

Literaturverzeichnis

1. Palitzsch K-D, Enger I, Nusser J, Zietz B, Arndt H, Cuk A et al. (1997): Diabetmobilgruppe, J. Schölmerich. Klinik und Poliklinik für Innere Medizin 1, Universität Regensburg: Über 6% einer bevölkerungsrepräsentativen Stichprobe Deutschlands hat Diabetes mellitus. Med. Klein. 92(103. Kongress der Deutschen Gesellschaft für Innere Medizin):123(P160), suppl .II
2. Huse, D.M., Oster, G., Killen, A.R., Lacey, M.J., Colditz, G.A.: The economic costs of non-insulin-dependent diabetes mellitus. JAMA 262(1989) 2708-2713.
3. Michaelis D, Jutzi E.: Epidemiologie des Diabetes mellitus in der Bevölkerung der ehemaligen DDR: Alters- und geschlechtsspezifische Inzidenz und Prävalenzrends im Zeitraum 1960-1987. Z. klin. Med. 46(1991):59-64.
4. King H, Rewers M. WHO Ad Hoc Diabetes Reporting Group: Global estimates for prevalence of diabetes mellitus and impaired glucose tolerance in adults. Diabetes Care 16(1993):157-177.
5. Andersson DKG, Svärdsudd K, Tibblin G. Prevalence and incidence of diabetes in a Swedish community 1972-1987. Diabet Med 8(1991):428-434.
6. Tuolimeneto J, Nissinen A, Kivilä S-L, Pekkanen J, Kaarsalo E, Wolf E, Aro A, Punsar S.: Prevalence of diabetes mellitus in elderly men aged 65 to 84 years in eastern and western Finland. Diabetologia 29(1986):611-615.
7. Ohlson L-O, Larsson B, Eriksson H, Svärdsudd K, Welin L, Tibblin G.: Diabetes mellitus in Swedish middle-aged men: the study of men born in 1913 and 1923. Diabetologia 30(1987):386-393.
8. Ohlson L-O, Larsson B, Svärdsudd K, et al. The influence of body fat distribution on the incidence of diabetes mellitus. Diabetes 34(1985):1055-58.
9. Gnanalingham MG, Manns JJ. Patient awareness of genetic and environmental risk factors in non-insulin-dependent diabetes mellitus-relevance to first-degree relatives. Diabet. Med 14(1997):660-662.
10. Barnett AH, Eff C, Leslie RDG, Pyke DA .: Diabetes in identical twins: a study of 200 pairs. Diabetologia 20(1981):87-93.
11. Newman B, Selby JV, King MC, Slemenda C, Fabsitz R, Friedman GD: Concordance for type 2 (non-insulin-dependent) diabetes mellitus in male twins. Diabetologia 30(1987):763-768.
12. Granner DK, O'Brien RM. Molecular physiology and genetics of NIDDM. Importance of metabolic staging. Diabetes Care 15(1992):369-395.
13. Turner RC, Hattersley AT, Shaw JT, Levy JC. Type II diabetes: clinical aspects of molecular biological studies. Diabetes 44(1995)1-10.
14. De Fronzo RA. The triumvirate: beta-cell, muscle, liver. A collusion responsible for NIDDM. Diabetes 37(1988):667-687.
15. Ward WK, Beard JC, Porte D. Clinical aspects of islet B-cell function in non-insulin-dependent diabetes mellitus. Diabetes Metabolism Rev 2(1986):297-313.
16. Porte D. Beta-cell in type II diabetes mellitus. Diabetes 40(1991):166-80.
17. Weir G. Non-insulin-dependent diabetes mellitus: interplay between beta-cell inadequacy and insulin resistance. Am J Med 73(1982):461-464.

18. Reaven GM. Role of insulin resistance in human diseases. *Diabetes* 37(1988):1595-160.
19. Zimmet P, Whitehouse S: Bimodality of fasting and two-hour glucose tolerance distributions in Micronesian population. *Diabetes* 27(1978):793-800.
20. Eriksson J, Fransilla-Kallunki A, Ekstrand A, Saloranta C, Widen E, Schalin C, Groop L: Early metabolic defects in persons at increased risk for non-insulin-dependent diabetes mellitus. *N Engl J Med* 321(1989):337-343.
