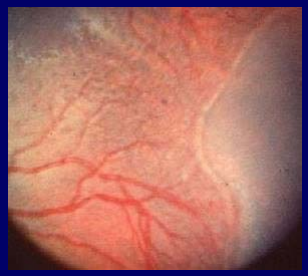


9º Reunión Nacional de Prevención de la Ceguera en la Infancia por ROP

Vasculogénesis: factores de crecimiento y desarrollo de ROP

Ernesto Alda
Bahía Blanca

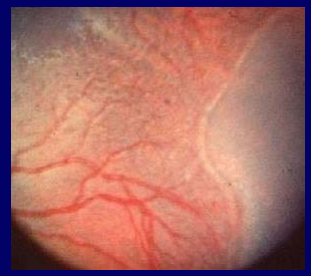
Sociedad Argentina de Pediatría



9º Reunión Nacional de Prevención de la Ceguera en la Infancia por ROP

~~Vasculogenesis~~: factores de crecimiento y desarrollo de ROP

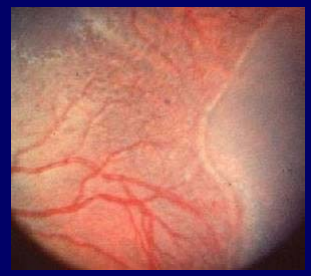
Ernesto Alda
Bahía Blanca



9º Reunión Nacional de Prevención de la Ceguera en la Infancia por ROP

Angiogénesis: factores de crecimiento y desarrollo de ROP

Ernesto Alda
Bahía Blanca



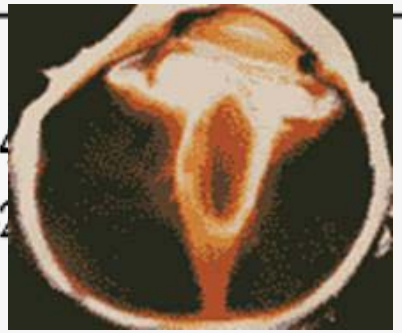
Declaro no tener conflictos de interés

Ernesto Alda
Bahía Blanca

Retinopatía del prematuro

Es una enfermedad del desarrollo de los vasos retinianos que puede producir disminución de la agudeza visual y aún ceguera.

Oxygen group	Number of infants	Blood vessel changes of RLF		Scarring RLF	
		Number	%	Number	%
Singleton					
Routine oxygen	4		70	8	17
Curtailed oxygen	42		31	20	5
Multiple birth					
Routine Oxygen	6	5	83	4	67
Curtailed oxygen	108	45	42	15	14



Frequency of RLF in the Cooperative Study, by Multiplicity of Birth and Severity of RLF (July 1, 1953–June 30, 1954)

Nombre: Stevie Wonder
Fecha de nacimiento:13 de mayo de 1950
Lugar de Nacimiento: Michigan, Estados Unidos

Al nacer su parto fue prematuro por lo que tuvo que ser transferido inmediatamente a una incubadora, en la que por equivocación se le administró demasiado oxígeno, lo que le ocasionó una ceguera permanente.

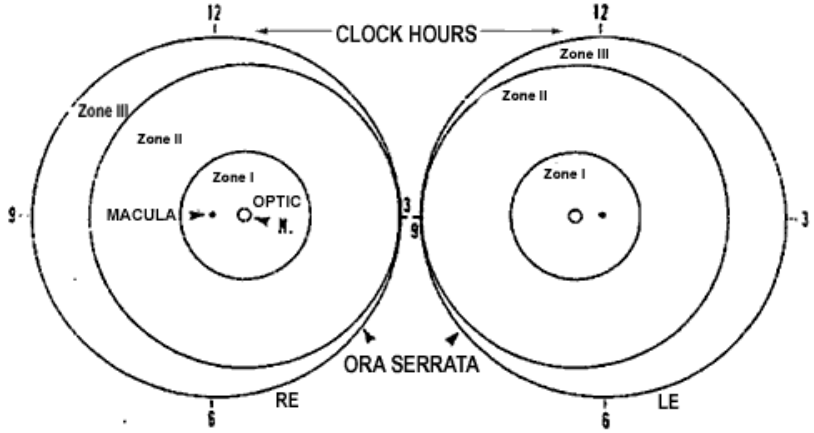
An International Classification of Retinopathy of Prematurity

The Committee for the Classification of Retinopathy of Prematurity

Arch Ophthalmol. 1984 Aug;102(8):1130-4

● **Because of modern life-support systems capable of keeping tiny premature infants alive, retinopathy of prematurity has recurred. No classification system currently available adequately describes the observations of the disease being made today. A new classification system, the work of 23 ophthalmologists from 11 countries, is presented in an attempt to meet this need. It emphasizes the location and the extent of the disease in the retina**

of *retinopathy of pre*
This term is preferre
be used to describe a
retinal changes obse
ture infants. The tr
retrolental fibroplasia
ate in the acute phase
for it describes solely
tricial changes that in
only the most se
infants. Much of w

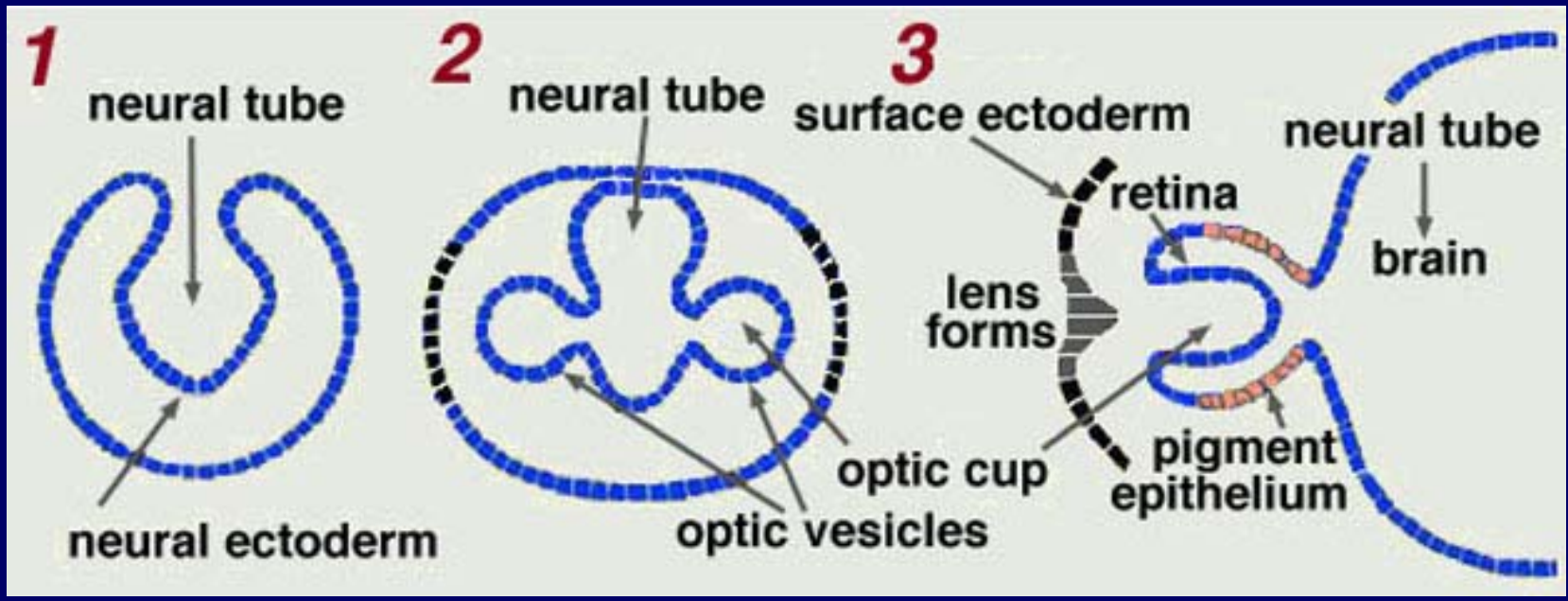


For editorial c
see p 11

arned during the pa
bout the disease in i

Isaac Ben-Sira	Israel
August Deutman	Netherlands
Hans Fledelius	Denmark
John Flynn	United States
Alec Garner (Chairman)	Great Britain
Glen Gole	Australia
N. Warren Hindle	Canada
Hidenao Ideta	Japan
James Kingham	United States
Fritz Koerner	Switzerland
Walter Konen	West Germany
Akio Majima	Japan
Andrew McCormick	Canada
Alan Mushin	Great Britain
Illana Nissenkorn	Israel
Earl Palmer	United States
Graham Quinn	United States
Arthur Rosenbaum	United States
David Schaffer	United States
Dennis Stark	Australia
Björn Svedbergh	Sweden
Karl Tan	Netherlands
Yasuhiko Tanaka	Japan

