

UNIVERSITAT DE BARCELONA
FACULTAT DE MEDICINA
DEPARTAMENT D'OBSTETRÍCIA i GINECOLOGIA, PEDIATRIA,
RADIOLOGIA i MEDICINA FÍSICA

**ESTUDI DE LA REACTIVITAT
PLAQUETÀRIA EN LA GESTACIÓ
NORMAL I EN ELS TRASTORNS
HIPERTENSIUS DE L'EMBARÀS**

Montserrat Palacio i Riera
Barcelona, juliol de 1995

BIBLIOGRAFIA

- 1.- Lindheimer MD, Katz AI: Current concepts: Hypertension in pregnancy. *N Engl J Med* 1985;313:675-680.
- 2.- Weiner CP. Clotting alterations associated with the pre-eclampsia-eclampsia syndrome. In: Rubin PC, ed. *Hypertension in pregnancy*. New York: Elsevier 1988;241-57.
- 3.- Abdul-Karim R, Assali NS. Pressor response to angiotensin in pregnant and nonpregnant women. *Am J Obstet Gynecol* 1961; 82:246-51.
- 4.- Oney T, Kaulhausen H. The value of the angiotensin sensitivity test in the early diagnosis of hypertensive disorders of pregnancy. *Am J Obstet Gynecol* 1982;126:821-829.
- 5.- Fitzgerald DJ, Mayo G, Catella F, Entman SS, FitzGerald GA. Increased thromboxane biosynthesis in normal pregnancy is mainly derived from platelets. *Am J Obstet Gynecol* 1987;157:325-330.
- 6.- Walker JJ, Cameron A, Bjornsson S, Singer CRJ, Fraser C. Can platelet volume predict progressive hypertensive disease in pregnancy?. *Am J Obstet Gynecol* 1989;161:676-9.
- 7.- Morrison R, Crawford J, MacPherson M, Hepinstall S. Platelet behaviour in normal pregnancy, pregnancy complicated by essential hypertension and pregnancy induced hypertension. *Thromb Haemostasis* 1985;54:607-11.
- 8.- Sowers JR, Zemel MB, Walsh MF, *et al.* Effects of normal pregnancy on cellular cation metabolism and peripheral vascular resistance. *Am J Hypertens* 1990;3:16-22.
- 9.- Fitzgerald DJ, Entman SS, Mulloy K, FitzGerald GA. Decreased prostacyclin synthesis preceding the clinical manifestations of pregnancy-induced hypertension. *Circulation* 1987;75:956-63.
- 10.- Fitzgerald DJ, Rocki W, Murray R, Mayo G, FitzGerald GA. Thromboxane A₂ synthesis in pregnancy-induced hypertension. *Lancet* 1990;335:751-54.
- 11.- Andrews NP, Broughton Pipkin F, Hepinstall S. Blood platelet behaviour in mothers and neonates. *Thromb Haemostasis* 1985;53:428-32
- 12.- Singer CRJ, Walker JJ, Cameron A. Platelet studies in normal pregnancy and pregnancy-induced hypertension. *Clin Lab Haematol* 1986;8:10-32.
- 13.- Ashby B. Prostaglandin regulation of cyclic AMP metabolism in human platelets. *Platelets* 1990;1:2-10.
- 14.- Friedman SA. Preeclampsia: A review of the role of prostaglandins. *Obstet Gynecol* 1988;71:122.
- 15.- Satoh K, Seki H, Sakamoto H. Role of prostaglandins in pregnancy-induced hypertension. *Am J Kidn Dis* 1991;XVII:133-138.
- 16.- Cooper RS, Shamsi N, Katz S. Intracellular calcium and sodium in hypertensive patients. *Hypertension* 1987;9:224-229.
- 17.- Haller H, Lenz T, Luedersdorf M, *et al.* Intracellular free calcium in platelets and hypertension. *J Clin Hypertens* 1987;3:12-18.

- 18.- Kilby MD, Broughton Pipkin F, Cockbill S, Heptinstall S, Symonds EM. A cross-sectional study of basal platelet intracellular free calcium concentration in normotensive and hypertensive primigravid pregnancies. *Clin Sci* 1990;78:75-80.
- 19.- Barr SM, Lees KR, Butters L, O'Donnell A, Rubin PC. Platelet intracellular free calcium concentration in normotensive and hypertensive pregnancies in the human. *Clin Sci* 1989;76:67-71.
- 20.- Zemel MB, Zemel PC, Berry S, et al. Altered platelet calcium metabolism as an early predictor of increased peripheral vascular resistance and preeclampsia in urban black women. *N Engl J Med* 1990;323:434-8.
- 21.- Haller H, Oeney T, Hauck U, Distler A, Philipp T. Increased intracellular free calcium and sensitivity to angiotensin II in platelets of preeclamptic women. *Am J Hypertens* 1989;2:238-243.
- 22.- Baker PN, Kilby MD, Pipkin FB. The effect of angiotensin II on platelet intracellular free calcium concentration in human pregnancy. *Am J Hyper* 1992;10:55-60.
- 23.- Gilabert J, Estellés A, Aznar J, Lago V, Triguero P. Alteraciones de la hemostasia en la preeclampsia y eclampsia: Importancia del factor parietal vascular en su patogenia. En: Gilabert J, Gálbis M, Aznar J, Monleón J, eds. *Clinica ginecológica: Alteraciones de la hemostasia en obstetricia*. Barcelona: Salvat Eds., 1988; 144-168.
- 24.- Escolar G, Garrido M, Mazzara R, Castillo R, Ordinas A. Experimental basis for the use of red cell transfusion in the management of anemic-thrombocytopenic patients. *Transfusion* 1988;28:406-.
- 25.- Diuguid DL, Furie B. Molecular genetics of hemophilia B. In: Hoffman R, Benz EJ, Shattil SJ, Furie B, Cohen HJ, eds. *Hematology. Basic principles and practice*. New York: Churchill Livingstone, 1991:1316-1324.
- 26.- Labat-Robert J, Bihari-Varga M, Robert L. Extracellular matrix. *FEBS Lett* 1990; 268:386-393.
- 27.- Aarts PA, van den Broek SA, Prins GW, Kuiken GD, Sixma JJ, Heethaar RM. Blood platelets are concentrated near the wall and red blood cells, in the center in flowing blood. *Arteriosclerosis* 1988; 8:819-824.
- 28.- White JG. Platelet ultrastructure. In: Bloom AL, Thomas DP, eds. *Haemostasis and thrombosis*. 2nd ed. London: Churchill Livingstone, 1987:20-46.
- 29.- Colman RW. Receptors that activate platelets. *Proc Soc Exp Biol Med* 1991; 197:242-248.
- 30.- Bevers EM, Comfurius P, Zwaal RFA. Platelet Procoagulant Activity - Physiological Significance and Mechanisms of Exposure. *Blood Rev* 1991; 5:146-154.
- 31.- Marcus AJ. The role of lipids in platelet function with particular reference to the Araquidonic pathway. *J Lipid Res* 1978;19:793-.
- 32.- Kroll MH, Schafer AI. Biochemical mechanisms of platelet activation. *Blood* 1989; 74:1181-1195.
- 33.- White JG. Platelet morphology and function. In: Williams WJ, Beutler E, Erslev AJ, Lichtman MA, eds. *Hematology*. 3rd ed. New York: McGraw-Hill, 1983:1121-1135.

- 34.- Fox JEB. The platelet cytoskeleton. In: Verstraete M, Vermylen J, Lijnen R, Arnout J, eds. *Thrombosis and Haemostasis*. Leuven: Leuven University Press, 1987:175-225.
- 35.- White JG. Platelet membrane ultrastructure and its changes during platelet activation. In: Jamieson GA, ed. *Platelet membrane receptors: molecular biology, immunology, biochemistry and pathology*. New York: Alan R. Liss, 1987:1-32.
- 36.- Vermylen J, Badenhorst PN, Deckmyn H, Arnout J. Normal mechanisms of platelet function. *Clin Haematol* 1983; 12:107-151.
- 37.- White JG, Leistikow EL, Escolar G. Platelet membrane responses to surface and suspension activation. *Blood Cells* 1990; 16:43-72.
- 38.- White JG, Escolar G. The Blood Platelet Open Canalicular System - A Two-Way Street. *Eur J Cell Biol* 1991; 56:233-242.
- 39.- Skaer RJ. Platelet degranulation. In: Gordon JL, ed. *Platelets in Biology and Pathology 2*. Elsevier-North-Holland-Amsterdam 1981; 321.
- 40.- Gerrard JM, White JG, Peterson DA. The platelet dense tubular system: its relationship to prostaglandin synthetic and calcium flux. *Thromb Haemost* 1978; 40:224-231.
- 41.- Haslam RJ, Lynham JA. Activation and inhibition of blood platelet adenylate cyclase by adenosine or by 2-chloroadenosine. *Life Sci* 1972; 2:1143-1154.
- 42.- Gordon JL, Pearson JD. Biology of the vascular endothelium. In: Bloom AL, Thomas DP, eds. *Haemostasis and thrombosis*. London: Churchill Livingstone, 1987:303-311.
- 43.- Menashi S, Auhti KS, Carey F, Crafowrd N. Characterisation of the calcium-sequestering process associated with human platelet intracellular membranes isolated by free flow electrophoresis. *Biochem J* 1984; 222:413-417.
- 44.- Bastida E, Escolar G, Ordinas A, Sixma JJ. Fibronectin is required for platelet adhesion and for thrombus formation on subendothelium and collagen surfaces. *Blood* 1987; 70:1437-1442.
- 45.- Chesterman CN, Berndt MC. Platelet and vessel wall interaction and the genesis of atherosclerosis. *Clin Haematol* 1986;15:323.
- 46.- Ashby B, Daniel JL, Smith JB. Mechanisms of platelet activation and inhibition. *Hematol Oncol Clin North Am* 1990; 4:1-26.
- 47.- Van Willigen G, Akkerman J-WN. Protein kinase C and cyclic AMP regulate reversible exposure of binding sites for fibrinogen on the glycoprotein IIB- IIIA complex of human platelets. *Biochem J* 1991; 273:115-120.
- 48.- Holmsen H. *Biochemistry of the platelet release reaction*. Ciba Found. Symp. 35: 175-205, 1975.
- 49.- Steen VM, Tysnes OB, Holmsen H. Synergism between thrombin and epinephrine in human platelets. *Biochem J* 1988; 253:581-586.
- 50.- Bills TK, Smith JB, Silver MJ. Selective release of arachidonic acid from the phospholipids of human platelets in response to thrombin. *J Clin Invest* 1977; 60:1-6.