21. O'Rahilly SP, Nugent Z, Rudenski AS, Hosker JP, Burnett MA, Darling P, Turner RC: Beta-cell dysfunction, rather than insulin insensitivity is the primary defect in familial type 2 diabetes. *Lancet* (1986):360-363.
22. Weyer C, Bogardus C, Mott DM, Pratley RE: The natural history of insulin secretory dysfunction and insulin resistance in the pathogenesis of type 2 diabetes mellitus. *J Clin Invest* 1999;104: 787-794.
23. Haffner SM, Stern MP, Hazuda HP, Pugh JA, Patterson JK: Hyperinsulinaemia in a population at high risk for non-insulin-dependent diabetes mellitus. *N Engl J Med* 315 (1986):220-224.
24. Lilloija S, Mott DM, Howard B, Bennett PH, Yki-Yärvinen H, Freymond D, Nyomba BL, Zurlo F, Swinburn B, Bogardus C: Impaired glucose tolerance as a disorder of insulin action: longitudinal and cross-sectional studies in Pima Indians. *N Engl J Med* 321(1988):337-343.
25. Lehtovirta M, Kaprio J, Forsblom C, Eriksson J, Tuomilehto J, Groop L. Insulin sensitivity and insulin secretion in monozygotic and dizygotic twins. *Diabetologia* 43 (2000):285-293.
26. Pimenta W, Korytkowski M, Mitrakou A et al. Pancreatic beta-cell dysfunction as the primary genetic lesion in NIDDM. *JAMA* 273(1995):1855-1861.
27. Van Haeften TW, Dubbeldam S, Zonderland ML, Erkelens DW. Insulin secretion in normal glucose-tolerant relatives of type 2 diabetic subjects. Assessments using hyperglycemic glucose clamp and oral glucose tolerance tests. *Diabetes Care* 21(1998):278-282.
28. Yalow RS, Berson SA.: Plasma insulin concentrations in nondiabetic and early diabetic subjects. *Diabetes* 9(1960): 254.
29. Cerasi E, Luft R.: The plasma insulin response to glucose infusion in healthy subjects and in diabetes mellitus. *Acta Endocrinol* 55(1967):278-304.
30. Brunzell JD, Robertson RP, Lerner RL, Hazzard WR, Ensinek JW, Bierman EL, Porte D Jr.: Relationships between fasting plasma glucose levels and insulin secretion during intravenous glucose tolerance test. *J Clin Endocrinol Metab* 42(1976):222-229.
31. Luzi L, DeFronzo RA.: Effect of loss of first-phase insulin secretion on hepatic glucose production and tissue glucose disposal in humans. *Am J Physiol* 257(1989):E241-E246.
32. Castillo C, Bogardus C, Bergman R, Thuillez P, Lilloija S.: Interstitial insulin concentrations determine glucose uptake rates but not insulin resistance in lean and obese men. *J Clin Invest* 83(1994):10-16.
33. Getty L, Hamilton-Wessler M, Adler M, Dea MK, Bergman RN.: Biphasic insulin secretion during intravenous glucose tolerance test promotes optimal interstitial insulin profile. *Diabetes* 47(1999):1941-1947.
34. Rebrin K, Steil GM, Mittelman SD, Bergmann RN.: Causal linkage between insulin suppression of lipolysis and suppression of liver glucose output in dogs. *J Clin Invest* 98(1996): 741-749.
35. Yki-Järvinen H. Glucose toxicity. *Endocr Rev* 13(1992):415-431.

36. Pimenta W.: Insulin secretion and insulin deficiency in people with impaired glucose tolerance. *Diabet Med* 13(1996):S33-S36.
37. Matsumoto K, Miyake S, Yano M.: Glucose tolerance, insulin secretion, and insulin sensitivity in non obese and obese Japanese subjects. *Diabetes Care* 20(1997):1562-1568.
38. Reaven GM, Hollenbeck CB, Chen YDI. Relationship between glucose tolerance, insulin secretion, and insulin resistance in non-obese individuals with varying degrees of glucose tolerance. *Diabetologia* 32(1989): 53-55.
