8. REFERENCES

1. Leduc S. Introduction of medical substances into the depth of tissues by electric current. *Ann d'electrobiologie.* 1900;3:545-560.
2. Gibson LE, Cooke RE. A test for the concentration of electrolytes in sweat in cystic fibrosis of pancreas utilizing pilocarpine by iontophoresis. *Pediatrics.* 1959;23:545-549.
3. Murray W, Lavine LS, Seifter E. The iontophoresis of C_{21} esterified glucocorticoids: preliminary report. *J Am Phys Ther Assoc.* 1963;43:579-581.
4. Rothfield SH, Murray W. The treatment of Peyronie's disease by iontophoresis of C_{21} esterified glucocortoids. *J Urol.* 1967;97:874-875.
5. Corneau M, Brummett R, Vernon J. Local anesthesia of the ear by iontophoresis. *Arch Otolaryngol.* 1973;98:114-120.
6. Gangarosa LP. Hill JM. Iontophoresis of vidarabine monophosphate for herpes orolabialis. *J Infect Dis.* 1986;154:930-4.
7. Rigano W, Yanik M, Barone FA, Baibak G, Cislo C. Antibiotic iontophoresis in the management of burned ears. *J Burn Care Rehabilitation.* 1992;13:407-409.
8. Gangarosa LP. Iontophoresis in dental practise. *Quintessence Chicago* 1983.
9. Sloan JB, Soltani K. Iontophoresis in dermatology. A review. *J Am Acad Dermatol.* 1986;15:671-84.
10. Wirtz R. die Ionentheraphie in der Augenheilkunde. *Klin Monatsbl Augenheilkd.* 1908;46:543-579.
11. Karbowski M. Iontophoresis in ophthalmology. *Ophthalmologica.* 1939;38:317-328.
12. Birkhauser R. Resultats d'etudes cliniques et experimentales sur la iontophorese. *Rev Gen Ophtalmol.* 1921;35:312-318.
13. Fietta P. Quelques essais d'iontophorese a l'atropine. *Rev Gen Ophtalmol.* 1924;38:317-328.
14. Morisot. L'ionopherapie ou ionisation appliquee au traitement des affections oculaires. *Clin Ophtalmol.* 1927;31:5-16.
15. Erlanger G. On the scientific and practical value of ionization in ophthalmology. Recent advantages and researches. *Br J Ophthalmol.* 1936;20:213-229.
16. Seech SG, LeGrande Cooper W. Experimental iontophoresis of rabbits'corneas. *Arch. Ophthalmol.* 1938;20:624-640.
17. Boyd JL. Sodium sulfathiazole iontophoresis. *Arch Ophthalmol.* 1942;28:205-213.
18. Fleming N. Iontotherapy as an aid in ophthalmic therapeutics. *Br J Ophthalmol.* 1943;27:254-367.
19. Swan KC. Corneal diseases. Treatment . Trans. *Am Acad Ophthalmol Otolaryngol.* 1951;55:387-400.
20. Witzel SH, Fielding IZ, Ormsby HL. Ocular penetration of antibiotics by iontophoresis. *Am J Ophthalmol.* 1956;42:89-95.
21. Von Sallmann L. Sulfadiazine iontophoresis in pyocyaneus infection of rabbit cornea. *Am J Opthalmol.* 1942;25:1292-1300.
22. Von Sallmann L. Iontophoretic introduction of atropine and scopolamine into the rabbit eye. *Arch Opthalmol.* 1943;29:711-719.
23. Von Sallmann L. Penecillin and sulfadiazine in the treatment of experimental intraocular infection with pneumococcus. *Arch Opthalmol.* 1943;30:426-436.
24. Von Sallmann L. Penetration of penicillin into the eye. Further studies. *Arch Opthalmol.* 1945;34:195-201.