- 51.- Holmsen H. Prostaglandin endoperoxides: thromboxane synthesis and dense granule secretion as positive feed-back loops in the propagation of platelet responses during the basic platelet reaction. *Thromb Haemostasis* 1977; 38:1030-1041.
- 52.- Broekman MJ, Handin RI, Derksen A, Cohen P. Distribution of phospholipids, fatty acids, and platelet factor 3 activity among subcellular fractions of human platelets. *Blood* 1976; 47:963-971.
- 53.- Fauvel J, Chap H, Roques V, Levy-Toledano S, Douste-Blazy L. Biochemical characterization of plasma membranes and intracellular membranes isolated from human platelets using percoll gradients. *Biochim Biophys Acta* 1986; 856:155-164.
- 54.- McIntyre DE. Platelet prostaglandin receptors. In: Gordon JL, ed. *Platelets in Biology and Pathology 2*. Elsevier-North-Holland-Amsterdam 1981; 211-227.
- 55.- Rittenhouse-Simmonds S. Differential activation of platelet phospholipases by thrombin and ionophore A23187. *J Biol Chem* 1981; 256:4153.
- 56.- Hanasaki K, Nakano T, Arita HJ. Involvement of the Na⁺/H⁺ antiporter in the activation of rat platelets by collagen. *Biochem* 1987; 102:5-8.
- 57.- Rasmussen H. The calcium messenger system. *N Eng J Med* 1986;314: 1094-1101, 1164-1170.
- 58.- Berridge MJ. Inositol triphosphate and diacylglycerol as second messengers. *Biochem J* 1984; 220:345-360.
- 59.- Brass LF, Joseph SK. A role for inositol triphosphate in intracellular Ca²⁺ mobilization and granule secretion in platelets. *J Biol Chem* 1985; 260:151-172.
- 60.- Berridge MJ. Inositol triphosphate and diacylglycerol: two interacting second messengers. *Annu Rev Biochem* 1987; 56: 159-193.
- 61.- Knight DE, Scrutton MC. Cyclic nucleotides control a system which regulates Ca²⁺ sensitivity of platelet secretion. *Nature* 1984; 309:66.
- 62.- Pannochia A, Hardisty RM. Cyclic AMP inhibits platelet activation independently of its effect on cytosolic free calcium. *Biochem Biophys Res Commun* 1985; 127:339.
- 63.- Nakashima S, Hattori H, Shirato L, Takenaka A, Nozawa Y. Differential sensitivity of arachidonic acid release and 1,2-diacylglycerol formation to pertussis toxin, GDP beta S and NaF in saponin-permeabilized human platelets: possible evidence for distinct GTP-binding proteins involving Phosphorilase C and A₂ activation. *Biochem Biophys Res Commun* 1987; 148:971-978.
- 64.- Dickzalusy V, Falardean P, Hammarstrom S. Conversion of prostaglandin endoperoxides to C17-Hydroxy acids catalyzed by human platelet thromboxane synthetase. *FEBS Lett* 1987; 84:217.
- 65.- Bastida E. Estructura y funcionalismo plaquetar. *Sangre* 1984; 29:777.
- 66.- Moncada S, Gryglewski RJ, Bunting S, Vane JR. An enzyme isolated from arteries transforms prostaglandin endoperoxides to an unstable substance that inhibits platelet aggregation. *Nature* 1976; 263:663-665.

- 67.- Bunting S, Gryglewsky RJ, Moncada S, Vane JR. Arteral wall generates from prostaglandins a substance (Prostaglandin X) which relaxes strips of mesenteric and coeliac arteries and inhibits platelet aggregation. *Prostaglandins* 1976; 12:897.
- 68.- de Castellarnau. Prostaglandinas en el periodo perinatal. En: Cabero LI, ed. *Perinatologia Tomo I*. Barcelona: Salvat Ed, 1986:139-157.
- 69.- Moncada S, Vane JR. Arachidonic acid metabolites and the interactions between platelets and blood-vessel walls. *N Engl J Med* 1979; 300:1142-1147.
- 70.- Lorenzet L, Niemetz N, Marcus AJ, Broekman MJ. Enhancement of mononuclear procoagulant activity by platelet 12-Hydroxyeicosatetraenoic acid. *J Clin Invest* 1986; 78:418.
- 71.- Buchanan MR, Bastida E. The role of 13-HODE and HETES in vessel wall/circulating blood cells interactions. *Agents and actions* 1987; 22:1-3.
- 72.- Soberman RJ, Harper TW, Betteridge D, Lewis RA, Ansten MF. Characterization and separation of the arachidonic acid, 5-lipoxygenase and linoleic acid w-6 lipoxygenase (Arachidonic 15-lipoxygenase) of human polymorphonuclear leukocytes. *J Biol Chem* 1985; 260:4508.
- 73.- Siess W. Molecular mechanisms of platelet activation. *Physiol Rev* 1989; 69:58-178.
- 74.- Martin BM, Wasiewski WW, Fenton II JW, Detwiler TC. Equilibrium binding of thrombin to platelets. *Biochemistry* 1976; 15:4886-4892.
- 75.- Erne P, Resnik TJ, Bürgisser E, Bühler FR. Platelets and hypertension. *J Cardiovasc Pharmacol* 1985; 7(Suppl 6):103-108.
- 76.- Hallam TJ, Sanchez A, Rink TJ. Stimulus-response coupling in human platelets. *Biochem J* 1984; 218:819-827.
- 77.- Zavoico GB, Feinstein MB. Cytoplasmic Ca²⁺ in platelets is controlled by cyclic AMP: antagonism between stimulators and inhibitors of adenylate cyclase. *Biochem Biophys Res Commun* 1984; 120:579-585.
- 78.- Pollack H. Microsurgical studies in cell physiology. VI. Calcium ions in living protoplasm. *J Gen Physiol* 1928; 11:539-545.
- 79.- Scharff O, Foder B. Regulation of cytosolic calcium in blood cells. *Physiol Rev* 1993; 73:547-582.
- 80.- Sage SO, Rink TJ. Kinetic differences between thrombin-induced and ADP-induced calcium influx and release from internal stores in fura-2-loaded human platelets. *Biochem Biophys Res Commun* 1986; 136:1124-1129.
- 81.- Sage SO, Rink TJ. The kinetics of changes in intracellular calcium concentrations in fura-2-loaded human platelets. *J Biol Chem* 1987; 262:16364-16369.
- 82.- Laher I, Hwa JJ, Bevan JA. Calcium and vascular myogenic tone. In: Paoletti R, Vanhoute P, eds. *Calcium antagonists, Pharmacology and Clinical Research. Proceedings of the Annals of the New York Academy of Sciences* 1988; 552:216-225.

- 83.- Khalil RA, van Breemen C. Sustained contraction of vascular smooth muscle: calcium influx or C-kinase activation? *J Pharmacol Exp Ther* 1988; 244: 537-542.
- 84.- Schultz G, Rosenthal J, Hescheler J, Trautwein W. Role of G proteins in calcium channel modulation. *Annu Rev Physiol* 1990; 52:275-292.
- 85.- Blache D, Ciavatti M, Ojeda C. The effect of calcium channel blockers on platelet function, especially calcium uptake. *Biochem Biophys Acta* 1987; 923:401-412.
- 86.- Palés J, Palacios-Araus L, López A, Gual A. Effects of dihydropyridines and inorganic calcium blockers on aggregation and on intracellular free calcium in platelets. *Biochem Biophys Acta* 1991; 1064:169-174.
- 87.- Sage SO, Reast R, Rink TJ. ADP evokes a biphasic Ca^{2+} influx in fura-2-loaded human platelets. Evidence for a Ca^{2+} entry regulated by the intracellular Ca^{2+} store. *Biochem J* 1990;265:675-680.
- 88.- Rink TJ, Sage SO. Calcium signalling in human platelets. *Annu Rev Physiol* 1990; 52:431-449.
- 89.- Valone FH, Johnson B. Modulation of platelet-activating-factor-induced calcium influx and intracellular calcium release in platelets by phorbol esters. *Biochem J* 1987; 247:669-674.
- 90.- Berridge MJ, Irvine RF. Inositol phosphates and cell signalling. *Nature Lond* 1989; 341:197-205.
- 91.- Iino M, Endo M. Calcium-dependent immediate feedback control of inositol 1,4,5-triphosphate-induced Ca^{2+} release. *Nature Lond* 1992; 360:76-78.
- 92.- Missiaen LH, de Smedt H, Droogmans G, Casteels R. Ca^{2+} release induced by inositol 1,4,5-triphosphate is a steady-state phenomenon controlled by luminal Ca^{2+} in permeabilized cells. *Nature Lond* 1992; 357:599-602.
- 93.- Berridge MJ. Inositol triphosphate and calcium signalling. *Nature Lond* 1993; 361:315-325.
- 94.- Carafoli E. Calcium pump of the plasma membrane. *Physiol Rev* 1991; 71:129-153.
- 95.- Rink TJ, Sage SO. Stimulated calcium efflux from fura-2 loaded human platelets. *J Physiol Lond* 1987; 393:513-524.
- 96.- Borlé AB. Control, modulation and regulation of cell calcium. *Rev Physiol Biochem Pharmacol* 1981; 90:130-153.
- 97.- Haynes DH, Valant PA, Adjei PN. Calcium extrusion by the sodium-calcium exchanger of the human platelet. *Ann NY Acad Sci* 1991; 639:592-603.
- 98.- Rengasany A, Soura S, Feinberg H. Platelet Ca^{2+} homeostasis: Na^+ - Ca^{2+} exchange in plasma membrane vesicles. *Thromb Haemost* 1987; 57:337-340.
- 99.- Schaeffer J, Blaustein MP. Platelet free calcium concentrations measured with fura-2 are influenced by the transmembrane sodium gradient. *Cell Calcium* 1989; 10:101-113.
- 100.- Roevens P, de Chaffoy de Courcelles. Ouabain increases the calcium concentration in intracellular stores involved in stimulus-response coupling in human platelets. *Circ Res* 1990; 67:1494-1502.