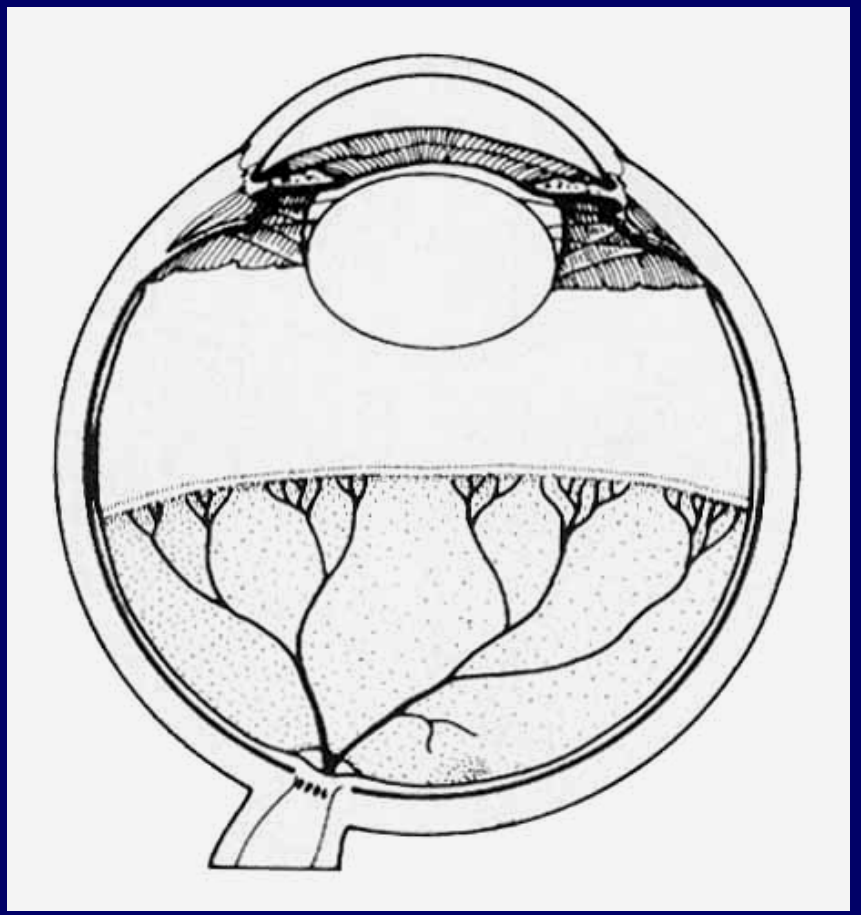
Embriogénesis de la retina

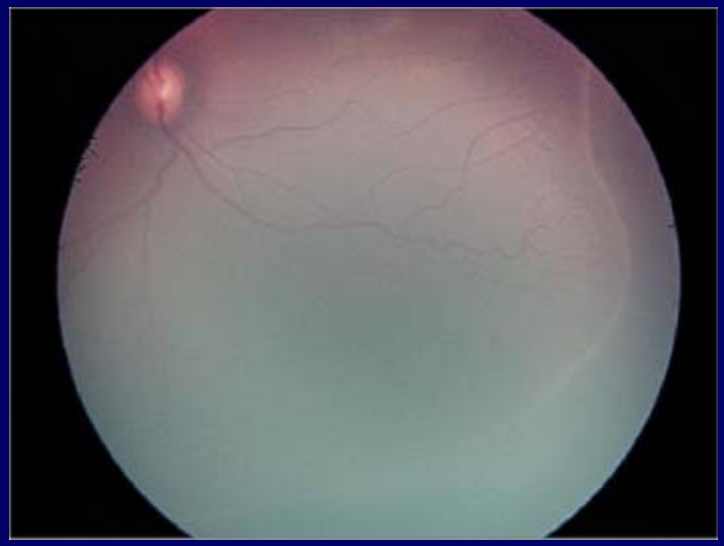


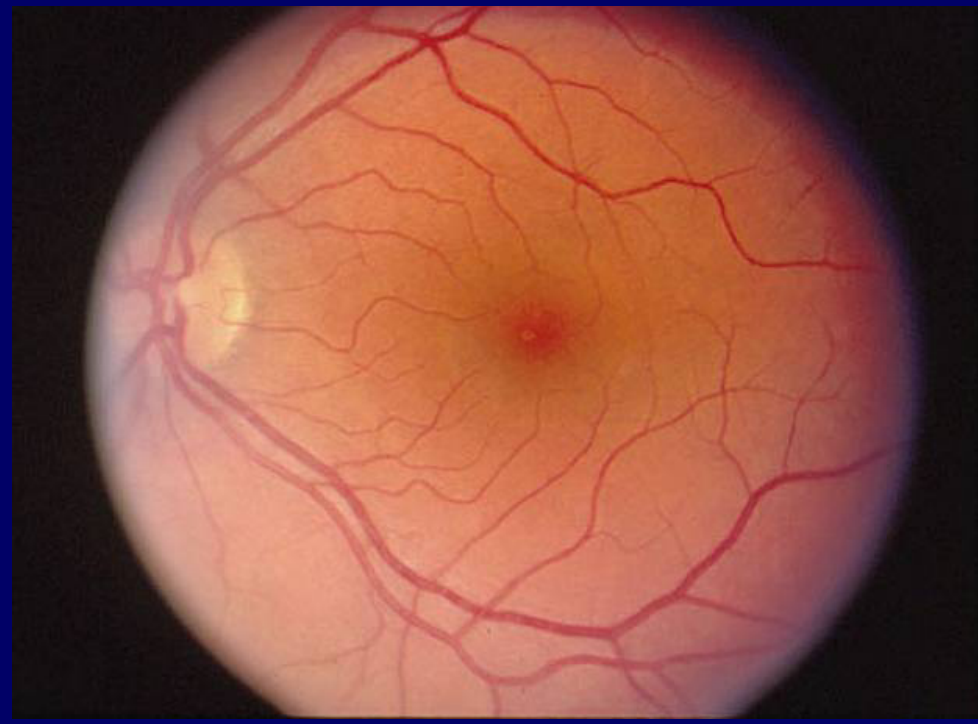
Este proceso comienza alrededor de los 22 días de la etapa embrionaria

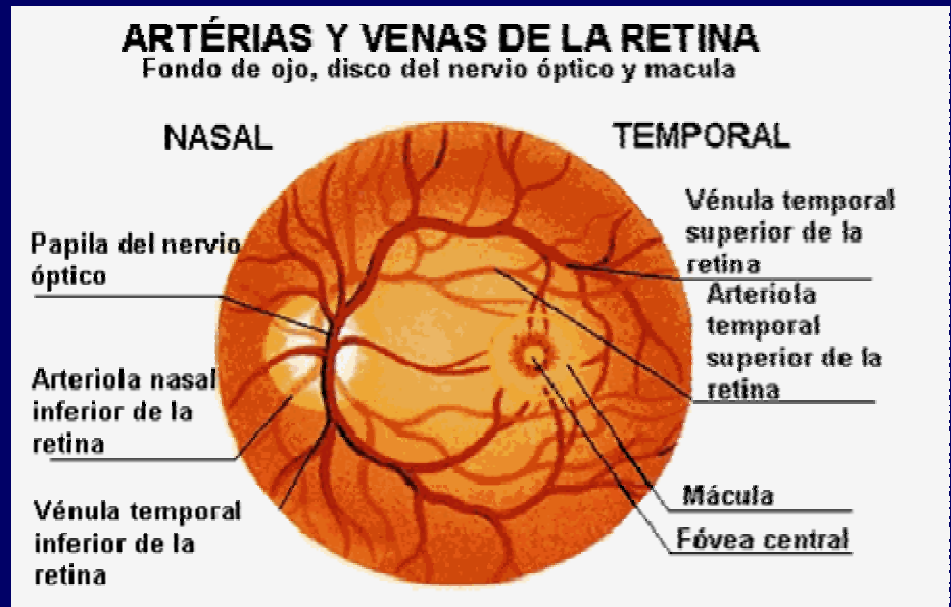
Desarrollo de los vasos retinianos

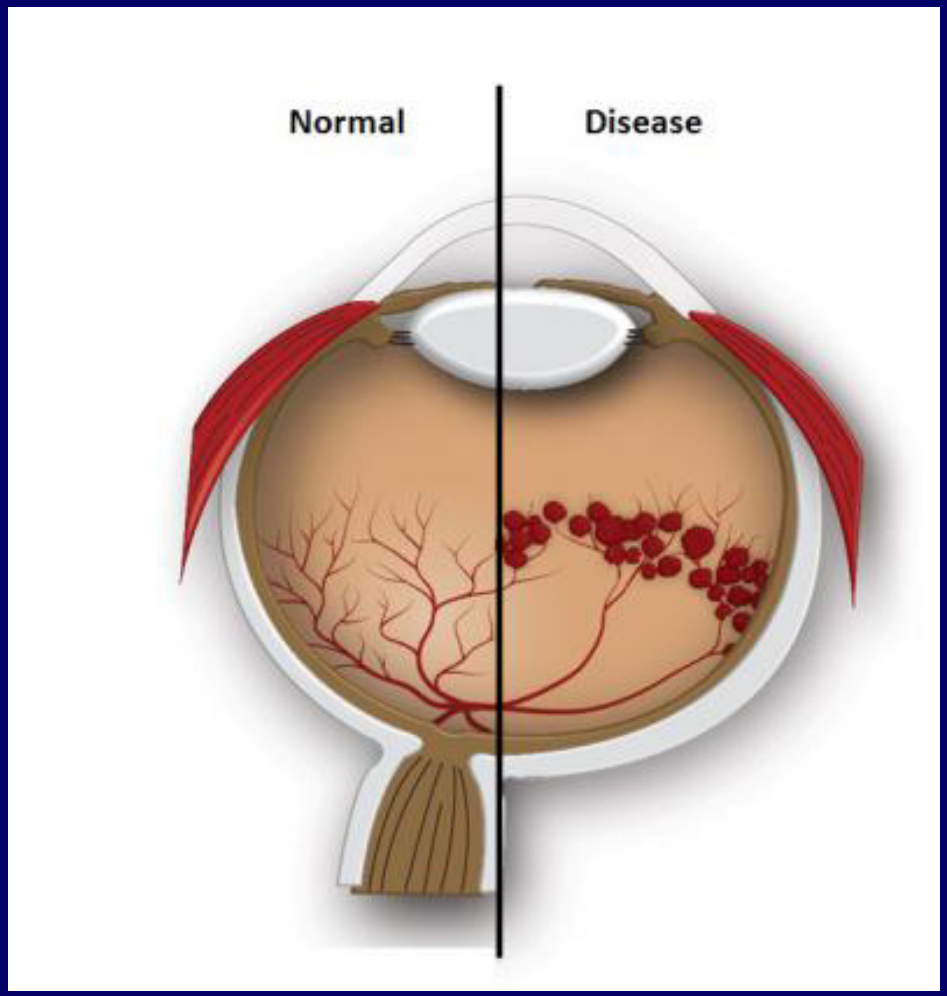
- Los vasos retinianos comienzan a desarrollarse a las 16 semanas desde la papila hacia la periferia de la retina. Los recién nacidos prematuros tienen la vascularización incompleta, con zonas avasculares periféricas inversamente relacionadas con la edad gestacional.