25. Von Sallmann L. Penecillin and sulfadiazine in the treatment of experimental intraocular infections with Staphylococcus aureus and Clostridium welchii. *Arch Opthalmol.* 1947;31:54-63.
26. Von Sallmann L. Controversial points in ocular penicillin therapy. *Trans Am Ophthalmol Soc.* 1947;45:570-636.
27. Smith VL. Iontophoresis in ophthalmology. *Am J Ophthalmol*. 1951;34:698-704.
28. Erlanger G. Iontophoresis, a scientific and practical tool in ophthalmology. *Ophthalmologica*. 2954;128:232-246.
29. Sarraf D, LeeDA. The role of iontophoresis in ocular drug delivery. *J Ocul Pharmacol*. 1994;10:69-81.
30. Hughes L, Maurice DM. A fresh look at iontophoresis. *Arch Ophthalmol*. 1984;102:1825-9.
31. Fishman PH, Jay WM, Rissing JP, et al. Iontophoresis of gentamicin into aphakic rabbit eyes. Sustained vitreal levels. *Invest Ophthalmol Vis Sci.* 1984; 25:343-5.
32. Burstein NL, Leopold LH, Bernacchi DB. Trans-scleral iontophoresis of gentamicin. *J Ocul Pharmacol.* 1985;1:363-8.
33. Grossman RE, Chu DF, Lee DA. Regional ocular gentamicin levels after transcorneal and transscleral iontophoresis. *Invest Ophthalmol Vis Sci*. 1990;31:909-16.
34. Barza M, Peckman C, Baum J. Transscleral iontophoresis of cefazolin, ticarcillin, and gentamicin in the rabbit. *Ophthalmology*. 1986;93:133-9.
35. Barza M, Peckman C, Baum J. Transscleral iontophoresis of gentamicin in monkeys. *Invest Ophthalmol Vis Sci.* 1987, 28:1033-6.
36. Frucht-Pery J, Goren D, Solomon A, et al. The distribution of gentamicin in the rabbit cornea following iontophoresis to the central cornea. *J Ocul Pharmacol Ther.* 1999;15:251-6.
37. Rootman, DS, Hobden JA, Jantzen JA, et al. Iontophoresis of tobramycin for the treatment of experimental Pseudomonas keratitis in the rabbit. *Arch Ophthalmol*. 1988;106:262-5.
38. Hobden JA, Rootman DS, O'Callaghan RJ, et al. Iontophoretic application of tobramycin to uninfected and Pseudomonas aeruginosa-infected rabbit corneas. *Antimicrob Agents Chemother.* 1988;32:978-81.
39. Choi TB, Lee DA. Transscleral and transcorneal iontophoresis of vancomycin in rabbit eyes. *J Ocul Pharmacol.* 1988;4:153-64.
40. Yoshizumi MO, Cohen D, Verbukh I, et al. Experimental transscleral iontophoresis of ciprofloxacin. *J Ocul Pharmacol*. 1991;7:163-7.
41. Hobden JA, Reidy JJ, O'Callaghan, RJ,et al. Ciprofloxacin iontophoresis for aminoglycoside-resistant pseudomonal keratitis. *Invest Ophthalmol Vis Sci.* 1990;31:1940-4.
42. Sarraf D, Equi RA, Holland GN, et al. Transscleral iontophoresis of foscarnet. *Am J Ophthalmol*. 1993;115:748-54.
43. Yoshizumi MO, Roca JA, Lee DA, et al. Ocular iontophoretic supplementation of intravenous foscarnet therapy. *Am J Ophthalmol.* 1996;122:86-90.
44. Hill, JM, Park NH, Gangarosa LP, et al. Iontophoresis of vidarabine monophosphate into rabbit eyes. *Invest Ophthalmol Vis Sci*. 1978;17:473-6.
45. Lam TT, Fu J, Chu R, et al. Intravitreal delivery of ganciclovir in rabbits by transscleral iontophoresis. *J Ocul Pharmacol*. 1994;10:571-5.

46. Chapon P, Voigt M, Gautier S, Behar-Cohen FF, et al. Intraocular tissues pharmacokinetics of ganciclovir transscleral coulomb controlled iontophoresis in rabbits. ARVO *Invest Ophthalmol Vis Sci* 1999; 40:S189.
47. Hill JM, Kwon BS, Burch KD, et al. Acyclovir and vidarabine monophosphate: comparison of iontophoretic and intravenous administration for the treatment of HSV-1 stromal keratitis. *Am J Med*. 1982;73:300-4.
48. Grossman RE, Chu DF, Lee DA. Regional ocular gentamicin levels after transcorneal and transscleral iontophoresis. *Invest Ophthalmol Vis Sci*. 1990;31:909-16.
49. Grossman R, Lee DA. Transscleral and transcorneal iontophoresis of ketoconazole in the rabbit eye. *Ophthalmology*. 1989;96:724-9.
50. Lam TT, Edward DP, Zhu XA, et al. Transscleral iontophoresis of dexamethasone. *Arch Ophthalmol.* 1989;107:368-71.
51. Behar-Cohen FF, Parel JM, Pouliquen Y,et al. Iontophoresis of dexamethasone in the treatment of endotoxin-induced- uveitis in rats. *Exp Eye Res*. 1997;65:533-45.
52. Behar-Cohen FF, El Aouni A, Gautier S, et al. Transscleral Coulomb-controlled iontophoresis of methylprednisolone into the rabbit eye: influence of duration of treatment, current intensity and drug concentration on ocular tissue and fluid levels. *Exp Eye Res.* 2002; 74:51-9.
53. Voigt M, Kralinger MT, Kieselbach G. et al. Ocular Aspirin distribution: a comparison of intravenous, topical and Coulomb controlled iontophoresis administration. *Invest Ophthalmol Vis Sci* 2002. [in press]
54. Kondo M, Araie M. Iontophoresis of 5-fluorouracil into the conjunctiva and sclera. *Invest Ophthalmol Vis Sci.* 1989;30:583-5.
55. Behar-Cohen FF, Savoldelli M,Parel JM, et al. Reduction of corneal edema in endotoxin-induced uveitis after application of L-NAME as nitric oxide synthase inhibitor in rats by iontophoresis. *Invest Ophthalmol Vis Sci.* 1998;39:897-904.
56. Asahara T, Shinomiya K, Naito T, et al. Induction of genes into the rabbit eye by iontophoresis. *Nippon Ganka Gakkai Zasshi.* 1999;103; 178-85.
57. Voigt M, de Kozak Y, Halhal M, et al. Down-regulation of NOSII gene expression by iontophoresis of anti-sense oligonucleotide in endotoxin-induced uveitis. *Biochem Biophys Res Commun*. 2002;295:336-41.
58. Swarbrick, J, Lee G, Brom J, et al. Drug permeation through human skin II: Permeability of ionizable compounds. *J Pharm Sci.* 1984;73:1352-5.
59. Abramson HA, Gorin MH. Skin reactions: IX. The electrophoretic demonstration of the patent pores of the living human skin: Its relation to the charge of the skin. *J Phys. Chem*. 1940;44:1094.
60. Wearly LL, Liu JC, Chien YW. Iontophoresis facilitated transdermal delivery of verapamil: I. In vitro evaluation and mechanistic studies. *J Cont Rel.* 1989;8:237.
61. Srinivasan V, Higuchi WI. A model for iontphoresis incorporating the effect of convective solvent flow. *Int J Pharm*. 1990;60,1094.
62. Chien YW, Lelawongs P. Siddiqui O, et al. Facilitated transdermal delivery of therapeutic peptides and proteins by iontophoretic delivery devices. *J Cont Rel.* 1990;13:263.
63. Singh P, Maibach HI. Iontophoresis in drug delivery: basic principles and applications. *Crit Rev Ther Drug Carrier Syst*. 1994;11:161-213.
64. Li LC, Scudds RA. Iontophoresis: an overview of the mechanisms and clinical application. *Arthritis Care Res.* 1995;8:51-61.