39. Ryan EA, Imes S, Liu D, McManus R, Finegood DT, Plonsky KS, Sturis J.: Defects in insulin secretion and action in women with a history of gestational diabetes. *Diabetes* 44(1995): 506-512.
40. Ward W, Johnston C, Beard J, Benedetti T, Halter J, Porte D.: Insulin resistance and impaired insulin secretion in subjects with histories of gestational diabetes mellitus. *Diabetes* 34(1985):861-869.
41. Köbberling J, Tillil H, Lorenz H-J: Genetics of type 2 A- and type 2 B-diabetes mellitus (Abstract). *Diabetes Res Clin Pract* 1 (Suppl. 1) (1985):311.
42. Rojas L, Soeldner JS, Gleason RE, Kahn CB, Marble A.: Offspring of two diabetic parents: differential serum insulin response to intravenous glucose and tolbutamide. *J Clin Endocrinol Metab* 29(1969): 1569-1579.
43. Vauhkonen I, Niskanen L, Vanninen E, Kainulainen S, Uusitupa M, Laakso M.: Defects in insulin secretion and insulin action in non-insulin-dependent diabetes mellitus are inherited: metabolic studies of offspring of diabetic probands. *J Clin Invest* 101(1998): 86-96.
44. Roder M, Eriksson J, Hartling S, Groop L, Binder C. Proportional proinsulin response in first-degree relatives of patients with type 2 diabetes. *Acta Diabetol* 30(1993):132-137.
45. Johnston C, Ward K, Beard C, McKnight B, Porte D.: Islet function and insulin sensitivity in the nondiabetic offspring of conjugal type II diabetic patients. *Diabetic Med* 7(1990):119-125.
46. Gulli G, Ferranini E, Stern M, Haffner S, DeFronzoR.: The metabolic profile of NIDDM is fully established in glucose-tolerant offspring of two Mexican-American NIDDM parents. *Diabetes* 41(1992):1575-1586.
47. Osei K, Cottrell D, Orabella M. Insulin sensitivity, glucose effectiveness, and body fat distribution pattern in nondiabetic offspring of patients with NIDDM. *Diabetes Care* 14(1991): 890-896.
48. Lillioja S, Mott DM, Spraul M, Ferraro R, Foley JE, Ravussin E, Knowler WC, Bennett PH, Bogardus C.: Insulin resistance and insulin secretory dysfunction as precursors of non-insulin-dependent diabetes mellitus. *N Engl J Med* 329(1993): 1988-1992.
49. Haffner SM, Miettinen H, Gaskill SP, Stern MP.: Decreased insulin secretion and increased insulin resistance are independently related to the 7-year risk of NIDDM in Mexican - Americans. *Diabetes* 44(1995): 1386-1391.
50. Chiu KC, Lee NP, Cohan P, Chuang L-M. B-cell function declines with age in glucose tolerant Caucasians. *Clin Endocrinol* 53 (2000):569-575.
51. Bergman RN.: Lilly lecture 1989. Toward physiological understanding of glucose tolerance. Minimal-model approach. *Diabetes* 38 (1989) 1512-1518.

52. Coates PA, Luzio SD, Brunel P.: Comparison of estimates of insulin sensitivity from minimal model analyses of the insulin-modified frequently sampled intravenous glucose tolerance test and the isoglycemic hyperinsulinemic clamp in subjects with NIDDM. *Diabetes* 44(1995) 631-637.
53. Faber OK, Binder C.: C-Peptide response to glucagon: a test for the residual beta-cell function in diabetes mellitus. *Diabetes* 26(1977):605-610.
54. Gjessing HJ, Reinholdt B, Pedersen O. The plasma C-Peptide and insulin responses to stimulation with intravenous glucagon and a mixed meal in well-controlled type 2 (non-insulin-dependent) diabetes mellitus: dependency on acutely established hyperglycemia. *Diabetologia* 32(1989): 858-863.
55. WHO: Diabetes mellitus. Report of a WHO study group. *Tech Rep Ser* 17(1985):45-51.
56. Stumvoll M, Mitrakou A, Pimenta W, Jenssen T, Yki-Jarvinen H, Van Haefen T, Renn W, Gerich J.: Use of the oral glucose tolerance test to assess insulin release and insulin sensitivity. *Diabetes Care* 23 (2000) 295-301.
57. Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC.: Homeostasis model assessment: Insulin resistance and β -cell function from fasting plasma glucose and insulin concentrations in man. *Diabetologia* 28 (1985):412-419.
58. Haffner SM, Kennedy E, Gonzalez C, Stern MP, Miettinen H.: A prospective analysis of the HOMA model: The Mexico City Diabetes Study. *Diabetes Care* 19 (1996) 1138-41.
59. Hosker JP, Matthews DR, Rudenski AS, Burnett MA, Darling P, Bown EG, Turner RC.: Continuous infusion of glucose with model assessment: Measurement of insulin resistance and B-cell function in man. *Diabetologia* 28(1985):401-411.
60. De Fronzo, R.A., Tobin, J.D., Andres, R. :Glucose clamp technique : a method for quantifying insulin secretion and resistance. *Am. J. Physiol.*237(1979): E214-E223.
61. Fritsche A, Stefan N, Hardt E, Schützenauer S, Häring H, Stumvoll M.: A novel hyperglycemic clamp for characterisation of islet function in humans: assessment of the three different secretagogues, maximal insulin response and reproducibility. *Eur J Clin Invest* 30(2000): 411-418.
62. Elahi D, Raizes G, Anders R, Hershof RJ, Muller D, Tobin J, Andersen DK.: Interaction of arginine and gastric inhibitory polypeptide (GIP) on insulin release in man. *Am J Physiol* 242(1982):E343-E351.
63. Meier JJ, Hücking K, Holst JJ, Deacon CF, Schmiegel WH, Nauck MA.: Reduced Insulinotropic Effect of Gastric Inhibitory Polypeptide in First-Degree Relatives of Patients with Type 2 Diabetes. *Diabetes* 50(2001):2497-2504.
64. Boden G, Chen X, Rosner J, Barton M.: Effects of 48-h fat infusion on insulin secretion and glucose utilization. *Diabetes* 44(1995):1239-1242.
65. Stefan N, Fritsche A, Häring H, Stumvoll M.: Effect of experimental elevation of free fatty acids on insulin secretion and insulin sensitivity in healthy carriers of the Pro 12Ala Polymorphism of the Peroxisome Proliferator-Activated Receptor- γ 2 Gene. *Diabetes* 50(2001):1143-1148.
66. Mitrakou A, Vuorinen-Mrkkola H, Raptis G, Toft I, Mokan M, Strumph P, Pimenta W, Veneman T, Jenssen T, Bolli G, Korytkowski M, Yki-Järvinen H, Gerich J.: Simultaneous assessment of insulin secretion and insulin sensitivity using a hyperglycemic clamp. *J Clin Endocrinol Metab* 75(1992):379-382.
67. Tillil H, Shapiro ET, Rubenstein AH, Galloway JA, Polonsky KS.: Reduction of insulin clearance during hyperglycemic clamp. Dose-Response Study in normal humans. *Diabetes* 37(1988):1351-1357.

68. Nauck MA, Homberger E, Siegel EG, Allen RC, Eaton RP, Ebert R.: Incretin effects of increasing glucose loads in man calculated from venous insulin and C-peptide responses. *J Clin Endocrinol Metab* 63 (1986): 492-498.
69. Creutzfeldt W, Nauck M.: Gut hormones and diabetes mellitus. *Diabetes/Metab Rev* 8(1992):149-17.
70. Buchan AMJ, Polak JM, Capella C, Solcia E, Pearse AGE.: Electron immunocytochemical evidence of the K cell localisation of gastric inhibitory polypeptide (GIP) in man. *Histochemistry* 56(1978): 37-44.
71. Essele R, Göke R, Willemer S. Glucagon-like peptide-1 cells in the gastrointestinal tract and pancreas of rat, pig and man. *Eur J Clin Invest* 22(1992):283-291.
72. Nauck MA, Bartels E, Ørskov C, Ebert R, Creutzfeldt W.: Additive insulinotropic effects of exogenous synthetic human gastric inhibitory polypeptide and glukagon-like polypeptide-1 (7-36) amide infused at near-physiological insulinotropic hormone and glucose concentration. *J Clin Endocrinol Metab* 76(1993): 912-17.