- 101.- Kimura M, Aviv A, Reeves JP. K⁺-dependent Na⁺/Ca²⁺ exchange in human platelets. *J Biol Chem* 1993; 268:6874-6877.
- 102.- Carafoli E. Intracellular calcium homeostasis. *Annu Rev Biochem* 1987; 56:395-433.
- 103.- Enyedi A, Sarkadi B, Foldes-Papp Z, Monostory S, Gardos G. Demonstration of two distinct calcium pumps in human platelet membrane vesicles. *J Biol Chem* 1986;261:9558-9563.
- 104.- Johansson JS, Nied LE, Haynes DH. Cyclic AMP stimulates Ca²⁺-ATPase-mediated Ca²⁺ extrusion from human platelets. *Biochem Biophys Acta* 1992; 1105:19-28.
- 105.- Tao J, Johansson JS, Haynes DH. Protein kinase C stimulates dense tubular Ca²⁺ uptake in the intact human platelet by increasing the V_m of the Ca²⁺-ATPase pump: stimulation by phorbol ester, inhibition by calphostin C. *Biochem Biophys Acta* 1992; 1107:213-222.
- 106.- Heizmann CW, Hunziker W. Intracellular calcium binding proteins: more sites than insights. *Trends Biochem Sci* 1991; 16:98-103.
- 107.- Burgoyne RD, Geisow MJ. The annexin family of the calcium-binding proteins. *Cell Calcium* 1989; 10:1-10.
- 108.- Koch GL. The endoplasmic reticulum and calcium storage. *Bioessays* 1990; 12:527-531.
- 109.- Janis RA, Silver PJ, Triggle DJ. Drug action and cellular calcium regulation. *Adv Drug Res* 1987; 16:309-591.
- 110.- Howie PW. Blood clotting and fibrinolysis in pregnancy. *Postgrad Med J* 1979; 55:362-366.
- 111.- McKay DG. Chronic intravascular coagulation in normal pregnancy and pre-eclampsia. *Contr Nephrol* 1983; 25:108-119.
- 112.- Bonnar J. Hemostatic function and coagulopathy during pregnancy. *Obstet Gynecol Annu* 1978; 7:195-217.
- 113.- Hellgren M, Blombäch M. Studies on blood coagulation and fibrinolysis in pregnancy, during delivery and in the puerperium. *Gynecol Obst Invest* 1981; 12:141-154.
- 114.- Letsky EA, Swiet M. Thromboembolism in pregnancy and its management. *Br J Haematol* 1984; 57:543-552.
- 115.- Kaunitz AM, Hughes JM, Grimes DA. Causes of maternal mortality in the United States. *Obstet Gynecol* 1985; 65:605-612.
- 116.- Fay RA, Hughes AO, Hughes O, Farron NT. Platelets in pregnancy: Hyperdestruction in pregnancy. *Obstet Gynecol* 1983; 61(2):238-240.
- 117.- O'Brien JR. Platelet counts in normal pregnancy. *J Clin Path* 1976; 29:174.
- 118.- Pitkin RM, Witte DL. Platelet and leukocyte counts in pregnancy. *JAMA* 1979; 242:24.
- 119.- Giles C. The platelet count and mean platelet volume. *Br J Haematol* 1981; 48:31-37.

- 120.- Harrison KL, Bramich L, Collins. Platelet count during normal pregnancy. *Aus NZ J Obstet Gynaecol* 1982; 22:74.
- 121.- Tygart SG, McRoyan DK, Spinnato JA, McRoyan CJ, Kitay DZ. Longitudinal study of platelet indices during normal pregnancy. *Am J Obstet Gynecol* 1986; 154:883-887.
- 122.- Sill PR, Lind T, Walker W. Platelet values during normal pregnancy. *Br J Obstet Gynecol* 1985;92:480-483.
- 123.- Paulus JM. Platelet size in man. *Blood* 1975; 46:3.
- 124.- Karpatkin S, Charnatz A. Heterogeneity of human platelets. *J Clin Invest* 1969; 48:1073-1081.
- 125.- Rakoczi I, Tallian F, Bagdany S, Gati I. Platelet life-span in normal pregnancy and pre-eclampsia as determined by a non-radioisotope technique. *Thromb Res* 1979; 15:553-556.
- 126.- Pekonen F, Rasi V, Ammala M, Viinikka L, Ylikorkala O. Platelet function and coagulation in normal and preeclamptic pregnancy. *Thromb Res* 1986; 43:553-560.
- 127.- Arocha-Pinago CL, López AOG, García L, Linares J. Beta-thromboglobulin (β -TG) and platelet factor 4 (PF₄) in obstetrical cases. *Acta Obstet Gynecol Scand* 1985; 64:115-120.
- 128.- Inglis ICM, Stuart, George AJ, Davies AJ. Haemostatic and rheological changes in normal pregnancy and preeclampsia. *Br J Haematol* 1982; 50:461-465.
- 129.- Dawes J, Smith RC, Pepper DS. The release distribution and clearance of human β -thromboglobulin and platelet factor 4. *Thromb Res* 1978; 12(5):851-861.
- 130.- Davison JM, Hytten FE. Glomerular filtration during and after pregnancy. *J Obstet Gynecol Br Commonw* 1974; 81:588.
- 131.- Whigham KAE, Howie PW, Drummond AH, Prentice CRM. Abnormal platelet function in preeclampsia. *Br J Obstet Gynaecol* 1978; 85:28-32.
- 132.- Gader AMA, Bahakim H, Jabbar FA, Lambourne AL, Gaafar TH, Edrees YB. Dose-response aggregometry in maternal/neonatal platelets. *Thromb Haemost* 1988; 60(2):314-318.
- 133.- O'Brien WF, Saba HI, Knuppel RA, Scerbo JC, Cohen GR. Alterations in platelet concentration and aggregation in normal pregnancy and pre-eclampsia. *Am J Obstet Gynecol* 1986; 155(3):486-490.
- 134.- Yamazaki H, Motomiya T, Kikutani N, Sakakibara C, Watanabe S, Numata M, Noguchi K. Platelet aggregation during menstrual cycle and pregnancy. *Thromb Res* 1979; 14(2):333-340.
- 135.- Lewis PJ, Boylan P, Friedman LA, Hensby CN, Downing I. Prostacyclin in pregnancy. *Br Med J* 1980; 280:1581-1582.
- 136.- Leuschen PM, Davis RB, Boyd D, Goodlin RC. Comparative evaluation of antepartum and postpartum platelet function in smokers and nonsmokers. *Am J Obstet Gynecol* 1986;155(6):1276-1280.

- 137.- Louden KA, Broughton Pipkin F, Hepinstall S, Fox SC, Mitchell JRA, Symonds EM. A longitudinal study of platelet behaviour and thromboxane production in whole blood in normal pregnancy and the puerperium. *Br J Obstet Gynaecol* 1990;97:1108-1114.
- 138.- Horn EH, Cooper J, Hardy E, Hepinstall S, Rubin PC. A cross-sectional study of platelet cyclic AMP in healthy and hypertensive human pregnancy. *Clin Sci* 1991;80:549-558.
- 139.- Ylikorkala O, Viinikka L. Thromboxane A₂ in pregnancy and puerperium. *Br Med J* 1980; 281:1601-1602.
- 140.- Hoche C, Kefalides A, Dadak C, Sinszinger H. Platelet sensitivity to prostacyclin and prostaglandins in pregnancy and puerperium. *Prostaglandins in pregnancy* 1983; 8:189-193.
- 141.- Briel R, Kieback DG, Lippert TH. Platelet sensitivity to prostacyclin analogue in normal and pathological pregnancy. *Prostagl Leuko and Med* 1984;13:335-340.
- 142.- Dadak CH, Kefalides A, Sinszinger H. Prostacyclin-synthesis stimulating plasma factor and platelet sensitivity in preeclampsia. *Biol Res Pregnancy Perinatol* 1985;6:65-69.
- 143.- Horn EH, Hepinstall S, Rubin PC. Preliminary studies on the effects of cyclic AMP manipulators *in vitro* in pregnancy. *Platelets* 1990;1:51.
- 144.- Horn EH, Cooper J, Hardy E, Hepinstall S, Rubin PC. Platelet adenylate cyclase activity in normal and hypertensive pregnancy. *Br J Haematol* 1990; 76(Suppl 1):32.
- 145.- Aznar, J, Estellés A, Gilabert J. Modificaciones de la hemostasia durante la gestación, parto y puerperio. En: Gilabert J, Galbis M, Aznar J, Monleón J, eds. *Clínica ginecológica: Alteraciones de la hemostasia en Obstetricia*. Barcelona: Salvat Ed 1988:90-102.
- 146.- Hepinstall S, Bevan J, Cockbill SR, Hanley SP, Parry MJ. Effects of a selective inhibitor of thromboxane synthetase on human blood platelet behaviour. *Thromb Res* 1980; 20:219-230.
- 147.- Mills DCB. The role of cyclic nucleotides in platelets. In: Keabian JW, Nathanson JA, eds. *Handbook of experimental pharmacology*. Berlin-New York 1982, 58 (2):723-761.
- 148.- Huang EM, Detwiler JC. Stimulus response coupling mechanisms. In: Phillips DR, Shuman MA, eds. *Biochemistry of platelets*. London: Academic Press Inc. 1986:39-42.
- 149.- Blockmans D, Gresele P, Deckmyn H, Vermeylen J. Responder-nonresponder behaviour of human platelets towards thromboxane synthase inhibitors (TSI) is due to differences in adenylate cyclase sensitivity. *Thromb Haemost* 1985; 54:114.
- 150.- Gray SJ. Studies on cyclic AMP in relation to human blood platelet behaviour. Ph.D. Thesis, University of Nottingham, 1988.
- 151.- Sills T, Hepinstall S. Effects of a thromboxane synthetase inhibitor and a cAMP phosphodiesterase inhibitor, singly and in combination, on platelet behaviour. *Thromb Haemost* 1986; 55(3):305-308.
- 152.- Rao GHR, Peller JD, White JG. Measurements of ionized calcium in blood platelets with a new generation calcium indicator. *Biochem Biophys Res Comm* 1985;132:652-657.