65. Siddiqui O, Roberts MS, Polack AE. The effect of iontophoresis and vehicle pH on the in-vitro permeation of lignocaine through human stratum corneum. *J Pharm Pharmacol.* 1985;37:732-5.
66. Siddiqui O, Roberts MS, Polack AE. Iontophoretic transport of weak electrolytes through the excised human stratum corneum. *J Pharm Pharmacol*. 1989;41:430-2.
67. Yoshida NH, Roberts MS. Solute molecular size and transdermal iontophoresis across excised human skin. J Cont Rel. 1993;9:239.
68. Green PG, Hinz RS, Cullander C, et al. Iontophoretic delivery of amino acids and amino acid derivatives across the skin in vitro. *Pharm Res.* 1991;8:1113-20.
69. Potts RO, Guy RH. A pore pathway is not necessary to explain skin permeability. Proceedings of the 18th *International Symposium on Controlled release of Bioactive Materials. Amsterdam* 1991;175.
70. Heit MC, Williams PL, Jayes FL, et al. Transdermal iontophoretic peptide delivery: in vitro and in vivo studies with luteinizing hormone releasing hormone. *J Pharm Sci.* 1993;82:240-3.
71. Siddiqui O, Sun Y, Liu JC, Chien YW. Facilitated transdermal transport of insulin. *J Pharm Sci.* 1987;76:341-5.
72. Kari B. Control of blood glucose levels in alloxan-diabetic rabbits by iontophoresis of insulin. *Diabetes.* 1986;35:217-21.
73. Phipps JB, Padmanabhan RV, Lattin GA. Transport of ionic species through skin. *Solid State Ionics.* 1988;28-30:1778-1783.
74. Phipps JB, Padmanabhan RV, Lattin GA. Iontophoretic delivery of model inorganic and drug ions. *J Pharm Sci.* 1989;78:365-9.
75. Del Terzo S, Behl CR, Nash RA. Iontophoretic transport of a homologous series of ionized and nonionized model compounds: influence of hydrophobicity and mechanistic interpretation. *Pharm Res.* 1989;6:85-90.
76. Lelawongs P LJ, Siddiqui O, Chien YW. Transdermal iontophoretic delivery of arginin-vasopressine (I):Physicochemical considerations. *J Pharm Sci.* 1989;56:13.
77. Bellantone NH RS, Francoeur ML, Rasadi B. Enhanced percutaneous absorption via iontophoresis: I. Evaluation of an in vitro system and transport of model compounds. *Int J Pharm.* 1986;30:63.
78. Millard J, Barry BW. The iontophoresis of water and glutaminic acid across full thickness human skin and shed snake skin. *J Pharm Pharmacol.* 1988;40. Suppl.:41.
79. O'Malley EP Oester YT. Influence of some chemical factors on iontophoresis using radio isotopes. *Arch Phys Med Rehabil.* 1955;36:310
80. Burnette RR, Marrero D. Comparison between the iontophoretic and passive transport of thyrotropin releasing hormone across excised nude mouse skin. *J Pharm Sci.* 1986;75:738-43.
81. Burnette RR, Ongpipattanakul B. Characterization of the permselective properties of excised human skin during iontophoresis. *J Pharm Sci.* 1987;76:765-73.
82. Roberts MS SJ, Yoshida N, Currie KI. Iontophoretic transport of selected solutes through human epidermis. *Prediction of Percutaneous Penetration, IBC Technical Services; London.* 1990:231.
83. Miller LL, Kolaskie CJ, Smith GA, Rivier J. Transdermal iontophoresis of gonadotropin releasing hormone (LHRH) and two analogues. *J Pharm Sci.* 1990;79:490-3.
84. Wearly LL CY. Transdermal permeation of verapamil (III): Effect of binding and concentration gradient on reversibility of skin permeation rate. *Int J Pharm.* 1990;59:87.