73. Dupre J, Ross SA, Watson D, Brown JC.: Stimulation of insulin secretion by gastric inhibitory polypeptide in man. *J Clin Endocrinol Metab* 37(1973): 826-828.
74. Nauck MA, Niedereichholz U, Ettler R, Holst JJ, Ørskov C, Ritzel R.: Glukagon-like polipeptide-1 inhibition of gastric emptying outwegs ist insulinotropic effects in healthy humans. *Am J Physiol* 273(1997): E981-E988.
75. Cleator JG, Gourlay RH.: Release of immunoreactive gastric inhibitory polypeptide (IR-GIP) by oral ingestion of food substances. *Am J Surg* 130(1975): 128-135.
76. Fieseler P, Bridenbaugh S, Nustede R, Martell J, Ørskov C, Holst JJ.: Physiological augmentation of amino acid-induced secretion by GIP and GLP-1 but not by CCK-8. *Am J Physiol* 268(1995): E949-55.
77. Nauck MA, Heimesaat MM, Ørskov C, Holst JJ, Ebert R, Creutzfeldt W.: Preserved incretin activity of glucagon-like-peptide 1(7-36 amide) but not of synthetic human gastric inhibitory polypeptide in patients with type-2 diabetes mellitus. *J Clin Invest* 91(1993): 301-7.
78. Nauck MA, Stöckmann F, Ebert R, Creutzfeldt W.: Reduced incretin effect in Type 2(non-insulin-dependent) diabetes. *Diabetologia* 29(1986): 46-54.
79. Jones JR, Owens DR, Luzio SD, Hayes TM.: Glucose dependent insulinotropic polypeptide (GIP) infused intravenously is insulinotropic in the fasting state in Type 2 (noninsulindependent) diabetes mellitus. *Horm Metab Res* 21(1988): 23-26.
80. Nauck MA, Heimesaat MM, Ørskov C, Holst JJ, Ebert R, Creutzfeldt W.: Preserved incretin activity of glucagon-like-peptide 1(7-36 amide) but not of synthetic human gastric inhibitory polypeptide in patients with type-2 diabetes mellitus. *J Clin Invest* 91(1993): 301-7.
81. Ward WK, Bolgiano DC, McKnight B, Halter JB, Porte D. Jr.: Diminished b cell secretory capacity in patients with non-insulin-dependent diabetes mellitus. *J Clin Invest* 74(1984):168-174.
82. Larsson H, Ahren B. Glucose-dependent arginine stimulation test for characterization of islet function: studies on reproducibility and priming effect of arginine. *Diabetologia* 41 (1998):772-777.
83. Van Haeften TW, Voetberg GA, Gerich J, van der Veen ED.: Dose-Response Characteristics for Arginine-stimulated insulin secretion in man and influence of hyperglycemia. *J Clin Enocrin Metab* 69(1989):1059-1064.

84. Steiner, D. F., Oyer, P.E.: The biosynthesis of insulin and a probable precursor of insulin by a human islet cell adenoma. *Proc. Natl. Acad. Sci. USA* 57(1967): 473-480.
85. Horwitz, D.L., Starr, J.I., Mako, M.E., Blackard, W.G., Rubenstein, A.H.: Proinsulin, insulin and C-peptide concentrations in human portal and peripheral blood. *J. Clin. Invest.* 55(1975):1278-1283.
86. Rubenstein AH, Clark JL, Melani F, Steiner DF.: Secretion of proinsulin and C-peptide by pancreatic beta cells and its circulation in blood. *Nature* 224(1969): 697-99.
87. Polonsky K., Jaspan J, Pugh W, Cohen D, Schneider M, Schwartz T, Moosa A R, Tager H, Rubenstein, A.H.: Metabolism of C-peptide in the dog : in vivo demonstration of the absence of hepatic extraction. *J. Clin. Invest.* 72 (1983): 1114-1123.
88. Tillil H, Shapiro ET, Miller A, Karrison T, Frank BH, Galloway JA.: Dose-dependent effects of oral and intravenous glucose on insulin secretion and clearance in normal humans. *Am J Physiol (Endocrinol Metab)* 254(1988): E349-357.
89. Henriksen JH, Tronier B, Blow JB.: Kinetics of circulating endogenous insulin, C-peptide and proinsulin in fasting nondiabetic man. *Metabolism* 36(1987): 463-468.