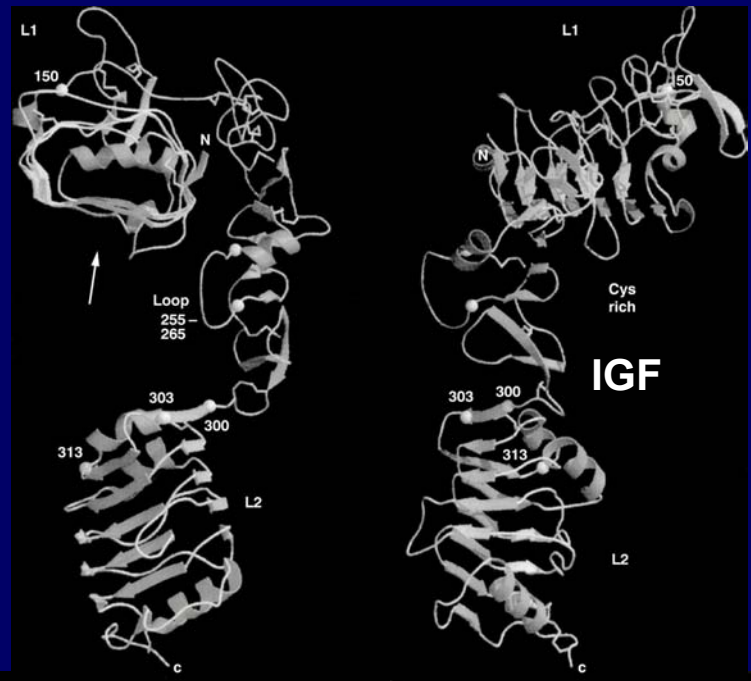


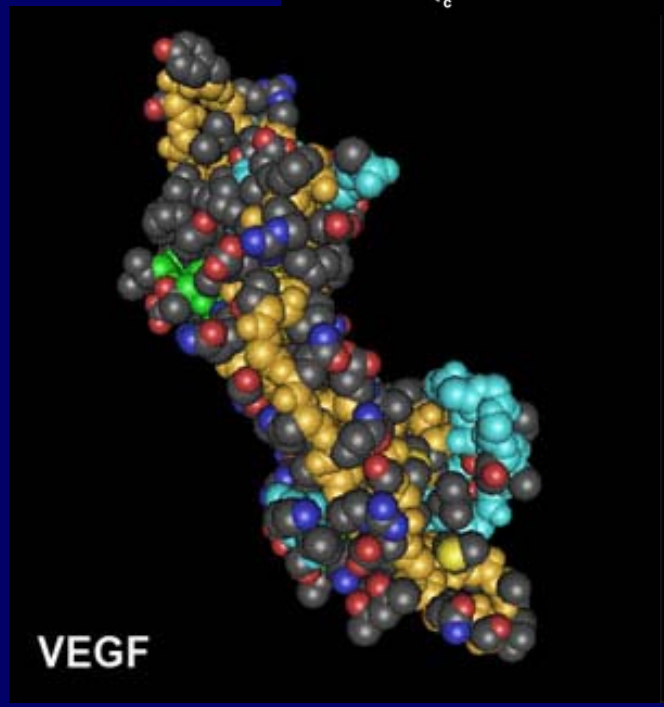

ARTÉRIAS Y VENAS DE LA RETINA
Fondo de ojo, disco del nervio óptico y macula
NASAL
TEMPORAL
Papila del nervio óptico
Arteriola nasal inferior de la retina
Vénula temporal inferior de la retina
Vénula temporal superior de la retina
Arteriola temporal superior de la retina
Mácula
Fóvea central

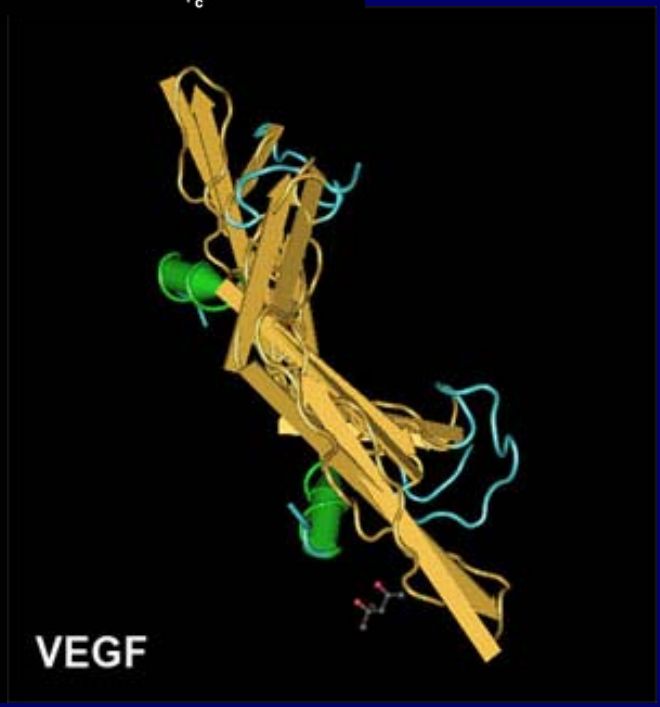

Normal
Disease

Desarrollo de los vasos sanguíneos

- Vasculogenesis
  - *De novo* formación de vasos desde progenitores vasculo endoteliales (angioblastos)
- Angiogenesis
  - Formación de nuevos vasos sanguíneos desde los vasos existentes.
  - Mecanismo principal en el desarrollo de los vasos retinianos.


L1
150
N
Loop
255 –
265
303
300
313
L2
C
L1
150
N
Cys
rich
IGF
303
300
313
L2
C


VEGF


VEGF

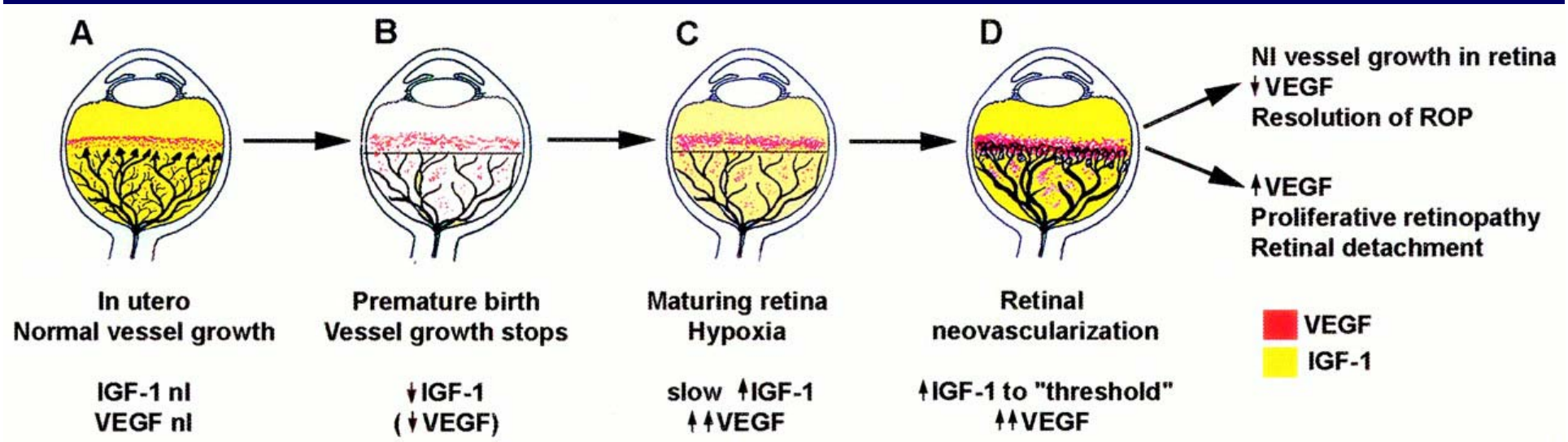
Low IGF-I suppresses VEGF-survival signaling in retinal endothelial cells: Direct correlation with clinical retinopathy of prematurity

Ann Hellstrom*†, Carole Perruzzi‡, Meihua Ju§, Eva Engström†, Anna-Lena Hård*, Jun-Li Liu¶, Kerstin Albertsson-Wikland†, Björn Carlsson‖, Aimon Niklasson†, Lena Sjödell*, Derek LeRoith¶, Donald R. Senger‡, and Lois E. H. Smith§**

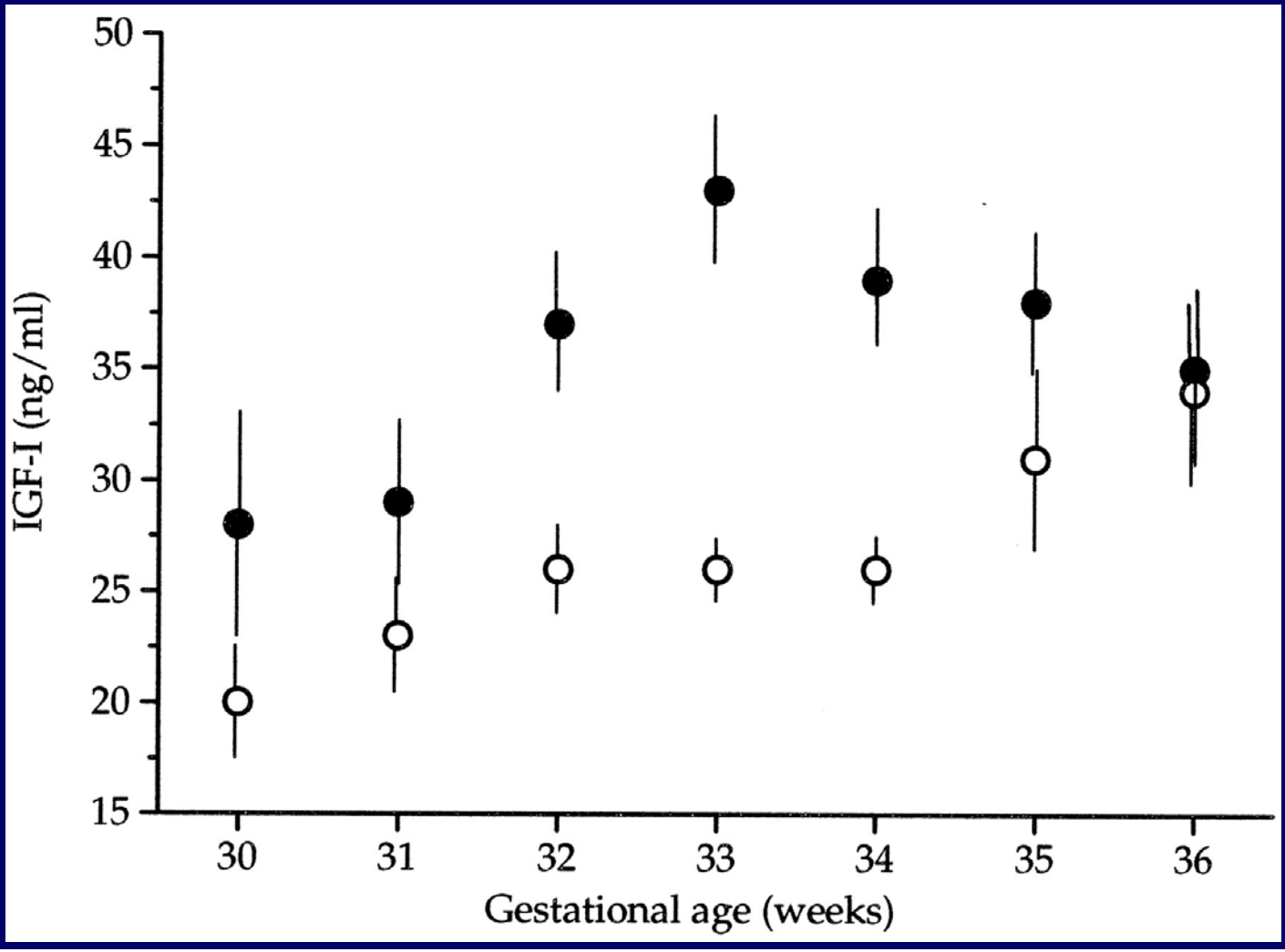
*Department of Clinical Neuroscience, Section of Ophthalmology, and †International Pediatric Growth Research Center, Department of Pediatrics, The Queen Silvia Children's Hospital, 41685 Göteborg, Sweden; ‡Department of Pathology, Beth Israel Deaconess Medical Center, Boston, MA 02215; §Department of Ophthalmology, Children's Hospital, Harvard Medical School, Boston, MA 02115; ¶Endocrine Branch, National Institutes of Health, Bethesda, MD 20892; and ‖Research Centre for Endocrinology and Metabolism, Department of Internal Medicine, University of Göteborg, 41345 Göteborg, Sweden