85. Gangarosa LP, Park NH, Fong BC, Scott DF, Hill JM. Conductivity of drugs used for iontophoresis. *J Pharm Sci.* 1978;67:1439-43.
86. Burnette RR. Iontophoresis. *Transdermal Drug Delivery, Hadgraft J, Guy RH, Eds., Marcel Decker, New Yorck* 1988;ch.11.
87. Grimnes S. Pathways of ionic flow through human skin in vivo. *Acta Derm Venereol.* 1984;64:93-8.
88. Papa CM KA. Mechanism of eccrine anhidrosis. *J Invest Dermatol.* 1966;97:55.
89. Cullander C, Guy RH. Sites of iontophoretic current flow into the skin: identification and characterization with the vibrating probe electrode. *J Invest Dermato.l* 1991;97:55-64.
90. Cullander C. What are the pathways of iontophoretic current flow through mammalian skin? *Adv Drug Del Rev.* 1992;9:119.
91. Turner NG, Guy RH. Iontophoretic transport pathways: dependence on penetrant physicochemical properties. *J Pharm Sci.* 1997;86:1385-9.
92. Turner NG, Guy RH. Visualization and quantitation of iontophoretic pathways using confocal microscopy. *J Invest Dermatol Symp Proc.* 1998;3:136-42.
93. Chien YW, Banga AK. Iontophoretic (transdermal) delivery of drugs: overview of historical development. *J Pharm Sci.* 1989;78:353-4.
94. Jung JE KH, Schmidt KP, Voges G, Menestria G, Boheim G. Conformational requirements for the potential dependent pore formation of the peptide antibiotic alamethicin, suzukacillin and trichtoxin. *In: Physical Chemistry of Transmembrane Ion Motion; Elsevier New York* 1983.
95. Chien YW, Siddiqui O, Sun Y, Shi WM, Liu JC. Transdermal iontophoretic delivery of therapeutic peptides/proteins. I: Insulin. *Ann N Y Acad Sci.* 1987;507:32-51.
96. Monteiro-Riviere NA, Inman AO, Riviere JE. Identification of the pathway of iontophoretic drug delivery: light and ultrastructural studies using mercuric chloride in pigs. *Pharm Res.* 1994;11:251-6.
97. Gangarosa LP, Park NH, Wiggins CA, Hill JM. Increased penetration of nonelectrolytes into mouse skin during iontophoretic water transport (iontohydrokinesis). *J Pharmacol Exp Ther.* 1980;212:377-81.
98. Kim A, Green PG, Rao G, Guy RH. Convective solvent flow across the skin during iontophoresis. *Pharm Res.* 1993;10:1315-20.
99. Pikal MJ, Shah S. Transport mechanisms in iontophoresis. III. An experimental study of the contributions of electroosmotic flow and permeability change in transport of low and high molecular weight solutes. *Pharm Res.* 1990;7:222-9.
100. Pikal MJ, Shah S. Transport mechanisms in iontophoresis. II. Electroosmotic flow and transference number measurements for hairless mouse skin. *Pharm Res.* 1990;7:213-21.
101. Pikal MJ. Transport mechanisms in iontophoresis. I. A theoretical model for the effect of electroosmotic flow on flux enhancement in transdermal iontophoresis. *Pharm Res.* 1990;7:118-26.
102. Praisman MI, Berkowitz JM. Ion mediated flow, electroosmosis. *J Membr Biol.* 1973;11.
103. Tyle P. Iontophoretic devices for drug delivery. *Pharm Res.* 1986;3:318-26.
104. Fay MF. Indications and applications for iontophoresis. *Todays OR Nurse.* 1989;11:10.
105. Lark MR, Gangarosa LP. Iontophoresis: an effective modality for the treatment of inflammatory disorders of the temporomandibular joint and myofascial pain. *Cranio.* 1990;8:108-19.