90. Matthews DR, Rudenski AS, Burnett MA, Darling P, Turner RC.: The half-life of endogenous insulin and C-peptide in man assessed by somatostatin suppression. *Clin. Endocrinol.* 23(1985): 71-79.
91. Tillil H, Shapiro ET, Rubenstein AH, Galloway JA, Polonsky KS.: Reduction of insulin clearance during hyperglycemic clamp. Dose response study in normal humans. *Diabetes* 37(1988):1351-57.
92. Faber OK, Hagen C, Binder C, Markussen J, Naithani VK, Blix PM, Kuzuya H, Horwitz DL, Rubenstein AH, Rossing N.: Kinetics of human connecting peptide in normal and diabetic subjects. *J Clin Invest* 62 (1978):197-203.
93. Eaton PR, Allen RC, Schade DS, Erickson KM, Standefer J.: Prehepatic insulin production in man : kinetic analysis using peripheral connecting peptide behaviour. *J Clin Endocrinol Metab* 51(1980): 520-28.
94. Eaton PR, Allen RC, Schade DS.: Hepatic removal of insulin in normal man: dose response to endogenous insulin secretion. *J Clin Endocrinol Metab* 56(1983):1294-1300.
95. Polonsky KS, Rubenstein AH.: C-Peptide as a measure of the secretion and hepatic extraction of insulin: pitfalls and limitations. *Diabetes* 33(1984):1821-1829.
96. Polonsky KS, Frank B, Pugh W, Addis A, Karrison T, Meier P, Tager H, Rubenstein AH.: The limitations to and valid use of C-peptide as a marker of the secretion of insulin. *Diabetes* 35 (1986):379-386.
97. Polonsky KS, Licinio-Paixao J, Given BD, Pugh W, Rue P, Galloway J, Karrison T, Frank B.: Use of biosynthetic human C-peptide in the measurement of insulin secretion rates in normal volunteers and type 1 diabetic patients. *J Clin Invest* 77 (1986): 98-105.
98. Morishima T, Pye S, Polonsky K, Radziuk J.: The measurement and validation of the nonsteady-state rates of C-peptide appearance in the dog. *Diabetologia* 29(1986): 440-446.
99. Licinio-Paixao J, Polonsky KS, Given BD, Pugh W, Ostrega D, Frank B, Rubenstein AH.: Ingestion of a mixed meal does not affect the metabolic clearance rate of biosynthetic human C-peptide. *J Clin Endocrinol Metab* 63(1986): 401-403.

100. Polonsky, K.; Jaspan, J., Emmanouel, D., Holmes, K., Moossa, A.R.: Differences in the hepatic and renal extraction of insulin and glucagon in the dog :evidence for saturability of insulin metabolism. *Acta Endocrinol.* 102(1983): 420-427.
101. Morishima T, Bradshaw C, Radziuk J.: Measurement using tracers of steady-state turnover and metabolic clearance of insulin in dogs. *Am J Physiol* 248(1985): E203-E208.
102. Cobelli C, Mari A, Ferrannini E.: Non linearity of insulin kinetics. *Am J Physiol* 251(1986):E247-E248.
103. Cohen P, Barzilai N, Barzilai D, Karnieli E.: Correlation between insulin clearance amid insulin responsiveness: studies in normal, obese, hyperthyroid and Cushing's syndrome patients. *Metabolism* 35 (1986) : 744-749.
104. Nijs HGT, Radder JK, Frölich M, Krans MJ.: In vivo relationship between insulin clearance and action in healthy subjects and IDDM patients. *Diabetes* 39(1990): 333-339.
105. Walton C, Godsland IF, Proudler AJ, Felton CV, Wynn V.: Effect of body mass index and fat distribution on insulin sensitivity, secretion, and clearance in non-obese healthy men. *J. Clin. Endocrinol. Metab.* 75 (1992): 170-175.
106. Rhodes CJ, Alarcon C.: What beta-cell defect could lead to hyperproinsulinemia in NIDDM ? Some clues from recent advances made in understanding the proinsulin-processing mechanism. *Diabetes* 43(1994): 511-517.