PNAS - The Proceedings of the National Academy of Sciences of the United States of America

Communicated by Mary Ellen Avery, Children's Hospital, Boston, MA, March 7, 2001 (received for review December 27, 2000)



. *The mean IGF-I level for infants with ROP (○) and without ROP (●) is shown vs. gestational age.*

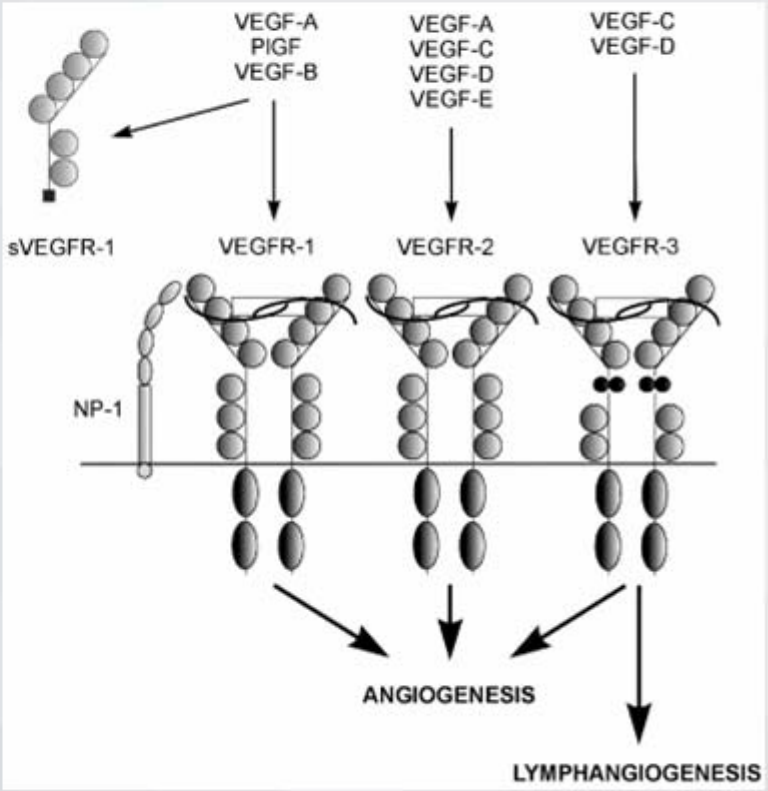


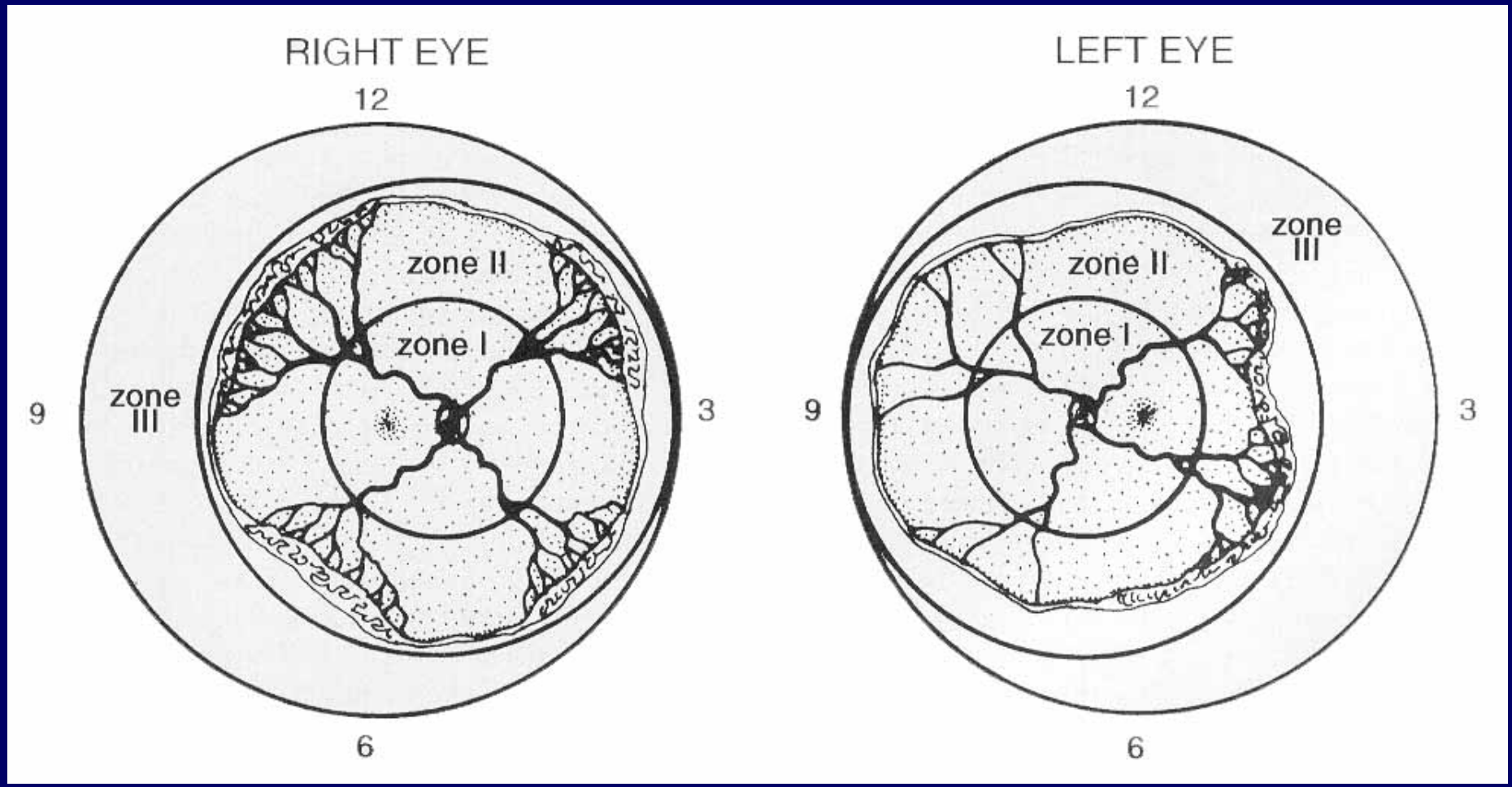
Hellstrom A et al. PNAS 2001;98:5804-5808