- 153.- Kilby MD, Platelet intracellular free calcium concentrations in normotensive and hypertensive pregnancy. D.M. Thesis. University of Nottingham 1990.
- 154.- Horn EH. Platelets in normal and hypertensive pregnancy. *Platelets* 1991; 2:183-195.
- 155.- Ardlie NG. Calcium ions, drug action and platelet function. *Pharmac Ther* 1982; 18:249-270.
- 156.- Wilson K, Baig MW, Lees AD. Increased platelet aggregation in hypertension- relationship to intraplatelet calcium. *Clin Sci* 1989; 76(suppl 20):17.
- 157.- Roberts JM, Lewis V, Mize N, Tsuchiya A, Starr J. Human platelet α -adrenergic receptors and responses during pregnancy: No change except that with differing hematocrit. *Am J Obstet Gynecol* 1986; 154:206-210.
- 158.- Cabero LI. Retardo de crecimiento intrauterino. En: Cabero LI, ed. *Perinatología* 1986 (I). Barcelona: Salvat Ed:281-312.
- 159.- Davey DA, McGillivray I. The classification and definition of the hypertensive disorders of pregnancy. *Am J Obstet Gynecol* 1988;158:892-898.
- 160.- Cabero LI, Santamaria R. Estados hipertensivos del embarazo (i). *Clin Invest Gin Obst* 1984; 11:161-182.
- 161.- Zuspan FP. Chronic hypertension in pregnancy. *Clin Obstet Gynecol* 1984; 27:854.
- 162.- Turnbull AC. Maternal mortality and present trends. In: Sharp F, Symonds EM, eds. *Hypertension in pregnancy*. Ithaca, NY: Perinatology Press, 1987:135.
- 163.- McGillivray I. Preeclampsia: the hypertensive disease of pregnancy. Philadelphia: WB Saunders, 1983:17.
- 164.- Stirrat GM. The immunology of hypertension in pregnancy. In: Sharp F, Symonds EM, eds. *Hypertension in pregnancy*. Ithaca, NY: Perinatology Press, 1987:249.
- 165.- Robertson WB, Khong TY. Pathology of the uteroplacental bed. In: Sharp F, Symonds EM, eds. *Hypertension in pregnancy*. Ithaca, NY: Perinatology Press, 1987:101.
- 166.- Silver RK, Turbov JM, Beaird JA, Golbus J. Soluble factors produced by isolated first-trimester chorionic villi directly inhibit proliferation of T cells. *Am J Obstet Gynecol* 1990; 163:1914.
- 167.- Sibai BM. Immunologic aspects of preeclampsia. *Clin Obstet Gynecol* 1991; 34:27.
- 168.- Feeney JG, Scott JS. Preeclampsia and changed paternity. *Eur J Obstet Gynecol Reprod Biol* 1980; 11:35.
- 169.- Klonoff-Cohen HS, Savitz DA, Cefalo RC, McCann MF. An epidemiologic study of contraception and preeclampsia. *JAMA* 1989; 262:3143.
- 170.- Arngrimsson R, Björnsson S, Geirsson RT, Björnsson H, Walker JJ, Snaedal G. Genetic and familial predisposition to eclampsia and preeclampsia in a defined population. *Br J Obstet Gynecol* 1990; 97:762.

- 171.- Redman CWG. The fetal allograft. *Fetal Medicine Review* 1990; 2:21.
- 172.- Favier R. Presence of elevated serum interleukin-2 levels in pregnant women. *N Engl J Med* 1990; 322:270.
- 173.- Greer IA, Butterworth B, Liston WA, Johnston TA, Dawes J. Neutrophil activation in PIH: localization to the placental bed. *Proceedings VII World Congress of Hypertension in Pregnancy, Perugia, Italy. October 7-11, 1990*:276
- 174.- Harlan JD. Neutrophil-mediated vascular injury. *Acta Med Scand* 1987; 715:123.
- 175.- Greer IA, Haddad NG, Dawes J, Johnstone FD, Calder AA. Neutrophil activation in pregnancy-induced hypertension. *Br J Obstet Gynaecol* 1989; 96:978.
- 176.- Pelusi G, Scagliarini G, Biagi G, de Rosa V, Busacchi P. Neutrophil production of leukotriene-B4 is increased in gestational hypertension. *Proceedings VII World Congress of Hypertension in Pregnancy, Perugia, Italy. October 7-11, 1990*:199.
- 177.- Rodgers GM, Taylor RN, Roberts JM. Preeclampsia is associated with a serum factor cytotoxic to human endothelial cells. *Am J Obstet Gynecol* 1988; 159:908.
- 178.- Rappaport VJ, Hirata G, Kim Yap H, Jordan SC. Anti-vascular endothelial cell antibodies in severe preeclampsia. *Am J Obstet Gynecol* 1990;162:138.
- 179.- Lazarchick J, Stubbs TM, Romein L, Van Dorsten JP, Loadholt CB. Predictive value of fibronectin levels in normotensive gravid women destined to become preeclamptic. *Am J Obstet Gynecol* 1986; 154:1050.
- 180.- Jaffe EA, Endothelial cells. In: Gallin JI, Goldstein IM, Snyderman R, eds. *Inflammation: basic principles and clinical correlates*. New York: Raven, 1988:559.
- 181.- Vanhoutte PM. Endothelium and control of vascular function. *Hypertension* 1989; 13:658.
- 182.- Vanhoutte PM, Lüscher TF. Peripheral mechanisms in cardiovascular regulation: transmitters, receptors and the endothelium. In: Zanchetti A, Tarazi RC, eds. *Handbook of Hypertension. Vol 8*. New York: Elsevier, 1986:96.
- 183.- Brenner BM, Try JL, Ballerman BJ. Endothelium-dependent vascular responses, mediators and mechanisms. *J Clin Invest* 1989; 84:1373.
- 184.- Palmer RMJ, Ferrige AG, Moncada S. Nitric oxide release accounts for the biological activity of the endothelium-derived relaxing factor. *Nature* 1987;327:524.
- 185.- Ignarro LJ. Biological actions and properties of the endothelium-derived nitric oxide formed and released from artery and vein. *Circ Res* 1989; 65:1.
- 186.- Gardiner SM, Compton AM, Bennett T, Palmer RMJ, Moncada S. Control of regional blood flow by endothelium-derived nitric oxide. *Hypertension* 1990; 15:486.
- 187.- Lüscher TF. The endothelium, target and promotor of hypertension? *Hypertension* 1990; 15:482.

- 188.- Yanagisawa M, Kurihara H, Kimura S. A novel potent vasoconstrictor peptide produced by vascular endothelial cells. *Nature* 1988; 332:411.
- 189.- Katusic ZS, Vanhoutte PM. Superoxide anion is an endothelium-derived contracting factor. *Heart Circ Physiol* 1989; 26:H33.
- 190.- Jörgensen M, Philips M, Thorsens Semer J, Zeuthen J. Plasminogen activator inhibitor-1 is the primary inhibitor of tissue-type plasminogen activator in pregnancy plasma. *Thromb Haemost* 1987; 58:872.
- 191.- Ballegeer V, Spitz B, Kieckens L, Moreau H, van Asche A, Collen D. Predictive value of increased plasma levels of fibronectin in gestational hypertension. *Am J Obstet Gynecol* 1990;162:358.
- 192.- Lockwood CJ, Peters JH. Increased plasma levels of ED1+ cellular fibronectin precede the clinical signs of preeclampsia. *Am J Obstet Gynecol* 1990; 162:358.
- 193.- de Boer K, Lecander I, Cate ten JW, Borm JJ, Treffers PE. Placental-type plasminogen activator inhibitor in preeclampsia. *Am J Obstet Gynecol* 1988; 158:518.
- 194.- Walsh SW. Preeclampsia: an imbalance in placental prostacyclin and thromboxane production. *Am J Obstet Gynecol* 1985; 152:335.
- 195.- Dekker GA. Prediction and prevention of pregnancy-induced hypertensive disorders: a clinical and pathophysiologic study. Thesis, Erasmus University, Rotterdam. The Hague: Pasmans, 1989:38.
- 196.- Roberts JM, Taylor RN, Musci TJ, Rodgers GM, Hubel CA, McLaughlin MK. Preeclampsia: an endothelial cell disorder. *Am J Obstet Gynecol* 1989; 161:1200.
- 197.- Shanklin DR, Sibai BM. Ultrastructural aspects of preeclampsia: I. Placental bed and uterine boundary vessels. *Am J Obstet Gynecol* 1989; 161:735.
- 198.- Roberts JM, Taylor RN, Friedman SA, Goldfien A. New developments in preeclampsia. *Fetal Medicine Review* 1990; 2:125.
- 199.- Friedman SA. Preeclampsia: a review of the role of the prostaglandins. *Am J Obstet Gynecol* 1989; 161:1605.
- 200.- Gant NF, Daley GI, Chand S, Whalley PJ, McDonald PC. A study of angiotensin II pressor response throughout primigravid pregnancy. *J Clin Invest* 1973; 52:2682.
- 201.- Conrad KP, Colpoys MC. Evidence against the hypothesis that prostaglandins are the vasodepressor agents of pregnancy. *J Clin Invest* 1986; 77:236.
- 202.- Ahokas RA, Mercer BM, Sibai BM. Enhanced endothelium-derived relaxing factor activity in pregnant spontaneously hypertensive rats. *Am J Obstet Gynecol* 1991; 164(suppl):242.
- 203.- Dekker GA, Kraayenbrink AA, van Kamp GJ, van Geijn HP. Endothelial vasoactive mediators in preeclampsia. *Am J Obstet Gynecol* 1991; 164(suppl):276
- 204.- Spokas J, Kuchel O, Hamet P, Cantin M. Prostaglandins in hypertension. In: Genest EG, Quilley J, McGiff JC, eds. *Hypertension*. Montreal: McGraw Hill, 1983:373.

- 205.- Weiner CE, Martínez E, Chestnut H, Ghosdi A. Effect of pregnancy on uterine and carotid artery response to norepinephrine, epinephrine and phenylephrine in vessels with documented functional endothelium. *Am J Obstet Gynecol* 1989;161:1605.
- 206.- Weiner CE, Martinez E, Zhu LK, Ghosdi A, Chesnut D. *In vitro* release of endothelium-derived relaxing factor by acetyl-choline is increased during the guinea pig pregnancy. *Am J Obstet Gynecol* 1989; 161:1599.
- 207.- Bell C. Dual vasoconstrictor and vasodilator innervation of the uterine arterial supply in the guinea pig. *Circ res* 1968; 23:279.
- 208.- Bell C. Oestrogen-induced sensitization of the uterine artery of the guinea pig to acetylcholine. *Br J Pharmacol* 1973; 49:595.
- 209.- Myatt L, Brewer A, Brockman DE. The action of nitric oxide in the perfused human fetal-placental circulation. *Am J Obstet Gynecol* 1991; 164:687.
- 210.- Pinto A, Sorrentino R, Sorrentino P. Endothelial-derived relaxing factor released by endothelial cells of human umbilical vessels and its impairment in pregnancy-induced hypertension. *Am J Obstet Gynecol* 1991; 164:507.
- 211.- Musci TJ, Roberts JM, Rodgers GM. Mitogenic activity is increased in the sera of preeclamptic women before delivery. *Am J Obstet Gynecol* 1988; 159:1446.
- 212.- King AJ, Mardsen PA, Brenner BM. Endothelin: a potent vasoactive peptide of endothelial origin. In: Laragh JH, Brenner BM, eds. *Hypertension: pathophysiology, diagnosis and management*. New York: Raven, 1990:649.
- 213.- de Nucci G, Thomas R, D'Orleans-Juste P. Pressor effects of circulating endothelin are limited by its removal in the pulmonary circulation and by the release of prostacyclin and endothelium-derived relaxing factor. *Proc Natl Acad Sci USA* 1988; 88:9797.
- 214.- Webb DJ, Cockcroft JR. Plasma immunoreactive endothelin in uraemia. *Lancet* 1989; 1:1211.
- 215.- Dekker GA, Kraayenbrink AA, Zeeman GG, van Kamp GJ. Increased plasma levels of the novel vasoconstrictor peptide endothelin in severe preeclampsia. *Eur J Obstet Gynecol Reprod Biol* 1991; 40:215.
- 216.- Kamoi K, Sudo N, Ishibashi M, Yamaji T. Plasma endothelin-1 levels in patients with pregnancy-induced hypertension. *N Engl J Med* 1990; 323:1486.
- 217.- Taylor RN, Varma M, Teng NH, Roberts JM. Women with preeclampsia have higher plasma endothelin levels than women with normal pregnancies. *J Clin Endocrinol Metab* 1990; 71:1675.
- 218.- Greer IA, Leask R, Hodson BA, Dawes J, Kilpatrick DC, Liston WA. Endothelin, elastase, and endothelial dysfunction in preeclampsia. *Lancet* 1991; 337:228.
- 219.- Nova A, Sibai BM, Barton JR, Mercer BM, Mitchell MD. Maternal plasma level of endothelin is increased in preeclampsia. *AM J Obstet Gynecol* 1991; 165:726.
- 220.- Scholtes MCW, Gerretsen G, Haak HL. The factor VIII ratio in normal and pathologic pregnancy. *Eur J Obstet Gynecol Reprod Biol* 1983; 16:89.