107. Tillil H, Frank BH, Pekar AH, Broelisch C, Rubenstein AH, Polonsky KS.: Hypoglycemic potency and metabolic clearance rate of intravenously administered human proinsulin and metabolites. *Endocrinology* 127(1990):2418-2422.
108. Yoshioka N, Kuzuya T, Matsuda A, Taniguchi M, Iwamoto Y.: Serum proinsulin concentrations at fasting and after oral glucose load in patients with Type II (non-insulin-dependent) diabetes mellitus. *Diabetologia* 31(1988): 355-360.
109. Saad MF, Kahn SE, Nelson RG.: Disproportionately elevated proinsulin in Pima Indians with noninsulin-dependent diabetes mellitus. *J Clin Endocrinol Metabol* 70(1990): 1247-1253.
110. Persson B, Hanson U, Hartling SG, Binder C.: Follow-up of women with previous GDM. Insulin, C-peptide, and proinsulin response to oral glucose load. *Diabetes* 40(1991) Suppl. 2 :136-141.
111. Davies MJ, Rayman G, Gray IP, Day JL, Hales CN.: Insulin deficiency and increased plasma concentration of intact and 32/33 split proinsulin in subjects with impaired glucose tolerance. *Diabetic Med* 10(1993): 313-320.
112. Reaven GM, Chen Y-DI, Hollenbeck CB, Shou WMH, Ostrega D, Polonsky KS.: Plasma insulin, C-peptide and proinsulin concentrations in obese and non obese individuals with varying degrees of glucose tolerance. *J Clin Endocrinol Metab* 76(1993):44-48.
113. Haffner SM, Gonzalez C, Mykkanen L, Stern M.: Total immunoreactive proinsulin, immunoreactive insulin in relation to conversion to NIDDM: the Mexico City Diabetes Study. *Diabetologia* 40(1997): 830-837.
114. Kahn SE, Leonetti DL, Prigeon RL, Boyko EJ, Bergstrom RW, Fujimoto WY.: Proinsulin as a marker for the development of NIDDM in Japanese-American men. *Diabetes* 44(1995): 173-179.
115. American Diabetes Association. : Report of the expert committee on the diagnosis and classification of diabetes mellitus (Committee Report) *Diabetes Care* 21(1998):S5-S19.

116. Van Cauter ,E., Mestrez, F., Sturis, J., Polonsky, K.S.: Estimation of insulin secretion rates from C-peptide levels. Comparison of individual and standard kinetic parameters for C-peptide clearance. *Diabetes* 41(1992): 368-377.
117. Holst JJ, Gromada J, Nauck MA: The pathogenesis of NIDDM involves a defective Expression of the GIP receptor. *Diabetologia* 40(1997):984-986.
118. Lynn FC, Pair N, Ng EH, Macintosh CH, Keiba TJ, Peterson RA.: Defective glucose-dependent insulinotropic polypeptide receptor expression in diabetic fatty Zucker rats. *Diabetes* 50(2001):1004-1011.
119. Kubota A, Yamada Y, Hayami T, Yasuda K, Someya Y, Ihara Y, Kagimoto S, Watanabw R, Taminato T, Tsuda K, Seino Y.: Identification of two missense mutations in the GIP receptor gene: a functional study and association analysis with NIDDM: no evidence of association with Japanese NIDDM subjects. *Diabetes* 45(1996)1701-1705.
120. Almind K, Ambye L, Urhammer SA, Hansen T, Echwald SM, Holst JJ, Gromada J, Thorens B, Pedersen O.: Discovery of amino acid variants in the human glucose-dependent insulinotropic polypeptide (GIP) receptor: the impact of the pancreatic beta cell responses and functional expression studies in Chinese hamster fibroblast cells. *Diabetologia* 41(1998)1194-1198.
121. Kahn SE, Prigeon RL, McCulloch DK, Boyko EJ, Bergman RN, Schwartz MW at all. Quantification of the relationship between insulin sensitivity and β -cell function in human subjects. Evidence for a hyperbolic function. *Diabetes* 1993; 42: 1663-1672.
122. Bühl A, Zöfel P.: SPSS Version 10. Einführung in die moderne Datenanalyse unter Windows. Addison-Weseley V.1999.
123. Pueyo ME, Clement K, Vaxillare M, Passa P, Froguel P, Robert J-J, Velho G.: Arginine-Induced Insulin release in glucokinase-Deficient Subjects.17(1994):1015-1021.