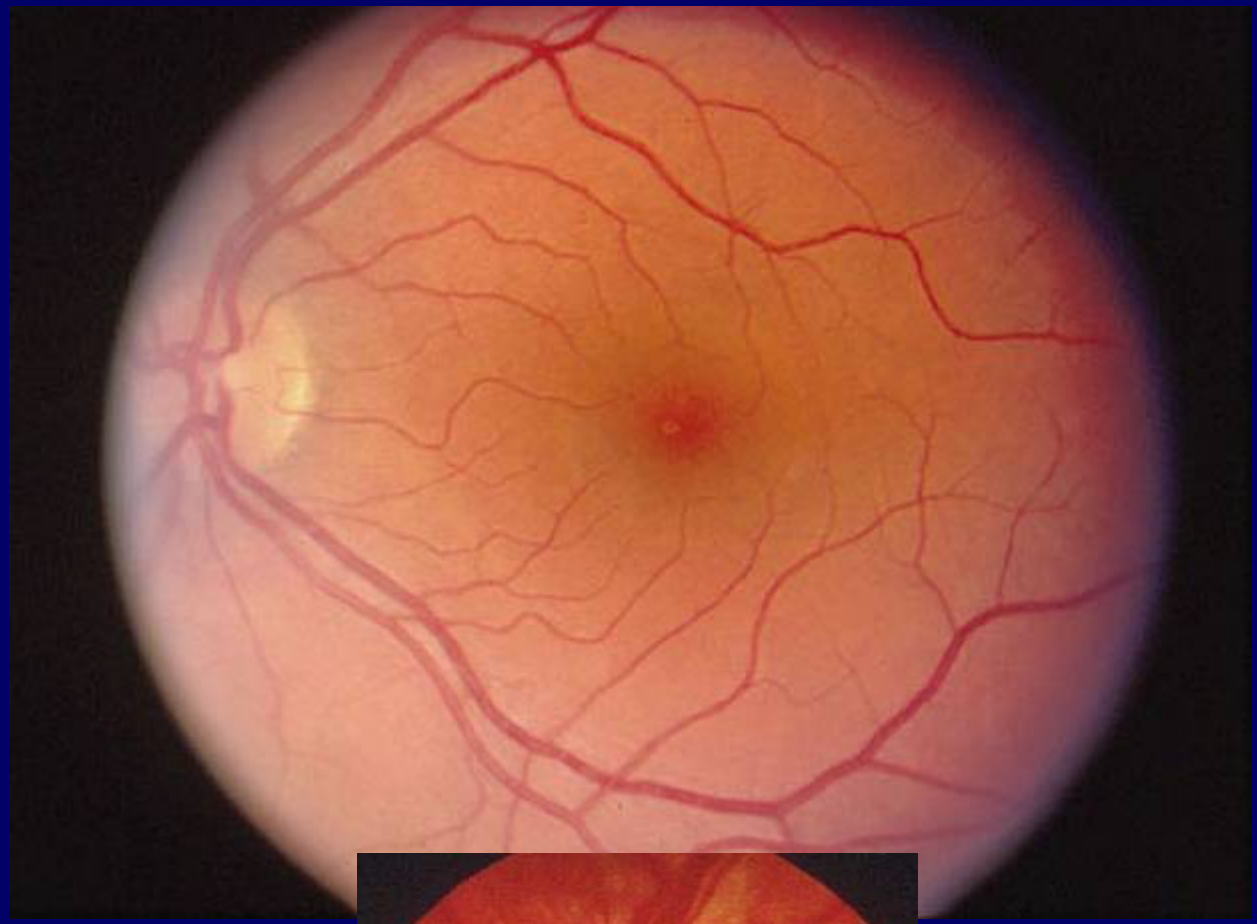
Mean serum IGF-I at matched gestational ages in infants with and without ROP.

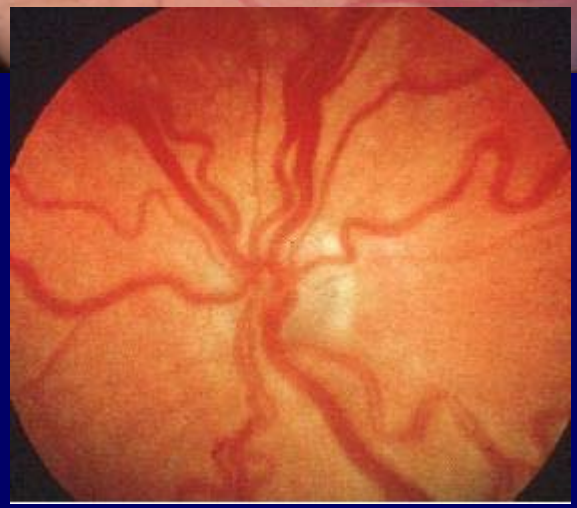
Vascular Endothelial Growth Factor

- Family of growth factors that regulates angiogenesis and vascular permeability
- 6 known members
- Vascular endothelial growth factors (VEGF) A-E and Placental growth factor (PlGF)
- 4 known receptors
  - VEGFR1 (Flt-1)
  - sVEGFR1
  - VEGFR2 (KDR or Flk-1)
  - VEGFR3 (Flt-4)
- NP-1 (neuropilin-1) co-receptor for VEGF-A




RIGHT EYE
12
zone II
zone I
zone III
9
3
6
LEFT EYE
12
zone III
zone II
zone I
9
3
6





Enfermedad plus

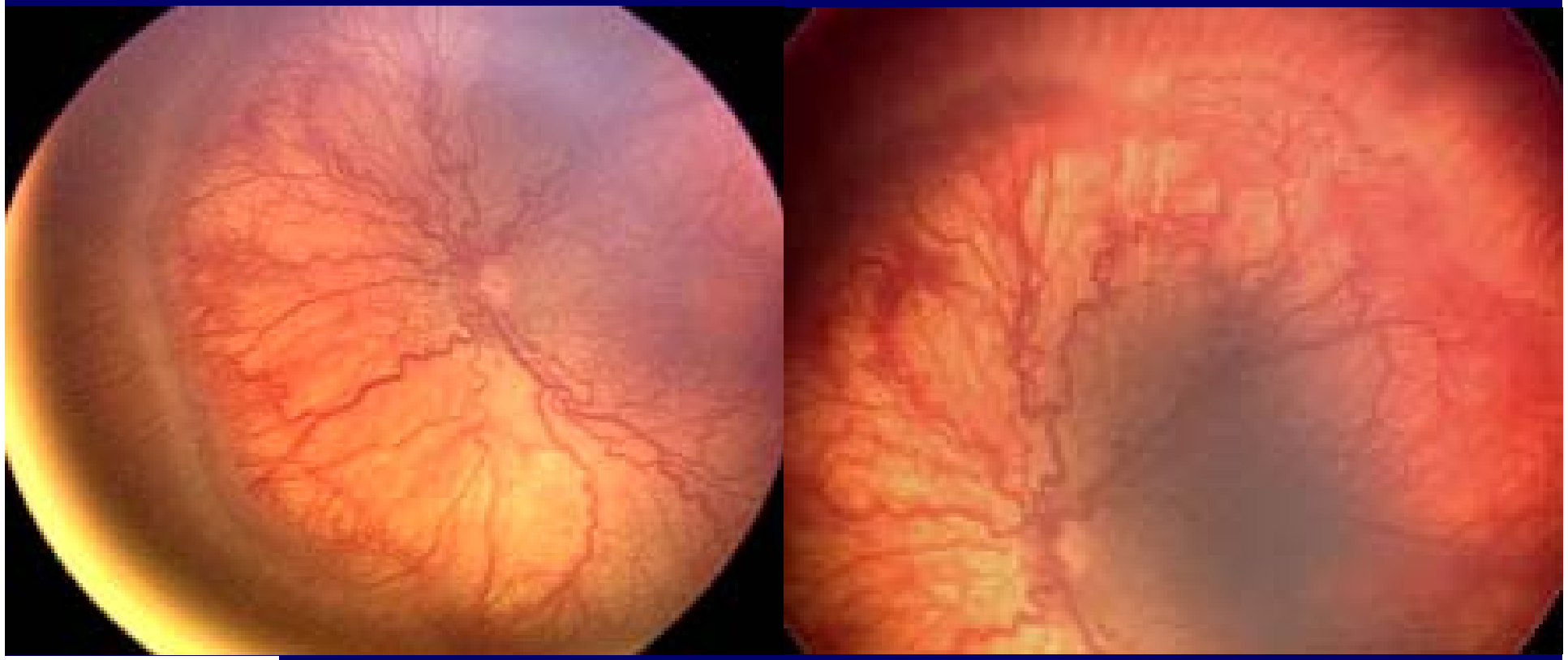
Molecular Vision 2006; 12:532-80 <http://www.molvis.org/molvis/v12/a63/>
Received 15 September 2005 | Accepted 26 April 2006 | Published 23 May 2006

Review

Proceedings of the Third International Symposium on Retinopathy of Prematurity: An update on ROP from the lab to the nursery (November 2003, Anaheim, California)

Gerard A. Lutty,[1] Tailoi Chan-Ling,[2] Dale L. Phelps,[3,4] Anthony P. Adamis,[5] Kenneth I. Berns,[6,7] Candy K. Chan,[8] Cynthia H. Cole,[9] Patricia A. D'Amore,[10,11] Arup Das,[12] Wen-Tao Deng,[13] Velma Dobson,[14] John T. Flynn,[15] Martin Friedlander,[16] Anne Fulton,[11,17] William V. Good,[18] Maria B. Grant,[19] Ronald Hansen,[11,17] William W. Hauswirth,[13] Robert J. Hardy,[20] David R. Hinton,[21,22,23] Suzanne Hughes,[2] D. Scott McLeod,[1] Earl A. Palmer,[24] Arnall Patz,[1] John S. Penn,[25] Brian J. Raisler,[26] Michael X. Repka,[1,27] Magali Saint-Geniez,[10,11] Lynn C. Shaw,[19] David T. Shima,[5] Bradley T. Smith,[28] Lois E. H. Smith,[17] Sjakon G. Tahija,[29] William Tasman,[28] Michael T. Trese[30]