- 221.- de Boer K, Cate ten JW, Sturk A, Borm JJJ, Treffers PE. Enhanced thrombin generation in normal and hypertensive pregnancy. *Am J Obstet Gynecol* 1989; 160:95.
- 222.- Condie RG, Ogston D. Sequential studies on components of the haemostatic mechanism in pregnancy with particular reference to the development of preeclampsia. *Br J Obstet Gynaecol* 1976; 83:938.
- 223.- Hathaway NE, Bonnar J. Hemostatic disorders of the pregnant woman and the newborn infant. New York: Elsevier, 1987:1.
- 224.- Feher J, Csomos G, Vereckei A. The chemistry of free radical reactions. In: Free radical reactions in medicine. Berlin: Springer-Verlag, 1987:2.
- 225.- Kloner RA, Pryklenk K, Whittaker P. Deleterious effects of oxygen radicals in ischemia/reperfusion, resolved and unresolved issues. *Circulation* 1989; 80:1115.
- 226.- Frank L, Massaro D. Oxygen toxicity. *Am J Med* 1980; 69:117.
- 227.- Klebanoff SJ. Phagocytic cells: products of oxygen metabolism. In: Gallin JI, Goldstein IM, Snydermann R, eds. Inflammation: basic principles and clinical correlates. New York: Raven Press, 1988:391.
- 228.- Uotila J, Tuimala R, Pyykko K. Erythrocyte glutathione peroxidase activity in hypertensive complications of pregnancy. *Gynecol Obstet Invest* 1990; 29:259.
- 229.- Gryglewski RJ, Palmer RMJ, Moncada S. Superoxide anion is involved in the breakdown of endothelium-derived vascular relaxing factor. *Nature* 1986; 320:454.
- 230.- Barrowcliffe TW, Gutteridge JMC, Dormancy TL. The effect of fatty-acid auto-oxidation products on blood coagulation. *Thromb Haemost* 1975; 33:271.
- 231.- Wickens D, Wilkins MH, Luneyc J, Ball G, Dormandy TL. Free radical oxidation (peroxidation) products in plasma in normal and abnormal pregnancy. *Ann Clin Biochem* 1981; 18:158.
- 232.- HubelCA, Roberts JM, Taylor RN, Musci TJ, Rodgers GM, McLaughlin MK. Lipid peroxidation in pregnancy: new perspectives on preeclampsia. *Am J Obstet Gynecol* 1989; 161:1025.
- 233.- Minakami H, Kimura K, Tamada T, Yasuda Y, Hirota N. Hepatocellular lipofuscin in preeclampsia. *Asia Oceania J Obstet Gynaecol* 1989; 15:277.
- 234.- Zeeman GG, Dekker GA. Pathogenesis of preeclampsia: A hypothesis. In: Pitkin RM, ed. *Clinical Obstetrics and Gynecology*. Maryland: Lippincott Co, 1992; 35(2):317.
- 235.- Maseki M, Nishigaki I, Hagihara M, Tomoda Y, Yagi K. Lipid peroxide levels and lipid content of serum lipoprotein fractions of pregnant subjects with or without preeclampsia. *Clin Chim Acta* 1981; 115:155.
- 236.- Erskine KJ, Iversen SA, Davies R. An altered ratio of 18:2(9,11) to 18:2(9,12) linoleic acid in plasma phospholipids as a possible predictor of preeclampsia. *Lancet* 1985; 1:554.
- 237.- Sane AS, Chokshi SA, Mishra VV, Barad DP, Shah VC, Nagpal S. Serum lipoperoxide levels in pregnancy-induced hypertension. *Panminerva Med* 1989; 31:119.

- 238.- Redman CWG. Platelets and the beginning of preeclampsia. *N Engl J Med* 1990; 323:478.
- 239.- Howie PW. The haemostatic mechanisms in pre-eclampsia. *Cli Obstet Gynecol*; 4(3):595-611.
- 240.- Redman CWG, Bonnar J, Beilin L. Early platelet consumption in pre-eclampsia. *Br Med J* 1978; 1:467-469.
- 241.- Beaufils M, Uzan S, Donsimoni R, Colau JC. Prevention of pre-eclampsia by early antiplatelet therapy. *Lancet* 1985; i:840-842.
- 242.- Wallenburg HCS, Dekker GA, Makovitz JW, Rotmans P. Low-dose aspirin prevents pregnancy-induced hypertension and pre-eclampsia in angiotensin-sensitive primigravidae. *Lancet* 1986;i:1-3.
- 243.- Schiff E, Peleg E, Goldenberg M *et al.* The use of aspirin to prevent pregnancy-induced hypertension and lower the ratio of thromboxane A₂ to prostacyclin in relative high risk pregnancies. *N Engl J Med* 1989; 321(6):351-356.
- 244.- Benigni A, Gregorini G, Frusca T *et al.* Effect of low dose aspirin on fetal and maternal generation of thromboxane by platelets in women at risk for pregnancy-induced hypertension. *N Engl J Med* 1989; 321(6):357-362.
- 245.- CLASP (Collaborative Low-dose Aspirine Study in Pregnancy) Collaborative Group. CLASP: A randomised trial of low-dose aspirin for the prevention and treatment of pre-eclampsia among 9364 women. *Lancet* 1994;343:619-929.
- 246.- Giles C. Intravascular coagulation in gestational hypertension and pre-eclampsia: the value of haemathological screening tests. *Clin Lab Haemat* 1982; 4:351-358.
- 247.- Giles C, Inglis TCM. Thrombocytopenia and macrothrombocytosis in gestational hypertension. *Br J Obstet Gynecol* 1981; 88:1115-1119.
- 248.- Fay RA, Bromham DR, Brooks JA, Gebiski VJ. Platelets and uric acid in the prediction of preeclampsia. *Am J Obstet Gynecol* 1985;1038-1039.
- 249.- Stubbs TM, Lazarchick J, Van Dorsten P, Cox J, Boyd, Loadholt C. Evidence of accelerated platelet production and consumption in nonthrombocytopenic preeclampsia. *Am J Obstet Gynecol* 1986; 155(2):263-265.
- 250.- Howie PW, Prentice CRM, McNicol GP. Coagulation, fibrinolysis and platelet function in pre-eclampsia, essential hypertension and placental insufficiency. *J Obstet Gynecol Brit Comm* 1971; 78:992-1003.
- 251.- Wallenburg HCS, Rotmans N. Enhanced reactivity of the platelet thromboxane pathway in normotensive and hypertensive pregnancies with insufficient fetal growth. *Am J Obstet Gynecol* 1982; 144(5):523-528.
- 252.- Redman CWG, Allington MJ, Bolton FG, Stirrat GM. Plasma β -thromboglobulin in pre-eclampsia. *Lancet* 1977; ii:248.
- 253.- Oian P, Lande K, Kjeldsen SE *et al.* Enhanced platelet release reaction related to arterial plasma adrenaline and blood pressure in pre-eclampsia. *Br J Obstet Gynecol* 1986; 93:548-553.

- 254.- Socol ML, Weiner CP, Louis G, Rhenberg K, Rossi EC. Platelet activation in preeclampsia. *Am J Obstet Gynecol* 1985; 151(4):494-497.
- 255.- Gilabert J, Estellés A, Aznar J, *et al.* Contribution of platelets to increased plasminogen activator inhibitor type I in severe preeclampsia. *Thromb Haemos* 1990; 63:361-366.
- 256.- Van Geet C, Spitz B, Vermeylen J, Van Assche FA. Urinary thromboxane metabolites in pre-eclampsia. *Lancet* 1990; 335i:1168-1169.
- 257.- Brash AR, Goodman RP, FitzGerald GA. Endogenous prostaglandin production in human pregnancy. In: Lewis PG, eds. *Prostacyclin in pregnancy*. New York: Raven Press 1983.
- 258.- Maki M. Coagulation, fibrinolysis, platelet and kinin-forming systems during toxemia in pregnancy. *Biol Res Preg* 1983; 4(4):152-154.
- 259.- Burgess-Wilson ME, Morrison R, Hepinstall S. Spontaneous platelet aggregation in heparinised blood during pregnancy. *Thromb Res* 1986; 37:385-393.
- 260.- Splawinska B, Skret A, Palczak R, Janeczko J, Furmaga W, Splawinski J. Whole blood platelet aggregation in normal pregnancy and pre-eclampsia. *Clin and Exper Hyper Hyper* 1987; B6 (2):311-319.
- 261.- Loudon KA, Broughton Pipkin F, Hepinstall S, Fox SC, Mitchell JRA, Symonds EM. Platelet reactivity and serum thromboxane B₂ production in whole blood in gestational hypertension and pre-eclampsia. *Br J Obstet Gynaecol* 1991;98:1239-1244.
- 262.- O'Brien JR. 'Exhausted' platelets continue to circulate. *Lancet* 1978;ii:1316-1317.
- 263.- Erne P, Mittelholzer E, Burgisser E, Fluckiger R, Buhler FR. Measurement of receptor induced changes in intracellular free calcium in human platelets. *J Receptor Res* 1984; 4:605-629.
- 264.- Baker PN, Broughton Pipkin F, Symonds EM. Platelet angiotensin II binding sites in hypertension in pregnancy. *Lancet* 1989; ii:1151.
- 265.- Born, GVR. Aggregation of blood platelets by adenosine-diphosphate and its reversal. *Nature* 194: 927-929, 1962.
- 266.- Tsien RY. New calcium indicators and buffers with high selectivity against magnesium and protons: design, synthesis and properties of prototype structures. *Biochemistry* 1980; 19:2396-2404.
- 267.- Gryniewicz G, Poenie M, Tsien RY. A new generation of Ca²⁺ indicators with greatly improved fluorescence properties. *J Biol Chem* 1985; 260:3440-3450.
- 268.- Mustard JF, Kinlough-Rathbone R, Packham MA. Isolation of human platelets from plasma by centrifugation and washing. *Methods Enzymol* 1989; 169:3-11.
- 269.- Baker VV, Bret Kort BS, Cefalo RC. Effects of plasma on the platelet antiaggregatory action of prostacyclin in pregnancy. *Am J Obstet Gynecol* 1987;156:974-977.
- 270.- Kitson GE, Broughton Pipkin F. Effects and interactions of prostaglandins E₁ and E₂ on human chorionic plate arteries. *Am J Obstet Gynecol* 1981;140:683.