124. Stumvoll M, Fritsche A, Häring H-U.: Clinical characterisation of insulin secretion as the basis for genetic analyses. *Diabetes* 51(2002)(Suppl.1):S122-S129.
125. Pick A, Clark J, Kubstrup C, Levisetti M, Pugh W, Bonner-Weir S, Polonsky KS.: Role of apoptosis in failure of β -cell mass compensation for insulin resistance and β -cell defects in the male Zucker diabetic fatty rat. *Diabetes*47(1998):358-364.
126. Jones CNO, Pei D, Staris P, Polonsky KS, Chen YD, Reaven GM.: Alterations in the glucose-stimulated insulin secretory dose-responce curve and in insulin clearance in nondiabetic insulin-resistant individuals *J Clin Endoc Metab* 82(1997):1834-1838.
127. Cozzolino D, Sessa G, Salvarore T.: Hyperinsulinemia in offspring of non-insulin-dependent diabetes mellitus patients: the role played by abnormal clearance of insulin. *Metabolism* (1995)44:1278-1282.
128. Haffner SM, Stern MP, Watanabe RM, Bergman RN.: Relationship of insulin clearance and secretion to insulinsensitivity in non-diabetic Mexican-Americans. *Eur J Clin Invest* 22(1992):147-153.
129. Osei K, Schuster DP.: Ethnic difference in secretion, sensitivity, and hepatic extraction of insulin in black and white Americans. *Diabetes Med* 11(1994):755-762.
130. Rocchini AP, Marker P, Cervenka T.: Time course of insulin resistance associated with feeding dogs a high-fat diet. *Am J Physiol* 272(1997):E147-E154.
131. Swinburn BA, Boyce VL, Bergman RN, Howard BV, Bogardus C.: Deterioration in carbohydrate metabolism and lipoprotein changes induced by modern, high fat diet in Pima Indians and Caucasians. *J Clin Endocrinol Metab* 73(1991):156-165.

132. Polonsky KS, Gumbiner B, Ostrega D, Griver K, Tager H, Henry RR.: Alterations in immunoreactive proinsulin and insulin clearance induced by weight loss in NIDDM. *Diabetes*43(1994):871-877.
133. Wesenthal SR, Sandhu H, McCall RH, Tchipashvili V, Yoshii, Polonsky K, Shi ZQ, Lewis GF, Mari A, Giacca A.: Free fatty acid impair hepatic insulin extraction in vivo. *Diabetes* 48(1999):766-774.
134. Shuster LT, Go VL, Rizza RA, O'Brien PC, Service FJ.: Incretin effect due to increased secretion and decreased clearance of insulin in normal humans. *Diabetes*37(1988):200-203.
135. Dupre J, Behme MT, Hramiak IM, Longo CJ.: Hepatic extraction of insulin after stimulation of secretion with oral glucose or parenteral nutrients. *Metabolism*42(1993):921-927.
136. Rhodes CJ, Alarcon C.: Waht β -cell defect could lead to hyperproinsulinemia in NIDDM: some clues from recent advances made in understanding the proinsulin conversion mechanism. *Diabetes* 43(1994):511-517.
137. Porte D, Kahn SE.: Hyperproinsulinemia and amyloid in NIDDM: Clues to etiology of islet β -cell dysfunction. *Diabetes* 38(1989):1333-1336.
138. Ward WK, LaCava EC, Paquette TL, Beard JC, Wallum BJ, Porte D Jr.: Disproportionate elevation of immunoreactive proinsulin in Typ 2 (non-insulin-dependent) diabetes mellitus and in experimental insulin resistance. *Diabetologia* 30 (1987):698-702.
139. Rasmussen H, Zawalich KC, Ganesan S, Calle R, Zawalich WS.: Physiology and pathophysiology of insulin secretion. *Diabetes Care* 13 (1990) 655-666.
140. Gerich JE, Charles MA, Grodsky GM. Charakterisation of the effect of arginine and glucose on glucagon and insulin release from the perfused rat pancreas. *J Clin Invest* 54(1974): 833-841.