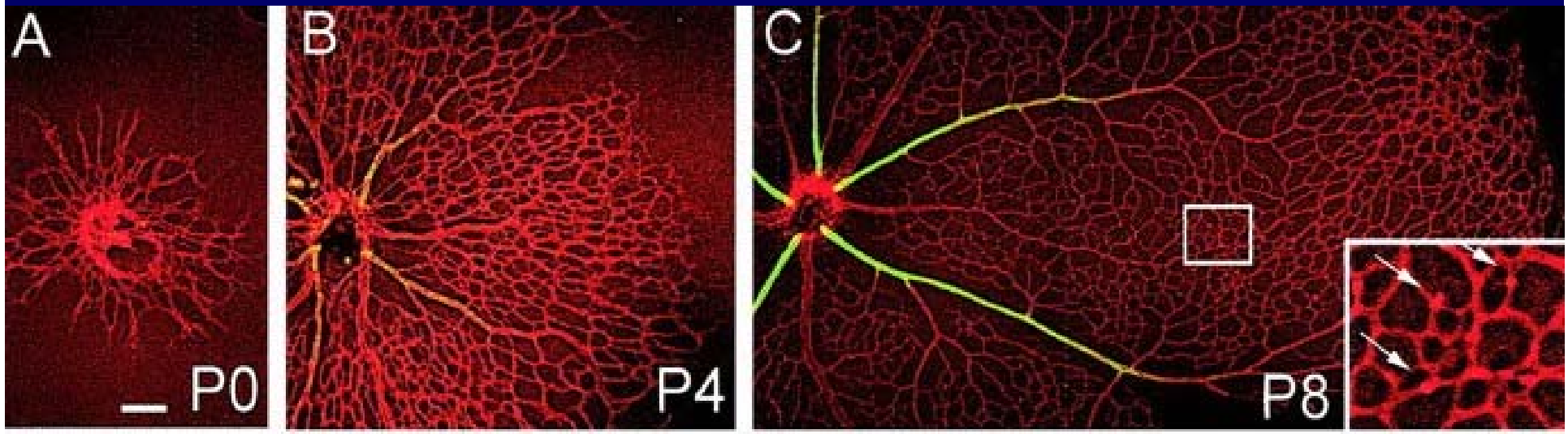
Biología Molecular de la ROP

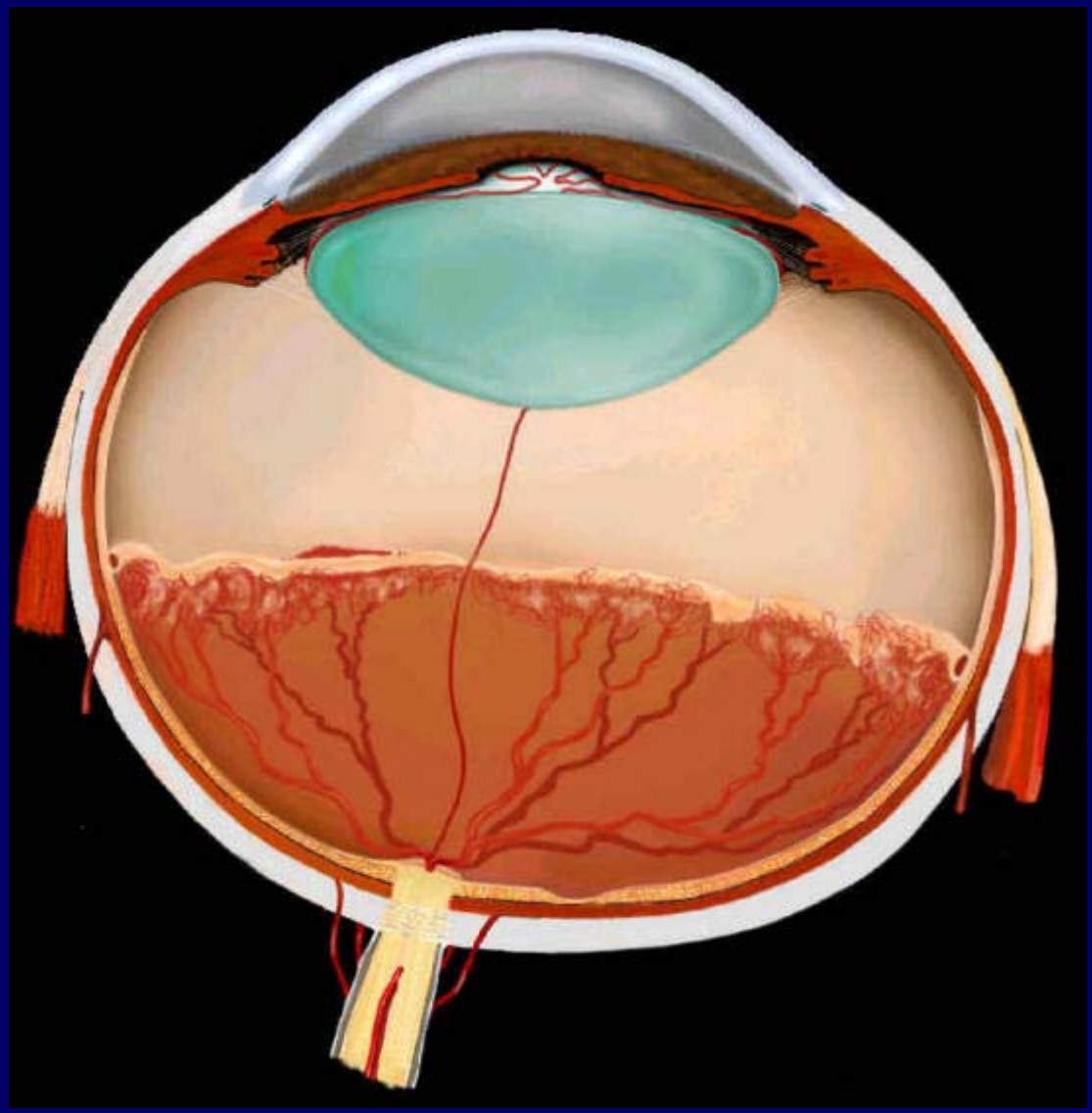


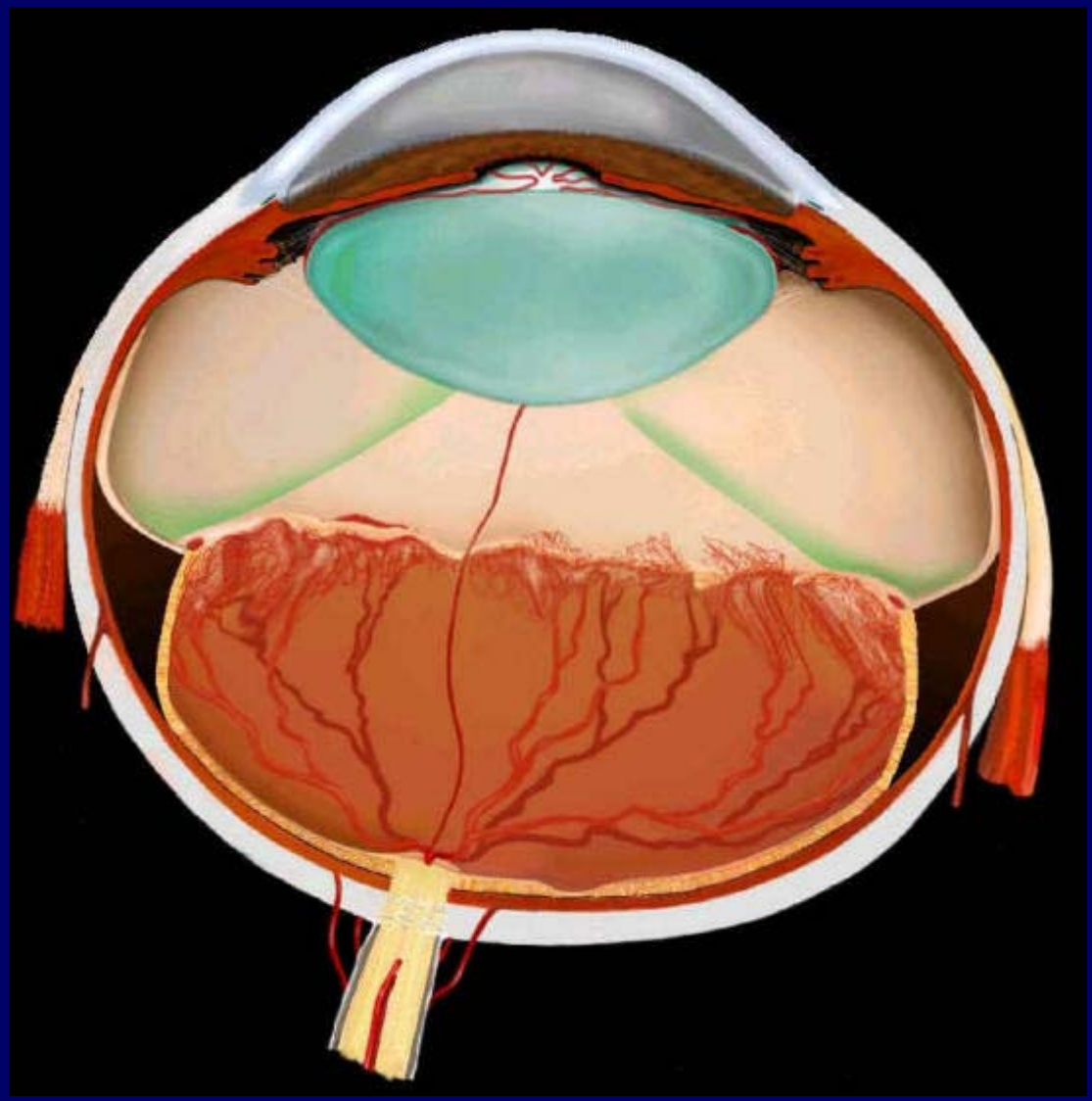
UNIVERSITY OF MANITOBA

John Baier MD

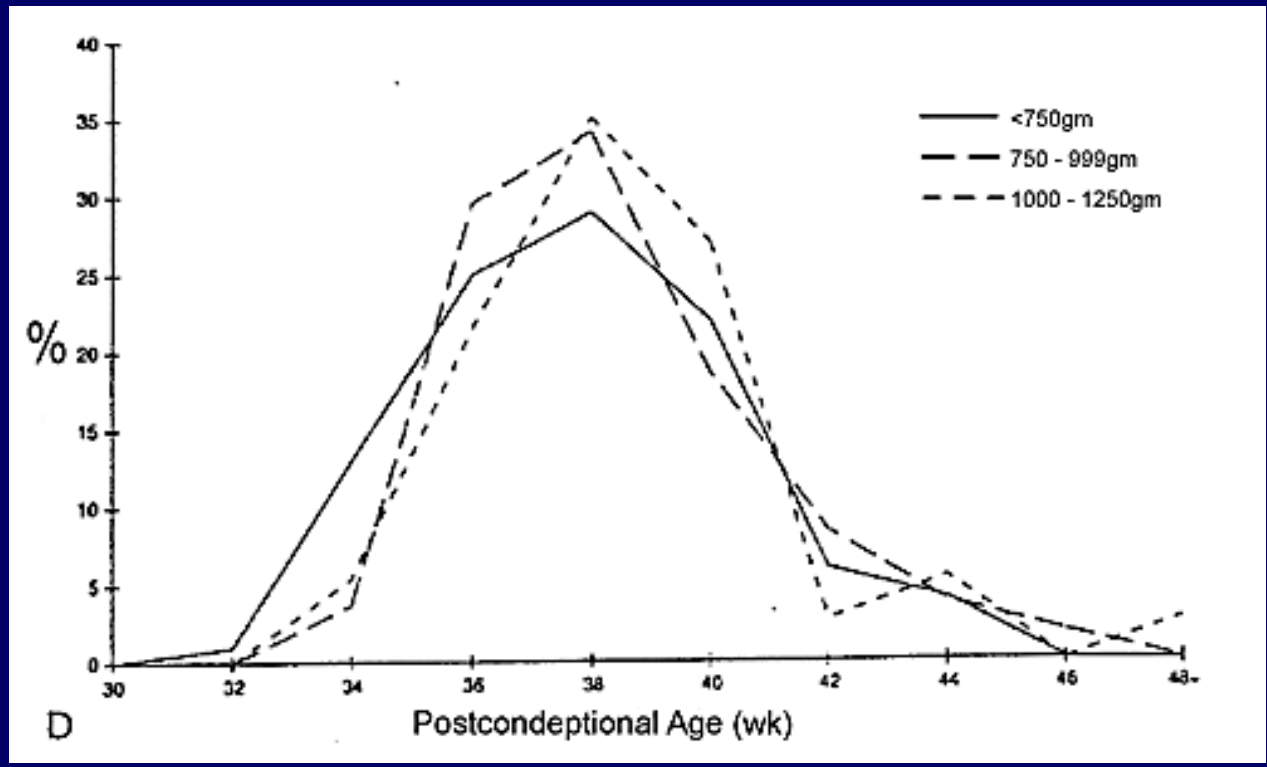
Angiogénesis retiniana








PULSE OXIMETER
STANDBY
BATTERY IN USE
PATIENT CONNECTION
ELECTRICALLY ISOLATED
PULSE SEARCH
OXYGEN SATURATION
PULSE RATE
HIGH SAT
LOW SAT
HIGH RATE
LOW RATE
AUDIO ALARM OFF