- 271.- Miller OV, Johnson RA, Gorman RR. Inhibition of PGE₁-stimulated cAMP accumulation in human platelets by thromboxane A₂. *Prostaglandins* 1977;13:599-609.
- 272.- Van Overloop B, Gairard A, Beretz A, Cazenave JP, Treisser A, Renaud R. Élévation du calcium libre intraplaquettaire dans l'hypertension artérielle gravidique avant traitement. *La Press Med* 1989;18:1208.
- 273.- Van der Post JAM, Konijnenberg A, Boer K, *et al*. Preeclampsia is not associated with altered platelet vasopressin binding and cytosolic Ca²⁺ concentration. *Am J Obstet Gynecol* 1993;169:1169-78.
- 274.- Kilby MD, Broughton Pipkin F, Symonds EM. Changes in platelet intracellular free calcium in normal pregnancy. *Br J Obstet Gynecol* 1993;100:375-379.
- 275.- Kunz FK, Perchlaner C, Tabarelli M, Soelder E, Zwierzina WD. Influence of oral contraceptives on coagulation tests in native blood and plasma. *Am J Obstet Gynecol* 1990;163:417-420.
- 276.- Sadurska B, Tacconi MT, Di Minno G, *et al* Plasma and platelet lipid composition and platelet aggregation by arachidonic acid in women on the pill. *Thromb Haemostasis* 1981;45:150-153.
- 277.- McCarron DA. Is calcium more than sodium in the pathogenesis of essential hypertension? *Hypertension* 1987;7:607-627.
- 278.- Heagerty AM, Ollerenshaw JD. The phosphoinositide signalling system and hypertension. *J Hypertens* 1987;5:515-524.
- 279.- Bühler FR, Resnik TJ. Plateletmembrane and calcium control abnormalities in essential hypertension. *Am J Hypertens* 1988;1:42-46.
- 280.- Hallam TJ, Thompson NT, Scrutton MC, Rink TJ. The role of cytoplasmic free calcium in the response of quin2-loaded human platelets to vasopressin. *Biochem J* 1984;221:897-901.
- 281.- Haslam RJ, Rosson GM. Aggregation of human blood platelets by vasopressin. *Am J Physiol* 1972;223:958-969.
- 282.- Pollock WK, McIntyre DE. Desensitization and antagonism of vasopressin-induced phosphoinositide metabolism and elevation of cytosolic free calcium concentration in human platelets. *Biochem J* 1986;234:67-73.
- 283.- Siess W, Stifel M, Binder H, Weber PC. Activation of V₁-receptors by vasopressin stimulates inositol phospholipid hydrolysis and arachidonate metabolism in human platelets. *Biochem J* 1986;234:67-73.
- 284.- Dominiczak AF, Morton JJ, Murray G, Semple PF. Platelet cytosolic free calcium in essential hypertension: responses to vasopressin. *Clin Sci* 1989;77:183-188.
- 285.- Lechi A, Lechi C, Bonadonna G, *et al*. Increased basal and thrombin-induced free calcium in platelets of essential hypertensive patients. *Hypertension* 1987;9:230-235.
- 286.- Zemel MB, Zemel PC. Correction: platelet calcium metabolism in the prediction of preeclampsia. *N Engl J Med* 1992;326:647.

- 287.- Pitkin RM. Calcium metabolism in pregnancy and the perinatal period: a review. *Am J Obstet Gynecol* 1985;151:99.
- 288.- Seki K, Makimura N, Mitsui C, Hirata J, Nagata I. Calcium-regulating hormones and osteocalcin levels during pregnancy: A longitudinal study. *Am J Obstet Gynecol* 1991;164:1248-1252.
- 289.- Stuart MJ, Sunderjii SG, Yambo T, Clark DA, Allen JB, Elrad H, Slott JH. Decreased prostacyclin production: a characteristic of chronic placental insufficiency syndromes. *Lancet* 1981;2:1126.
- 290.- Downing I, Shepherd GL, Lewis PJ. Reduced prostacyclin production in preeclampsia. *Lancet* 1980;2:1374.
- 291.- Goodman PR, Killam AP, Brash AR, Branch RA. Prostacyclin production during pregnancy: Comparison of production during normal pregnancy and pregnancy complicated by hypertension. *Am J Obstet Gynecol* 1982;142:817-822.
- 292.- Koullapis EN, Nicolaides KH, Collins BP, Rodeck CH, Campbell S. Plasma prostanoids in pregnancy induced hypertension 1982;89:617-621.
- 293.- Lewis PJ, Shepherd GL, Ritter J, Chan SMT, Bolton PJ, Jogee M, Myatt L, Elder MG. Prostacyclin and pre-eclampsia. *Lancet* 1981;1:559.
- 294.- Romanini C, Tranquilli AL, Cester H, Valensise H, Cugini AM, Rabini RA, Mazzanti L. Modifications induced by gestational hypertension on platelet calcium transport. *Exp Mol Path* 1991;54:122-128.
- 295.- Mochizuki M, Morikawa Hajime, Yamasaki M, Maruo T. Vascular reactivity in normal and abnormal gestation. *Am J Kidn Dis* 1991;17:139-143.
- 296.- Erne P, Bolli P, Burgisser E, Bühler FR. Correlation of platelet calcium with blood pressure: Effect of antihypertensive therapy. *N Engl J Med* 1984;310:1084-1088.
- 297.- Bruschi G, Bruschi ME, Caroppo M, *et al.* Cytoplasmic free $[Ca^{2+}]$ is increased in the platelets of spontaneously hypertensive rats and essential hypertensive patients. *Clin Sci* 1985;68:68-74.
- 298.- Le Quang Sang KH, Devynck MA. Increased platelet cytosolic free calcium concentration in essential hypertension. *J Hypertens* 1986;4:567-574.
- 299.- Lindner A, Kenny M, Meacham AJ. Effects of a circulating factor in patients with essential hypertension on intracellular free calcium in normal platelets. *N Engl J Med* 1987;316:509-513.
- 300.- Hvarfner A, Larson R, Morlin C, Rastad J, Wide L, Akerstrom G, Ljunghall S. Cytosolic free calcium in platelets: Relationships to blood pressure and indices of systemic calcium metabolism. *J Hypertens* 1988;6:71-77.
- 301.- Brickman AS, Nyby MD, von Hungen K, Eggena P, Tuck ML. Calcitropic hormones, platelet calcium and blood pressure in essential hypertension. *Hypertension* 1990;16:515-522.
- 302.- Poch E, Botey A, Gaya J, Darnell A, Rivera F, Revert L. Intracellular calcium concentration and activation of the Na^+/H^+ exchanger in essential hypertension. *Kidn Int* 1994;45:1037-1043.

- 303.- Haller H, Lindschau C, Quass P, Distler A. Protein Phosphorylation and intracellular free calcium in platelets of patients with essential hypertension. *Am J Hypertens* 1992;5:117-124.
- 304.- Lenz T, Haller H, Ludersdorg M, Kribben A, Thiede M, Distler A, Philipp T. Free intracellular calcium in essential hypertension. Effects of nifedipine and captopril. *J Hypertens* 1985;3:S13-S15.
- 305.- Scherrer U, Torriani S, Nussberger J, Maridor G, Waeber B, Hofstetter JR, Brunner HR. Weight reduction in obese patients reduces free cytosolic calcium of platelets together with ambulatory blood pressure. *J Hypertens* 1987;5:S629.
- 306.- Kilby MD, Broughton Pipkin F, Symonds EM. Platelet cytosolic calcium in human pregnancy complicated by essential hypertension. *Am J Obstet Gynecol* 1993;169:141-143.
- 307.- Taylor MA, Ayers CR, Gear ARL. Platelet calcium and quenched-flow aggregation kinetics in essential hypertension. *Hypertension* 1989;13:558-566.
- 308.- Norris LA, Sheppard BL, Burke G, Bonnar J. Platelet activation in normotensive and hypertensive pregnancies complicated by intrauterine growth retardation. *Br J Obstet Gynaecol* 1994;101:209-214.
- 309.- Wallenburg HCS, Van Kessel PH. Platelet lifespan in pregnancies resulting in small for gestational age infants. *Am J Obstet Gynecol* 1979;85:33-56.
- 310.- Stander HJ, Duncan EE, Sisson WE. Chemical studies in toxemias of pregnancy. *Bull Johns Hopkins Hosp* 1925;36:411-427.
- 311.- Frenkel Y, Barkai G, Mashiach S, Dolev E, Zimlichman R, Weiss M. Hypocalciuria of preeclampsia is independent of parathyroid hormone level. *Obstet Gynecol* 1991;77:689.
- 312.- Lancet M, Fisher IL. The value of blood uric acid levels in toxemia of pregnancy. *J Obstet Gynaecol Br Emp* 1956;63:116-113.
- 313.- Liedholm H, Montan S, Aberg A. Risk grouping of 113 patients with hypertensive disorders during pregnancy with respect to serum urate, proteinuria and time of onset of hypertension. *Acta Obstet Gynecol Scand* 1984;118(suppl):43-48.
- 314.- Redman CWG, Beilin LJ, Bonnar J, *et al.* Plasma-urate measurements in predicting fetal death in hypertensive pregnancy. *Lancet* 1976; i:1370-1373.
- 315.- Schuster E, Wepelmann B. Plasma urate measurements and fetal outcome in preeclampsia. *Gynecol Obstet Invest* 1981;12:162-167.
- 316.- Sibai BM, Anderson GD, McCubbin JH. Eclampsia. II. Clinical significance of laboratory findings. *Obstet Gynecol* 1982;59:153-157.
- 317.- Gallery EDM, Saunders DM, Boyce ES, Györy AZ. relation between plasma volume and uric acid in the development of hypertension in pregnancy. In: Bonnar J, McGillivray I, Symonds EM, eds. *Pregnancy hypertension*. Lancaster, England:MTP Press, 1980:175-179.
- 318.- Redman CWG, Williams GF, Jones DD, Wilkinson RH. Plasma urate and serum deoxycytidylate deaminase measurements for the early diagnosis of preeclampsia. *Br J Obstet Gynaecol* 1977;84:904-908.