106. Ledger PW. Skin biological issues in electrically enhanced transdermal delivery. *Adv Drug Del Rev.* 1992;9:289.
107. Behar-Cohen F, El Aouni A, Le Rouic JF, Parel JM, Renard G, Chauvaud D. Iontophoresis: past and future. *J Fr Ophtalmol.* 2001;24:319-27.
108. Lam TT, Fu J, Tso MO. A histopathologic study of retinal lesions inflicted by transscleral iontophoresis. *Graefes Arch Clin Exp Ophthalmol.* 1991;229:389-94.
109. Barza M, Peckman C, Baum J. Transscleral iontophoresis as an adjunctive treatment for experimental endophthalmitis. *Arch Ophthalmol.* 1987;105:1418-20.
110. Yoshizumi MO, Dessouki A, Lee DA, Lee G. Determination of ocular toxicity in multiple applications of foscarnet iontophoresis. *J Ocul Pharmacol Ther*. 1997;13:529-36.
111. Phoresor Iontophoretic Drug Delivery System: Package Insert, Motion Control, Salt lake City, UT.
112. Holzle E, Ruzicka T. Treatment of hyperhidrosis by a battery-operated iontophoretic device. *Dermatologica.* 1986;172:41-7.
113. Holzle E, Alberti N. Long-term efficacy and side effects of tap water iontophoresis of palmoplantar hyperhidrosis--the usefulness of home therapy. *Dermatologica*. 1987;175:126-35.
114. Chien YW LP, Siddiqui O, Sun Y, Shi WM. Facilitated transdermal delivery of therapeutic peptides and proteins by iontophoretic delivery devices. *J Cont Rel.* 1990;13:263.
115. Okabe K YH, Kawai Y. New iontophoretic transdermal administration of the betablocker metaprolol. *J Cont Rel.* 1986;4:79.
116. Brown MJ, Logan PM, O'Connell JX, et al. Diaphyseal telangiectatic osteosarcoma as a second tumor after bilateral retinoblastomas. *Skel Radio.* 1996;25:685–688.
117. Wong FL, Boice JD Jr, Abramson DH, et al. Cancer incidence after retinoblastoma: Radiation dose and sarcoma risk. *JAMA.* 1997;278:1262–1267.
118. Knudson AGJ, Hethcote HW, Brown BW. Mutation and childhood cancer: a probabilistic model for the incidenceof retinoblastoma. *Proc Natl Sci U S A.* 1975;72:5116–5120.
119. Mills MD, Windle JJ, Albert DM. Retinoblastoma in transgenic Mice: Models of Hereditary Retinoblastoma. *Surv Ophthalmol.* 1999;43:508-518.
120. Sparkes RS, Sparkes MC, Wilson MG, et al. Regional assignment of genes for human esterase D and retinoblastoma to chromosome band 13q14. *Science.* 1980;108:1042–1044.
121. Yunis JJ, Ramsay N. Retinoblastoma and subband deletion of chromosome 13. *Am J Dis Child.* 1978;132:161–163.
122. Dryja TP, Rapaport JM, Joyce JM, Petersen RA. Molecular detection of deletions involving band q14 of chromosome 13 in retinoblastomas. *Proc Natl Acad Sci U S A.*. 1986;83:7391–7394.
123. Friend SH, Bernards R, Rogelj S, et al. A human DNA segment with properties of the gene that predisposes to retinoblastoma and osteosarcoma. *Nature.* 1986;323:643–646.
124. Friend SH, Horowitz JM, Gerber MR, et al. Deletions of a DNA sequence in retinoblastomas and mesenchymal tumors:organization of the sequence and its encoded protein [published erratum appears in *Proc Natl Acad Sci U S A* 1988;85:2234]. *Proc Natl Acad Sci U S A.* 1987;84:9059–9063.
125. Fung YK, Murphree AL, T'Ang A. Structural evidence for the authenticity of the human retinoblastoma gene. *Science*. 1987;236:1657–1661.

126. Lee WH, Bookstein R, Hong F, et al. Human retinoblastoma susceptibility gene: cloning, identification, and sequence. *Science.* 1987;235:1394–1399.
127. Smith BJ, O'Brien JM. The genetics of retinoblastoma and current diagnostic testing. *J Pediatr Ophthalmol Strabismus.* 1996;33:120–123.
128. Ejima Y, Sasaki MS, Kaneko A, Tanooka H. Types, rates, origin and expressivity of chromosome mutations involving 13q14 in retinoblastoma patients. *Hum Genet.* 1988;79:118–123.
129. Hong FD, Huang HJ, To H, et al. Structure of the human retinoblastoma gene. *Proc Natl Acad Sci U S A.* 1989;86:5502–5506.
130. Weinberg RA. The retinoblastoma protein and cell cycle control. *Cell.* 1995;81:323–330.
131. Bandara LR, La Thangue NB. Adenovirus E1a prevents the retinoblastoma gene product from complexing with a cellular transcription factor. *Nature.* 1991;351:494–497.
132. Chellappan SP, Hiebert S, Mudryj M, et al. The E2F transcription factor is a cellular target for the RB protein. *Cell.* 1991;65:1053–1061.
133. Chittenden T, Livingston DM, Kaelin WG Jr. The T/E1Abinding domain of the retinoblastoma product can interact selectively with a sequence-specific DNA-binding protein. *Cell.* 1991;65:1073–1082.
134. Hiebert SW, Chellappan SP, Horowitz JM, et al. The interaction of RB with E2F coincides with an inhibition of the transcriptional activity of E2F. *Genes Dev.* 1992;6:177–185.
135. DeGregori J, Leone G, Ohtani K, et al. E2F-1 accumulation bypasses a G1 arrest resulting from the inhibition of G1 cyclin-dependent kinase activity. *Genes Dev.* 1995;9:2873–2887.
136. Sala A, Nicolaides NC, Engelhard A, et al. Correlation between E2F-1 requirement in the S phase and E2F-1 transactivation of cell cycle-related genes in human cells. *Cancer Res.* 1994;54:1402–1406.
137. Shirodkar S, Ewen M, DeCaprio JA, et al. The transcription factor E2F interacts with the retinoblastoma product and a p107-cyclin A complex in a cell cycle-regulated manner. *Cell.* 1992;68:157–166.
138. Buchkovich K, Duffy LA, Harlow E. The retinoblastoma protein is phosphorylated during specific phases of the cell cycle. *Cell.* 1989;58:1097–1105.
139. Chen PL, Scully P, Shew JY, et al. Phosphorylation of the retinoblastoma gene product is modulated during the cell cycle and cellular differentiation. *Cell.* 1989;58:1193–1198.
140. DeCaprio JA, Ludlow JW, Lynch D, et al. The product of the retinoblastoma susceptibility gene has properties of a cell cycle regulatory element. *Cell.* 1989;58:1085–1095.
141. Mihara K, Cao XR, Yen A. Cell cycle-dependent regulation of phosphorylation of the human retinoblastoma gene product. *Science.* 1989;246:1300–1303.
142. Hamel PA, Gallie BL, Phillips RA. The retinoblastoma protein and cell cycle regulation. *Trends Genet.* 1992;8:180–185.
143. Weinberg RA. The Rb gene and the negative regulation of cell growth. *Blood.* 1989;74:529–532.
144. Whyte P. The retinoblastoma protein and its relatives. *Semin Cancer Biol.* 1995;6:83–90
145. Gonzalez-Fernandez F, Garcia-Fernandez JM, Foster RG, et al. Expression of developmentally defined retinal phenotypes in the histogenesis of retinoblastoma. *Am J Pathol.* 1992;141:363-373.
146. Bogenmann E, Lochrie MA, Simon MI, et al. Cone cell-specific genes expressed in retinoblastoma. *Science.* 1988;240:76–78.