40
35
30
25
20
15
10
5
0
%
30
32
34
36
38
40
42
44
46
48+
D
Postcondeptional Age (wk)
<750gm
750 - 999gm
1000 - 1250gm

Journal of Perinatology

Original Article

Journal of Perinatology (2006) **26,** S46–S50. doi:10.1038/sj.jp.7211475; published online 16 February 2006

Oxygen and retinopathy of prematurity

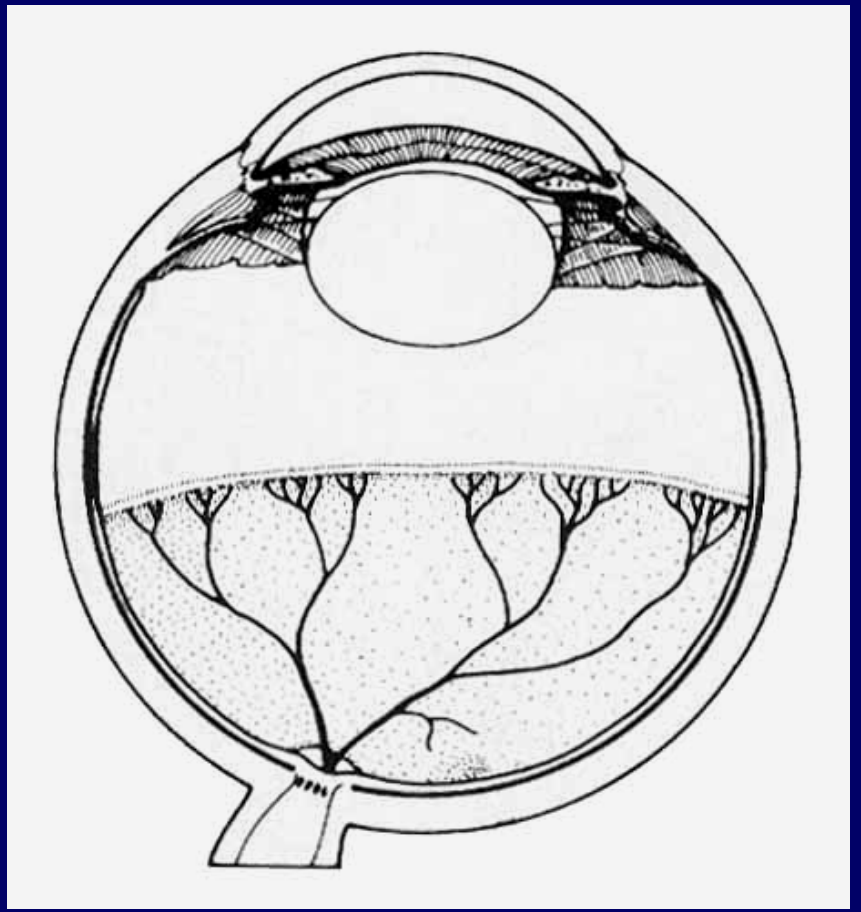
O D Saugstad[1]

[1]Department of Pediatric Research, Rikshospitalet University Hospital, University of Oslo, Oslo, Norway

Correspondence: Dr OD Saugstad, Pediatrisk Forskningsinstitutt, Rikshospitalet, 0027 Oslo, Norway. E-mail: o.d.saugstad@medisin.uio.no

Desarrollo de los vasos retinianos

- Los vasos retinianos comienzan a desarrollarse a las 16 semanas desde la papila hacia la periferia de la retina. Los recién nacidos prematuros tienen la vascularización incompleta, con zonas avasculares periféricas inversamente relacionadas con la edad gestacional.
- El mayor estímulo de la angiogénesis retiniana es la hipoxia.



DEVELOPMENTAL DYNAMICS 236:981–990, 2007

RESEARCH ARTICLE

Hyperoxia Inhibits Several Critical Aspects of Vascular Development

Koichi Uno, Carol A. Merges, Rhonda Grebe, Gerard A. Lutty, and Tarl W. Prow*

Normal human retinal vascular development uses angiogenesis and vasculogenesis, both of which are interrupted in the vaso-obliteration phase of retinopathy of prematurity (ROP). Canine oxygen-induced retinopathy (OIR) closely resembles human ROP. Canine retinal endothelial cells (ECs) and angioblasts were used to model OIR and characterize the effects of hyperoxia on angiogenesis and vasculogenesis. Cell cycle analysis showed that hyperoxia reduced the number of G1 phase cells and showed increased arrest in S phase for both cell types. Migration of ECs was significantly inhibited in hyperoxia ($P < 0.01$). Hyperoxia disrupted the cytoskeleton of angioblasts but not ECs after 2 days. Differentiation of angioblasts into ECs (determined by acetylated low-density lipoprotein uptake) was evaluated after basic fibroblast growth factor treatment. Differentiation of angioblasts into pericytes was determined by smooth muscle actin expression after treatment with platelet-derived growth factor. Differentiation into ECs was significantly inhibited by hyperoxia ($P < 0.0001$). The percentage of CXCR4$^+$ cells (a marker for retinal vascular precursors) increased in both treatment groups after hyperoxia. These data show novel mechanisms of hyperoxia-induced disruption of vascular development. *Developmental Dynamics 236:981–990, 2007.*

Key words: angioblasts; endothelial cells; hyperoxia; retina; vasculogenesis; angiogenesis; CXCR4

Accepted 25 January 2007

INTRODUCTION

sprout from pre-existing vessels by de- 1992; Smith et al., 1994; McLeod et

DEVELOPMENTAL DYNAMICS 236:981–990, 2007

RESEARCH ARTICLE

Hyperoxia Inhibits Several Critical Aspects of Vascular Development

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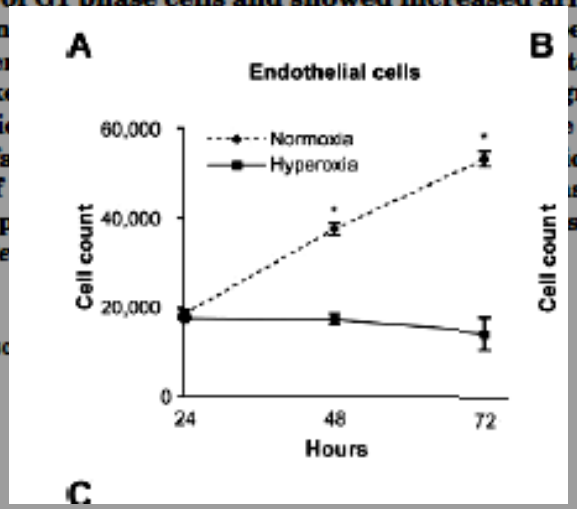
Key words: angioblasts; endothelial cells; hyperoxia; retina; vasc

Accepted 25 January 2007



INTRODUCTION

sprout from pre-existing vessels by de- 1992; Smith et al., 1994; McLeod et

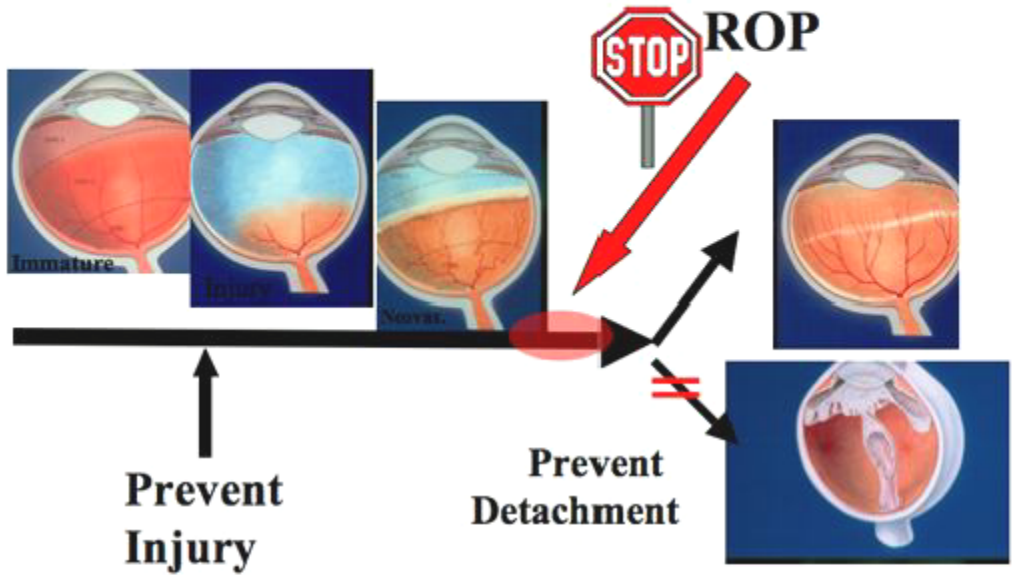


Figure 9. Rationale for the STOP-ROP study. Artist's concept of the sequential appearance of the growing preterm human retina as it develops ROP. From left to right, the normal immature retina, initial injury of the developing vessels, neovascularization with plus disease, involution (top) or retinal detachment (lower). The red arrow and circle indicates the hypothesized time/site of action of oxygen in the STOP-ROP study.