- 319.- Riedel H, Bahlmann J, Eisenbach GM. Results of a prospective study of toxemia in pregnancy. *Contrib Nephrol* 1981;25:137-144.
- 320.- Bonnar J. Haemostasis and coagulation disorders in pregnancy. In: Bloom AL, Thomas DP, eds. *Haemostasis and thrombosis*. Edinburgh: Churchill Livingstone 1981:454-471.
- 321.- O'Rourke FA, Halenda SP, Zavoico GB, Feinstein MB. Inositol 1,4,5-triphosphate releases Ca^{2+} from Ca^{2+} -transporting membrane vesicle fraction derived from human platelets. *J Biol Chem* 1985;260:956-962.
- 322.- Rink TJ, Hallman T. What runs platelets on? *Trends in Biochem Sci* 1984;9:215-219.
- 323.- Kuriyama H, Ito Y, Suzuki H, Kitamura K, Itoh T. Factors modifying contraction-relaxation cycle in vascular smooth muscle. *Am J Physiol* 1982;243:H641-H662.
- 324.- Robinson BF, Dobbs RJ, Kelsey CR. The effects of nifedipine on the resistance vessels, arteries and veins in man. *Br J Clin Pharmacol* 1980;10:433-438.
- 325.- Everett RB, Worley RJ, MacDonald PC, Gant NF. Oral administration of theophylline to modify pressor responsiveness to angiotensin II in women with pregnancy-induced hypertension. *Am J Obstet Gynecol* 1978;132:359-362.
- 326.- Rittenhouse SE. Synergistic activation by collagen and PGH_2 of phospho-inositide metabolism and arachidonate in human platelets. *J Clin Invest* 1982;70:1216-1224.
- 327.- Kikkawa U, *et al.* The role of protein Kinase C in calcium mediated signal transduction. In: Baker PJ, ed. *Calcium and the Cell*. Chichester UK: John Wiley:197-211.
- 328.- Kobayashi I, Fujita T, Yamazaki H. Platelet aggregability measured by screen filtration pressure method in cerebrovascular diseases. *Stroke* 1976;7:406-409.
- 329.- Poplawski A, Skorulska M, Niewiarowski S. Increased platelet adhesiveness in hypertensive cardiovascular disease. *J Atheroscler Res* 1968;8:721-723.
- 330.- Metha J, Metha P. Platelet function in hypertension and effect of therapy. *Am J Cardiol* 1981;47:331-334.
- 331.- Valachakis ND, Aledort L. Hypertension and propranolol therapy: effect on blood pressure, plasma catecholamines and platelet aggregation. *Am J Cardiol* 1980;45:321-325.
- 332.- Holme S, Sixma JJ, Wester J, Holmsen H. ADP-induced refractory state of platelets *in vitro*. Functional and ultra studies on gel-filtered platelets. *Scand J Haematol* 1977;18:267-278.
- 333.- Haver VM, Gear ARL. Functional fractionation of platelets. *J Lab Clin Med* 1981;97:187-204.
- 334.- Carty DJ, Gear ARL. Fractionation of platelets according to size: Functional and biochemical characteristics. *Am J Hematol* 1986;21:1-14.
- 335.- Loudon KA. Studies of platelet reactivity and thromboxane production in pregnancy and preeclampsia. The effect of low dose aspirin. DM Thesis. Nottingham: University of Nottingham 1988.

- 336.- Lucas IU, Skrinska UA, Chisolm GM, Hesse BL. Stability of prostaglandin in human and rabbit whole blood and plasma. *Thromb Haemost* 43, 379-387.
- 337.- Norris LA, Gleeson N, Sheppard BL, Bonnar J. Whole blood platelet aggregation in moderate and severe pre-eclampsia. *Br J Obstet Gynaecol* 1993;100:684-688.
- 338.- Greer IA, Calder AA, Walker JJ, Lunan CB, Tulloch I. Increased platelet reactivity in pregnancy-induced hypertension and uncomplicated diabetic pregnancy: an indication for antiplatelet therapy? *Br J Obstet Gynaecol* 1988;95:1204-1208.
- 339.- Ahmed Y, Sullivan MHF, Elder MG. Detection of platelet desensitization in pregnancy-induced hypertension is dependent on the agonist used. *Thromb Haemostasis* 1991;65:474-477.
- 340.- Sowers JR, Standley PR, Jacober S, Niyogi T, Simpson L. Postpartum abnormalities of carbohydrate and cellular calcium metabolism in pregnancy induced hypertension. *Am J Hypertens* 1993;6:302-307.
- 341.- Standley PR, Gangusani S, Prakash R, Sowers JR. Human platelet calcium measurements; methodological considerations and comparisons with calcium mobilization in vascular smooth muscle cells. *Am J Hypertens* 1991;4:546-549.
- 342.- Poch E, Botey A, Gaya J, Cases A, Rivera F, Revert F. Intracellular calcium mobilization and activation of the Na⁺/H⁺ exchanger in platelets. *Biochem J* 1993;290:617-622.
- 343.- Nakamura M, Suzuki H, Yamakawa, Saruta T. Role of platelet cytosolic calcium in regulation of blood pressure in patients of chronic hemodialysis. *Nephron* 1992;61:435-441.
- 344.- Rao GHR. Measurement of ionized calcium in normal human blood platelets. *Anal Biochem* 1988;169:400-404.
- 345.- Dekker GA, Makovitz JW, Wallenburg HCS. Comparison of prediction of pregnancy-induced hypertensive disease by angiotensin II sensitivity and supine pressor test. *Br J Obstet Gynaecol* 1990;97:817-821.
- 346.- Degani S, Abinader E, Eibschitz I, Oettinger M, Shapiro I, Sharf M. Isometric exercise test for predicting gestational hypertension. *Obstet Gynecol* 1985;65:652-4.
- 347.- Villar MA, Sibai BM. Clinical significance of elevated mean arterial pressure in second trimester and threshold increase in systolic or diastolic blood pressure during the third trimester. *Am J Obstet Gynecol* 1989;160:419-23.
- 348.- Moutquin JM, Rainville C, Giroux L, Raynaud P, Amyot G, Bilodeau R, Pelland N. A prospective study of blood pressure in pregnancy: prediction of preeclampsia. *Am J Obstet Gynecol* 1985;151:191-6.
- 349.- Gant NF, Chand S, Worley RJ, Whalley PJ, Crosby UD, McDonald PC. A clinical test useful for predicting the development of acute hypertension in pregnancy. *Am J Obstet Gynecol* 1974;120:1-6.
- 350.- Marya RK, Rathee S, Mittal R. Evaluation of three clinical tests for predicting pregnancy-induced hypertension. *Am J Obstet Gynecol* 1988;158:683-684.

- 351.- Baker PN, Broughton Pipkin F, Symonds EM. Platelet angiotensin II binding sites in hypertension of pregnancy. *Lancet* 1991;ii:1151.
- 352.- Campbell S, Pearce JMF, Hackett G, Cohen-Overbeek T, Hernandez C. Qualitative assessment of uteroplacental blood flow: early screening test for high-risk pregnancies. *Obstet Gynecol* 1986;668:649-653.
- 353.- Arduini D, Rizzo G, Romanini C, Mancuso S. Uteroplacental blood flow velocity waveforms as predictors of pregnancy-induced hypertension. *Eur J Obstet Gynecol Reprod Biol* 1987;26:335-341.
- 354.- López-Espinoza I, Dhar H, Humpreys S, Redman CWG. Urinary albumin excretion in pregnancy. *BR J Obstet Gynaecol* 1986;93:176-181.

LLISTA DE FIGURES

REVISIÓ BIBLIOGRÀFICA

Figura 1. Estructura de la paret vascular	17
Figura 2. Estructura plaquetària per microscòpia electrònica	21
Figura 3. Fisiologia plaquetària	26
Figura 4. Agregació plaquetària	28
Figura 5. Mecanismes d'actuació de l'AMPc	34
Figura 6. Metabolisme de l'àcid araquidònic	36
Figura 7. Contracció plaquetària	40
Figura 8. Regulació de la concentració de calci intraplaquetari	45

MATERIAL i MÈTODES

Figura 1. Exemple d'agregació plaquetària induïda per àcid araquidònic	113
Figura 2. Calci intraplaquetari posttrombina	119
Figura 3. Calci plaquetari postvasopressina	119

RESULTATS i DISCUSSIÓ

Figura 1.2.2.1 Recompte plaquetari. Gestació normal.	136
Figura 1.2.2.2 Volum plaquetari. Gestació normal.	137
Figura 1.2.2.3 Distribució plaquetària. Gestació normal.	138
Figura 1.2.2.4 Recompte plaquetari. Primer trimestre.	140
Figura 1.2.2.5 Recompte plaquetari. Segon trimestre.	140
Figura 1.2.2.6 Recompte plaquetari. Tercer trimestre.	143
Figura 1.2.2.7 Recompte plaquetari. Postpart.	143
Figura 1.2.2.8 Volum plaquetari. Primer trimestre.	146
Figura 1.2.2.9 Volum plaquetari. Segon trimestre.	146
Figura 1.2.2.10 Volum plaquetari. Tercer trimestre.	149

Figura 1.2.2.11 Volum plaquetari. Postpart.	149
Figura 1.2.2.12 Distribució plaquetària. Primer trimestre.	152
Figura 1.2.2.13 Distribució plaquetària. Segon trimestre.	152
Figura 1.2.2.14 Distribució plaquetària. Tercer trimestre.	155
Figura 1.2.2.15 Distribució plaquetària. Postpart.	155
Figura 1.2.3.1 Calci sèric. Gestació normal.	163
Figura 1.2.3.2 Àcid úric. Gestació normal.	164
Figura 1.2.3.3 Proteïnes totals. Gestació normal.	165
Figura 1.2.3.4 Albúmina sèrica. Gestació normal.	166
Figura 1.2.3.5 Calci sèric. Primer trimestre.	168
Figura 1.2.3.6 Calci sèric. Segon trimestre.	168
Figura 1.2.3.7 Calci sèric. Tercer trimestre.	171
Figura 1.2.3.8 Calci sèric. Postpart.	171
Figura 1.2.3.9 Àcid úric. Primer trimestre.	174
Figura 1.2.3.10 Àcid úric. Segon trimestre.	174
Figura 1.2.3.11 Àcid úric. Tercer trimestre.	177
Figura 1.2.3.12 Àcid úric. Postpart.	177
Figura 1.2.3.13 Proteïnes totals. Primer trimestre.	180
Figura 1.2.3.14 Proteïnes totals. Segon trimestre.	180
Figura 1.2.3.15 Proteïnes totals. Tercer trimestre.	183
Figura 1.2.3.16 Proteïnes totals. Postpart.	183
Figura 1.2.3.17 Albúmina sèrica. Primer trimestre.	186
Figura 1.2.3.18 Albúmina sèrica. Segon trimestre.	186
Figura 1.2.3.19 Albúmina sèrica. Tercer trimestre.	189
Figura 1.2.3.20 Albúmina sèrica. Postpart.	189
Figura 2.1 Test de sensibilitat a la PGE1. Gestació normal	196
Figura 2.2 Calci intracel·lular basal. Gestació normal.	203
Figura 2.3 Calci intracel·lular posttrombina. Gestació normal.	210
Figura 2.4 Calci intracel·lular postvasopressina. Gestació normal.	216
Figura 3.1.1 Test de sensibilitat a la PGE1. Primer trimestre.	223
Figura 3.1.2 Test de sensibilitat a la PGE1. Segon trimestre.	223
Figura 3.1.3 Test de sensibilitat a la PGE1. Tercer trimestre.	225
Figura 3.1.4 Test de sensibilitat a la PGE1. Postpart.	225
Figura 3.2.1 Calci basal. Primer trimestre.	233