147. Hurwitz RL, Bogenmann E, Font RL, et al. Expression of the functional cone phototransduction cascade in retinoblastoma. *J Clin Invest.* 1990;85:1872–1878.
148. Kyritsis AP, Tsokos M, Triche TJ. Retinoblastoma—origin from a primitive neuroectodermal cell? *Nature.* 1984;307:471–473.
149. Kyritsis AP, Tsokos M, Triche TJ, Chader GJ. Retinoblastoma: a primitive tumor with multipotential characteristics. *Invest Ophthalmol Vis Sci.* 1986;27:1760–1764.
150. Shields JA, Shields CL. Current Management of Retinoblastoma. *Mayo Clin Proc.* 1994;69:50-56.
151. Byckley JD. The aetiology of cancer in the very young. *Br J Cancer.* 1992;18(suppl):8-12.
152. Rubenfield M, Abramson DH, Ellsworth RM, et al. Unilateral vs bilateral retinoblastoma –correlations between age at diagnosis and stage of ocular disease. *Ophthalmology.* 1986;93:1016-1019.
153. Binder PS. Unusual manifestations of retinoblastoma. *Am J Ophthalmol.* 1974;77:674-679.
154. Bremner MH. Retinoblastoma in the anterior chamber of the eye. *Aust J Ophthalmol.* 1983;11:123-126.
155. Ohnishi Y, Yamana Y, Minei M, et al. Snowball opacity in retinoblastoma. *Jpn J Ophthalmol.* 1982;26:159-165.
156. Sheta A. Some aspects on the different clinical characteristics of retinoblastoma. *Bull Ophthalmol Soc Egypt.* 1971;64:413-424.
157. Takahashi T, Tamura S, Inoue M, et al. Retinoblastoma in a 26-year–old adult. *Ophthalmology.* 1983;90:179-183.
158. Haik BG, Siedlecki A, Ellsworth RM, et al. Documented delays in the diagnosis of retinoblastoma. *Ann Opthalmol*. 1985;17:731-732.
159. Murphree AL, Cibis GW. Retinoblastoma. In: Cibis GW, Tongue,AC, Stass-Isern ML. *eds: Decision making in pediatric ophthalmology. St Louis 1993*, Mosby.
160. Atchaneeyasakul L, Murphree AL, Retinoblastoma. In:Ryan S. *Retina*. *Mosby* 2001;1:513-570.
161. Shields CL, Shields JA. Recent developments in the Management of Retinoblastoma. *J Pediatr Ophthalmol Strabismus.* 1999;36:8-18.
162. de Sutter E, Havers W, Höpping W, et al. The prognosis of retinoblastoma in terms of globe saving treatment: a computer –assisted study. *Opthalmic Paediatr Genet.* 1987;8:77-84.
163. Rubin CM, Robison LL, Cameron JD, et al. Intraocular retinoblastoma group V-an analysis of prognostic factors. *J Clin Oncol.* 1985;3:680-685.
164. Shields JA, Shields CL, Sivalingam V. Decreasing frequency of enucleation in patients with retinoblastoma. *Am J Opthalmol.* 1989,108:185-188.
165. Roarty JD, McLean IW, Zimmerman LE. Incidence of second neoplasms in patients with bilateral retinoblastoma. *Ophthalmology*. 1988;95:1583-7.
166. Shields JA, Shields CL. Management and prognosis of retinoblastoma. In: Shields JA, Shields CL, eds. *Intraocular Tumors. A Text and Atlas*. Philadelphia, Pa: Saunders; 1992:377-392.
167. Dudgeon J. Retinoblastoma-trends in conservative management. *Br J Ophthalmol*. 1995;79:104.
168. Scott IU, O´Brian JM, Murray TG. Retinoblastoma: A review emphasizing genetics and management strategies. *Sem Ophthal*. 1997;12:59-71.
169. Shields CL, Shields JA, Minelli S, et al. Plaque radiotherapy in the management of retinoblastoma. Use as a primary and secondary treatment. *Ophthalmology.* 1993;100:216-224.