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High or Low Oxygen Saturation and Severe Retinopathy of Prematurity: A Meta-analysis

Minghua L. Chen, Lei Guo, Lois E. H. Smith, Christiane E. L. Dammann and Olaf Dammann

Pediatrics 2010;125;e1483-e1492; originally published online May 24, 2010;
DOI: 10.1542/peds.2009-2218

CONCLUSIONS

A sufficiently powered RCT on optimal oxygen delivery in the early and late stages of ROP is needed that also ensures long-term visual, pulmonary, and neurodevelopment follow-up. Moreover, we suggest that the PMA concept be embraced in such studies, because it is unclear currently whether clinical trials that investigate different lower oxygen-saturation protocols in very preterm infants have done this.[66–68] We speculate that low oxygen saturation in the first phase combined with high oxygen in the second phase of ROP pathogenesis might achieve greater protection than low oxygen alone.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Target Ranges of Oxygen Saturation in Extremely Preterm Infants

SUPPORT Study Group of the Eunice Kennedy Shriver NICHD Neonatal Research Network*

ABSTRACT

BACKGROUND

Previous studies have suggested that the incidence of retinopathy is lower in preterm infants with exposure to reduced levels of oxygenation than in those exposed to higher levels of oxygenation. However, it is unclear what range of oxygen saturation is appropriate to minimize retinopathy without increasing adverse outcomes.

METHODS

We performed a randomized trial with a 2-by-2 factorial design to compare target ranges of oxygen saturation of 85 to 89% or 91 to 95% among 1316 infants who were born between 24 weeks 0 days and 27 weeks 6 days of gestation. The primary outcome was a composite of severe retinopathy of prematurity (defined as the presence of threshold retinopathy, the need for surgical ophthalmologic intervention, or the use of bevacizumab), death before discharge from the hospital, or both. All infants were also randomly assigned to continuous positive airway pressure or intubation and surfactant.

*The authors are listed in the Appendix. The affiliations of the authors and other investigators in the Surfactant, Positive Pressure, and Pulse Oximetry Randomized Trial (SUPPORT) Study Group of the Neonatal Research Network of the Eunice Kennedy Shriver National Institute of Child Health and Human Development are listed in the Appendix. Address reprint requests to Dr. Waldemar A. Carlo at the University of Alabama at Birmingham, 176F Suite 9380, 619 S. 19th St., Birmingham, AL 35294-7335, or at wcarlo@peds.uab.edu.

This article (10.1056/NEJMoa0911781) was published on May 16, 2010, at NEJM.org.

N Engl J Med 2010.

Esquema de saturación óptima en prematuros

RN PREMATURO	SATURACIÓN DESEADA	ALARMA MÍNIMA DEL SATURÓMETRO	ALARMA MÁXIMA DEL SATURÓMETRO
< 1200 g ó < 32 semanas	**86 a 92%**	**85%**	**93%**
> 1200 g ó > 32 semanas	**86 a 94%**	**85%**	**95%**

Este criterio debe ser cumplido hasta las 8 semanas de vida postnatal y hasta completar la vascularización retiniana. En pacientes con displasia broncopulmonar el nivel de saturometría indicado es de 93%, sin superar ese valor hasta completar la vascularización retiniana.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Target Ranges of Oxygen Saturation in Extremely Preterm Infants

SUPPORT Study Group of the Eunice Kennedy Shriver NICHD

CONCLUSIONS

A lower target range of oxygenation (85 to 89%), as compared with a higher range (91 to 95%), did not significantly decrease the composite outcome of severe retinopathy or death, but it resulted in an increase in mortality and a substantial decrease in severe retinopathy among survivors. The increase in mortality is a major concern, since a lower target range of oxygen saturation is increasingly being advocated to prevent retinopathy of prematurity. (ClinicalTrials.gov number, NCT00233324.)

METHODS

We performed a randomized trial with a 2-by-2 factorial design to compare target ranges of oxygen saturation of 85 to 89% or 91 to 95% among 1316 infants who were born between 24 weeks 0 days and 27 weeks 6 days of gestation. The primary outcome was a composite of severe retinopathy of prematurity (defined as the presence of threshold retinopathy, the need for surgical ophthalmologic intervention, or the use of bevacizumab), death before discharge from the hospital, or both. All infants were also randomly assigned to continuous positive airway pressure or intubation and surfactant.

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tute of Child Health and Human Development are listed in the Appendix. Address reprint requests to Dr. Waldemar A. Carlo at the University of Alabama at Birmingham, 176F Suite 9380, 619 S. 19th St., Birmingham, AL 35294-7335, or at wcarlo@peds.uab.edu.

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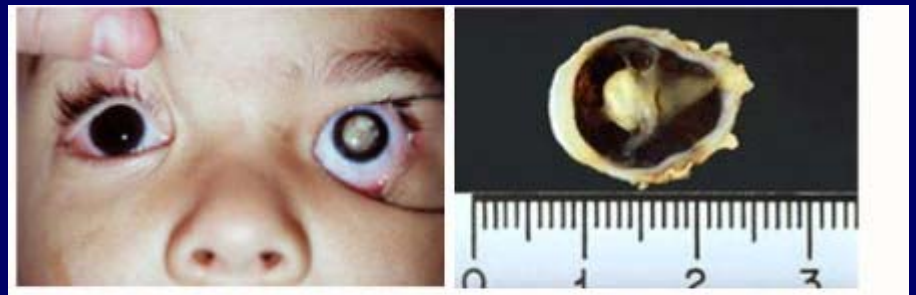
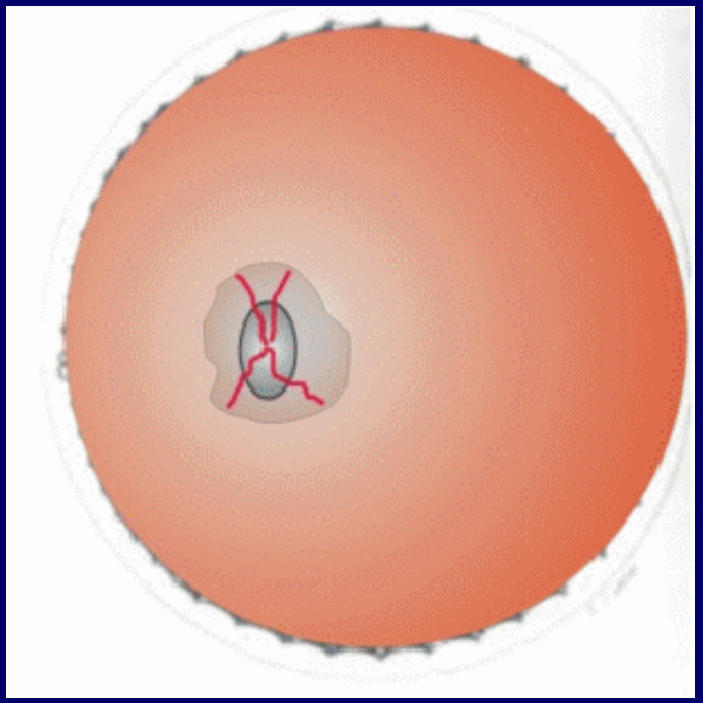
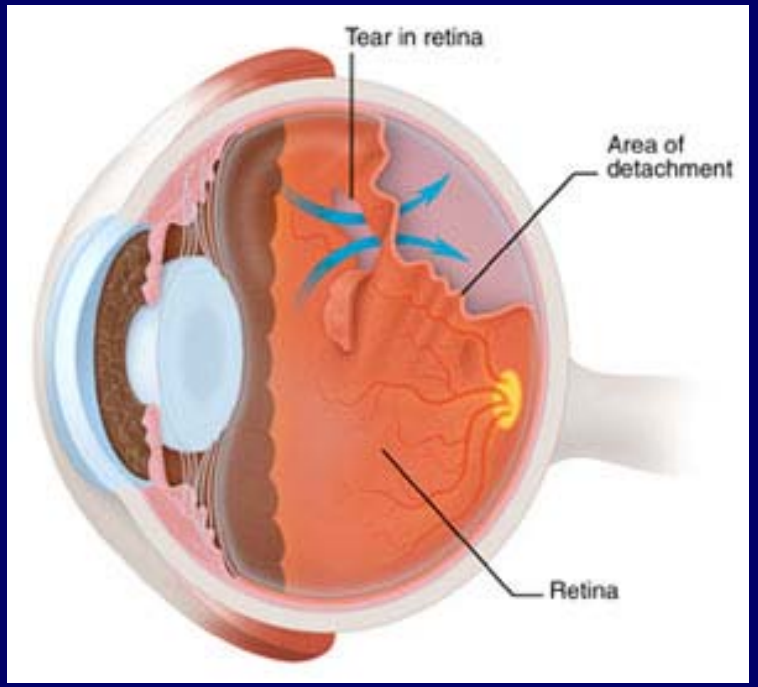


Leucocoria ojo izquierdo; y globo ocular que presenta ROP grado 5 (anatomía patológica)





Stevie Wonder habló en Ginebra en nombre de más de ***300 millones*** de personas que "viven en la oscuridad …"


Imagen: AFP PHOTO / Fabrice Coffrini

Sociedad | 21 de septiembre 2010 | 19:49 MSK

STEVIE WONDER: "O SI NO, TENDRÉ QUE ESCRIBIR UNA CANCIÓN"

El músico Stevie Wonder pidió modificar las leyes sobre la propiedad intelectual, para permitir que los ciegos y las personas con vista disminuida tengan acceso a millones de audiolibros sobre ciencia, historia y literatura que no pueden leer en formato electrónico.

Manifestó su petición en la sesión de la Organización Mundial sobre la Propiedad Intelectual de las Naciones Unidas, uno de los departamentos de la ONU encargado de los problemas al respecto.

Según el músico, en el mundo hay más de 300 millones de personas con vista debilitada que necesitan ayuda en la traducción de los libros a formatos accesibles, e incluso a los libros mismos.

Gracias por su atención

Proximamente en esta Sala