Figura 3.2.2 Calci basal. Segon trimestre.	233
Figura 3.2.3 Calci basal. Tercer trimestre.	236
Figura 3.2.4 Calci basal. Postpart.	236
Figura 3.3.1 Calci posttrombina. Primer trimestre.	243
Figura 3.3.2 Calci posttrombina. Segon trimestre.	243
Figura 3.3.3 Calci posttrombina. Tercer trimestre.	246
Figura 3.3.4 Calci posttrombina. Postpart.	246
Figura 3.4.1 Calci postvasopressina. Primer trimestre.	253
Figura 3.4.2 Calci postvasopressina. Segon trimestre.	253
Figura 3.4.3 Calci postvasopressina. Tercer trimestre.	256
Figura 3.4.4 Calci postvasopressina. Postpart.	256

LLISTA DE TAULES

REVISIÓ BIBLIOGRÀFICA

Taula 1. Molècules sintetitzades per l'endoteli	18
Taula 2. Contingut dels grànuls plaquetaris	23

RESULTATS i DISCUSSIÓ

Taula 1.1.1 Descripció de la població en estudi (I)	127
Taula 1.1.2 Descripció de la població en estudi (II)	128
Taula 1.1.3 Característiques de la població	128
Taula 1.1.4 Edat gestacional de les determinacions	129
Taula 1.1.5 Part (I)	129
Taula 1.1.6 Part (II)	130
Taula 1.1.7 Resultats perinatals	131
Taula 1.2.1 Tensió arterial al primer i segon trimestres.	133
Taula 1.2.2 Tensió arterial al tercer trimestre i postpart	134
Taula 1.2.2.1 Anàlisi estadística recompte plaquetari. Gestació normal.	136
Taula 1.2.2.2 Anàlisi estadística volum plaquetari. Gestació normal.	137
Taula 1.2.2.3 Anàlisi estadística volum plaquetari. Gestació normal.	138
Taula 1.2.2.4 Descripció dels paràmetres hematològics	139
Taula 1.2.2.5 Anàlisi estadística recompte plaquetari. Primer i segon trimestres.	141
Taula 1.2.2.6 Descripció variable recompte plaquetari. Primer i segon trimestres.	142
Taula 1.2.2.7 Anàlisi estadística recompte plaquetari. Tercer trimestre i postpart.	144
Taula 1.2.2.8 Descripció de la variable recompte plaquetari. Tercer trimestre i postpart.	145
Taula 1.2.2.9 Anàlisi estadística volum plaquetari. Primer i segon trimestres.	147
Taula 1.2.2.10 Descripció variable volum plaquetari. Primer i segon trimestres.	148
Taula 1.2.2.11 Anàlisi estadística volum plaquetari. Tercer trimestre i postpart.	150

Taula 1.2.2.12	Descripció variable volum plaquetari. Tercer trimestre i postpart. . .	151
Taula 1.2.2.13	Anàlisi estadística distribució plaquetària. Primer i segon trimestres.	153
Taula 1.2.2.14	Descripció variable distribució plaquetària. Primer i segon trimestres.	154
Taula 1.2.2.15	Anàlisi estadística distribució plaquetària. Tercer trimestre i postpart.	156
Taula 1.2.2.16	Descripció variable distribució plaquetària. Tercer trimestre i postpart.	157
Taula 1.2.3.1	Anàlisi estadística calci sèric. Gestació normal.	163
Taula 1.2.3.2	Anàlisi estadística àcid úric. Gestació normal.	164
Taula 1.2.3.3	Anàlisi estadística proteïnes totals. Gestació normal.	165
Taula 1.2.3.4	Anàlisi estadística albúmina sèrica. Gestació normal.	166
Taula 1.2.3.5	Descripció dels paràmetres bioquímics. Gestació normal.	167
Taula 1.2.3.6	Anàlisi estadística calci sèric. Primer i segon trimestres.	169
Taula 1.2.3.7	Descripció variable calci sèric. Primer i segon trimestres.	170
Taula 1.2.3.8	Anàlisi estadística calci sèric. Tercer trimestre i postpart.	172
Taula 1.2.3.9	Descripció variable calci sèric. Tercer trimestre i postpart.	173
Taula 1.2.3.10	Anàlisi estadística àcid úric. Primer i segon trimestres.	175
Taula 1.2.3.11	Descripció variable àcid úric. Primer i segon trimestres.	176
Taula 1.2.3.12	Anàlisi estadística àcid úric. Tercer trimestre i postpart.	178
Taula 1.2.3.13	Descripció variable àcid úric. Tercer trimestre i postpart.	179
Taula 1.2.3.14	Anàlisi estadística proteïnes totals. Primer i segon trimestres.	181
Taula 1.2.3.15	Descripció variables proteïnes totals. Primer i segon trimestres.	182
Taula 1.2.3.16	Anàlisi estadística proteïnes totals. Tercer trimestre i postpart.	184
Taula 1.2.3.17	Descripció variable proteïnes totals. Tercer trimestre i postpart.	185
Taula 1.2.3.18	Anàlisi estadística albúmina sèrica. Primer i segon trimestres.	187
Taula 1.2.3.19	Descripció variable albúmina sèrica.	188
Taula 1.2.3.20	Anàlisi estadística albúmina sèrica. Tercer trimestre i postpart.	190
Taula 1.2.3.21	Descripció variable albúmina sèrica. Tercer trimestre i postpart.	191
Taula 2.1.1	Anàlisi estadística Test de sensibilitat a la PGE ₁ . Gestació normal . . .	197
Taula 2.1.2	Descripció de la variable PGE ₁	198
Taula 2.2.1	Anàlisi estadística calci intracel·lular basal (CAB). Gestació normal.	204

Taula 2.2.2 Descripció de la variable CAB	205
Taula 2.3.1 Anàlisi estadística calci intracel·lular postestimulació amb trombina (CAT). Gestació normal.	211
Taula 2.3.2 Descripció de la variable CAT	212
Taula 2.4.1 Anàlisi estadística calci intracel·lular postestimulació amb vasopressina. Gestació normal.	217
Taula 2.4.2 Descripció de la variable CAV	218
Taula 3.1.1 Anàlisi estadística Test de sensibilitat a la PGE1. Primer i segon trimestres.	224
Taula 3.1.2 Anàlisi estadística Test de sensibilitat a la PGE1. Tercer trimestre i postpart.	226
Taula 3.1.3 Descripció variable PGE1	227
Taula 3.2.1 Anàlisi estadística calci basal. Primer i segon trimestres.	234
Taula 3.2.2 Descripció variable CAB. Primer i segon trimestres.	235
Taula 3.2.3 Anàlisi estadística calci basal. Tercer trimestre i postpart.	237
Taula 3.2.4 Descripció variable calci basal. Tercer trimestre i postpart.	238
Taula 3.3.1 Anàlisi estadística calci posttrombina. Primer i segon trimestres.	244
Taula 3.3.2 Descripció variable calci posttrombina. Primer i segon trimestres. ...	245
Taula 3.3.3 Anàlisi estadística calci posttrombina. Tercer trimestre i postpart.	247
Taula 3.3.4 Descripció variable calci posttrombina. Tercer trimestre i postpart. ...	248
Taula 3.4.1 Anàlisi estadística calc postvasopressina. Primer i segon trimestres. ...	254
Taula 3.4.2 Descripció variable calci postvasopressina. Primer i segon trimestres.	255
Taula 3.4.3 Anàlisi estadística calci postvasopressina. Tercer trimestre i postpart. ...	257
Taula 3.4.4 Descripció variable calci postvasopressina. Tercer trimestre i postpart.	258

ABREVIATURES

AA	àcid araquidònic.
AB	albúmina sèrica.
ADP	difosfat d'adenosina.
AINE	antiinflamatori no esteroïdal.
ATP	trifosfat d'adenosina.
AVP	vasopressina.
[Ca²⁺]_i	concentració de calci intraplaquetari.
CA	calci sèric.
CAB	calci intracel·lular basal.
CAT	calci intracel·lular posttrombina.
CAV	calci intracel·lular postvasopressina.
DAG	diacilglicerol.
EDCF	factor constrictor derivat de l'endoteli.
EDRF	factor relaxant derivat de l'endoteli.
FP4	factor plaquetari 4.
FvW	factor von Willebrand.
GPIb	glicoproteïna Ib
GPIIb-IIIa	glicoproteïna IIb-IIIa
GTP	guanosina trifosfat.
HTA	hipertensió arterial.
IP3	inositol trifosfat.
PAF	factor activador de les plaquetes.
PD	distribució plaquetària.
PG	prostaglandina.
PGI₂	prostaciclina.
PKC	proteïnaquinasa C.
PL	recompte plaquetari.
PLA₂	fosfolipasa A ₂ .
PLC	fosfolipasa C.

PR	proteïnes totals sèriques.
PRP	plasma ric en plaquetes.
RAAS	sistema renina-angiotensina-aldosterona.
SCO	sistema canalicular obert.
STD	sistema tubular dens.
TD	tensió arterial diastòlica.
THE	trastorns hipertensius de l'embaràs.
TS	tensió arterial diastòlica.
TSI	inhibidors de la tromboxàsintetasa.
TXA₂	tromboxà A ₂ .
TXB₂	tromboxà B ₂
UR	àcid úric.
VP	volum plaquetari.
X±IC	mitjana ± interval de confiança del 95%
X±SD	mitjana ± desviació estàndard

CLÍNIC
BARCELONA

Hospital Universitari

Obstetricia
Ginecología I



UNIVERSITAT DE BARCELONA



Centre de Recursos per a l'Aprenentatge
i la Investigació

Biblioteca de Medicina

(043)95

PAL

0701332597