170. Kock E, Rosengren B, Tengroth B, et al. Retinoblastoma treated with 60Co applicator. *Radiother Oncol.* 1986; 7:19-26.

171. Shields JA. The expanding role of laser photocoagulation for intraocular tumors. the 1993 H Christian Zweng Memorial Lecture. *Retina.* 1994;14:310-322.

172. Shields JA, Shields CL, Parsons H, et al. The role of photocoagulation in the management of retinoblastoma. *Arch Ophthalmol.* 1990;108:205-208.

173. Legendijk JJw. A microwave heating technique for the hyperthermic treatment of tumors in the eye, especially retinoblastoma. *Phys Med Biol.* 1995;27:1313-1324.

174. Shields JA, Parsons H, Shields CL, et al. The role of cryotherapy in the management of retinoblastoma. *Am J Ophthalmol.* 1989;108:260-264.

175. Shields CL, DePotter P, Himmelstein B, et al. Chemoreduction in the initial management of intraocular retinoblastoma. *Arch Ophthalmol.* 1996;114:1330-1338.

176. Ferris FL, Chew EY. A new era for the treatment of retinoblastoma. *Arch Ophthalmol.* 1996;114:1412.

177. Doz F, Khelfaoui F, Mosseri V, et al. The role of chemotherapy in orbital involvement of retinoblastoma. The experience of a single institution with 33 patients. *Cancer.* 1994;74:722-732.

178. Murphree Al, Villablanca JG, Deegan WF III, et al. Chemotherapy plus local treatment in the management of intraocular retinoblastoma. *Arch Ophthalmol.* 1996;114:1348-1356.

179. Gallie BL, Budning A, DeBoer G, et al. Chemotherapy with focal therapy can cure intraocular retinoblastoma without radiation. *Arch Ophthalmol.* 1996;114:1321-1328.

180. Shields CL, Shields JA, Needle M, et al. Combined Chemoreduction and adjuvant treatment for intraocular retinoblastoma. *Ophthalmology.* 1997;104:2101-2111.

181. Goble RR, McKenzie J, Kingston JE, Plowman PN, Hungerford JL. Orbital recurrence of retinoblastoma successfully treated by combined therapy. *Br J Ophthalmol.* 1990;74:97-98.

182. Kingston JE, Hungerford JL, Madreperla Sa, Plowman PN. Results of combined chemotherapy and radiotherapy for advanced intraocular retinoblastoma. *Arch Ophthalmol.* 1996;114:1339-1347.

183. Abramson DH, Niksarli K, Ellsworth RM, et al. Changing trends in the management of retinoblastoma: 1951-1965 vs 1966-1980. *J Pediatr Ophthalmol Strabismus.* 1994;31:32-37.

184. White L. The role of chemotherapy in the treatment of retinoblastoma. *Retina.* 1983;3:194-199.

185. White L. Chemotherapy in retinoblastoma: current status and future directions. *Am J Pediatr Hematol Oncol.* 1991;13:189-201.

186. Ettinger LJ, Gaynon PS, Krailo MD. A phase II study of carboplatin in children with recurrence of progressive solid tumors. *Cancer.* 1994;73:1297-1301.

187. Doz F, Pinkerton R. What is the place of carboplatin in the paediatric oncology? *Eur J Cancer.* 1994;30A:194-201.

188. Tucker MA, D´Angio GJ, Boice JD Jr., et al: Bone sarcomas linked to radiotherapy and chemotherapy in children. *N Enl J Med.* 1987;317:588-593.

189. Anagnoste SR, Scott IU, Murray TG, et al. Rhegmatogenous retinal detachment in retinoblastoma patients undergoing chemoreduction and Cryotherapy. *Am J Opthalmol.* 2000;129:817-9.

190. Mendelsohn ME, Abramson DH, Madden T, Tong W, Tran HT, Dunkel IJ. Intraocular concentrations of chemotherapeutic agents after systemic or local administration. *Arch Ophthalmol.* 1998;116:1209-12.

191. Abramson DH, Frank CM, Dunkel IJ. A Phase I/II Study of subconjunctival carboplatin for intraocular retinoblastoma. *Ophthalmology*.1999;106:1947-1950.

192. Harbour JW, Murray TG, Hamasaki D, et al. Local carboplatin therapy in transgenic murine retinoblastoma. *Invest Ophthalmol Vis Sci*. 1996;37:1892-8.

193. Murray TG, Roth DB, O'Brien JM, et al. Local carboplatin and radiation therapy in the treatment of murine transgenic retinoblastoma. *Arch Ophthalmol*. 1996;114:1385-9.

194. Murray TG, Cicciarelli N, O'Brien JM, et al. Subconjunctival carboplatin therapy and cryotherapy in the treatment of transgenic murine retinoblastoma. *Arch Ophthalmol*. 1997;115:1286-90.

195. DeCaprio JA, Ludlow JW, Figge J, et al. SV40 large tumor antigen forms a specific complex with the product of the retinoblastoma susceptibility gene. *Cell.* 1988;54:275–283.

196. Lane DP, Crawford LV. T antigen is bound to a host protein in SV40-transformed cells. *Nature.* 1979;278:261–263.

197. Linzer DI, Levine AJ. Characterization of a 54K dalton cellular SV40 tumor antigen present in SV40-transformed cells and uninfected embryonal carcinoma cells. *Cell.* 1979;17:43–52.

198. Windle JJ, Albert DM, O'Brien JM, et al. Retinoblastoma in transgenic mice. *Nature.* 1990;343:665–669.

199. O'Brien JM, Marcus DM, Bernards R, et al. A transgenic mouse model for trilateral retinoblastoma. *Arch Ophthalmol.* 1990;108:1145–1151.

200. O'Brien JM, Marcus DM, Niffenegger AS, et al. Trilateral Trans *Am Ophthalmol Soc.* 1989;87:301–326.

201. al-Ubaidi MR, Font RL, Quiambao AB, et al. Bilateral retinal and brain tumors in transgenic mice expressing simian virus 40 large T antigen under control of the human nterphotoreceptor retinoid-binding protein promoter. *J Cell Biol.* 1992;119:1681–1687.

202. Kivela T, Virtanen I, Marcus DM, et al. Neuronal and glial properties of a murine transgenic retinoblastoma model. *Am J Pathol.* 1991;138:1135–1148.

203. Marcus DM, O'Brien JM, Sahel J, et al. The histogenesis of transgenic murine retinoblastoma (abstract). *Invest Ophthalmol Vis Sci.* 1992;33 (Suppl):875.

204. Hsieh CL, Lee WH, Lee EY, et al. Assignment of retinoblastoma susceptibility gene to mouse chromosome 14. *Somat Cell Mol Genet.* 1989;15:461–464.

205. Drummer O, Proudfoot A, Howes L, et al. High-performance liquid chromatographic determination of platinum (II) in plasma ultrafiltrate and urine: comparison with a flameless atomic absorption spectrometric method. *Clin Chim Acta*. 1984;136:65-74.

206. van Warmerdam L, van Tellingen O, Maes R, et al. Validated method for the determination of carboplatin in biological fluids by Zeeman atomic absorption spectrometry. *Fresenius J Anal Chem.* 1995;351:777-781.

207. Graver R, George A, Deeb G. In vitro stabiltity, plasma protein binding and blood cell partintioning of 14C-carboplatin. *Cancer Chemother Pharmacol.* 1987;20:271-276.

208. Bornfeld N, Schuler A, Bechrakis N, et al. Preliminary results of primary chemotherapy in retinoblastoma. *Klin Padiatr*. 1997;209:216-21.

209. Finger PT, Czechonska G, Demirci H. et al. Chemotherapy for retinoblastoma: a current topic. *Drugs.* 1999;58:983-96.

210. Levy C, Doz F, Quintana E, et al. Role of chemotherapy alone or in combination with hyperthermia in primary treatment of intraocular retinoblastoma: preliminary results. *Br J Opthalmol.* 1998;82:1154-8.

211. Friedman DL, Himelstein B, Shields CL, et al. Chemoreduction and local ophthalmic therapy for intraocular retinoblastoma. *J Clin Oncol*. 2000;18;12-7.

212. Hayden BC, Murray Tg, Scott IU, et al. Subconjunctival carboplatin in retinoblastoma: Impact of tumor burden and dose schedule. *Arch Opthalmol*. 2000;118:1549-54.

213. Nose I, Parel J-M, Lee W, et al. Ocular Coulomb Controlled Iontophoresis (OCCI) [ARVO Abstract]. *Invest Ophthalmol Vis Sci.* 1996; 37(3):**S**41. Abstract nr 185.

214. Scott IU, Myrray TG, Toledano S, et al. New retinoblastoma tumorsin children undergoing systemic chemotherapy. *Arch Opthalmol.* 1998, 116:1685-86.

215. Benz MS, Scott IU, Murray TG, et al. Complications of systemicchemotherapy as treatment of retinoblastoma. *Arch Opthalmol.* 2000;118:577-578.

216. White L, Ortega JA, Ying KL. Acute non-lymphocytic leukemia following multimodality therapy for retinoblastoma. *Cancer.* 1985;55:469-8.

217. Chauveaud D, Behar-Cohen FF, Parel JM, Renard G. Transscleral iontophoresis of corticosteroids: Phase II Clinical trial [ARVO Abstract]. *Invest Ophthalmol Vis Sci.* 2000;41(4):**S**79. Abstract nr 414.