

Curriculum vitae et studiorum

Dario Iafusco was born in Naples on 8th October 1959

He is married with Giovanna Tortorella Esposito from 1990 and he has two lovely daughters:
Fernanda born on 23 th April 1994 and Elena born on 19 th March 2002

He graduated in Medicine and Surgery at the Second University of Naples on 26th July 1984 and obtained

- a post-graduate Specialization in Pediatrics on 27/5/1988 and
- a post-graduate Specialization in Endocrinology and Metabolism Diseases - Diabetology on 26th October 1999.

In 1988 he was appointed “Medical Technician” with Medical Functions at the Second University of Naples and since 1st October 2001 he is Confirmed Researcher at the Department of Pediatrics of the University of Campania “Luigi Vanvitelli” and his job is in the Regional Center for Pediatric Diabetology “G.Stoppoloni”

He teaches

Pediatrics at the English Course of Medicine and Surgery of the University of Campania “Luigi Vanvitelli”

Pediatric Diabetology at the Specialization of Pediatrics School of the University of Campania “Luigi Vanvitelli”

Pediatric Diabetology at the Pediatric Nurse Course of the University of Campania “Luigi Vanvitelli” and

Pediatrics at General Nurse Course of the University of Campania “Luigi Vanvitelli”.

From 2007 to 2009 he was the National Coordinator of Italian Study Group of Pediatric Diabetology of Italian Society of Pediatric Endocrinology and Diabetology (ISPED)

In 2010/2014/2016/2018 he was in the Faculty of the National School of Pediatrics Endocrinology and Diabetology of the Italian Society of Pediatric Endocrinology and Diabetology (ISPED)

In 2011-2012 he was the Coordinator of the National School of Pediatrics Endocrinology and Diabetology of the Italian Society of Pediatric Endocrinology and Diabetology (ISPED)

In 2017-2018 he was in the Faculty of the International School of Pediatrics Endocrinology and Diabetology of International Society of Pediatric Endocrinology and Diabetology (ISPED)

In 2013-2015 he was the Vice President of the Italian Society of Pediatric Endocrinology and Diabetology (ISPED)

In 2015-2017 he was the General Secretary of the Italian Society of Pediatric Endocrinology and Diabetology (ISPED)

From 2007 to 2016 Dario Iafusco was in the Working Group of Italian Society of Pediatric Endocrinology and Diabetology (ISPED) for the Italian guidelines and raccomandations on “Treatment of Diabetic Ketoacidosis”, “Treatment of Pediatric Diabetes by Insulin Pumps”, “Treatment of Hypoglycaemia in Pediatric Diabetes”, “Insulin Therapy in Pediatrics” and “raccomandations for the physical activity in children and adolescents with diabetes”

The principal investigating Area of Dario Iafusco is the Pediatric Diabetology.

Personal contribution to the definition and characterization of Monogenic Diabetes of Infancy

In particular from 1990 he collected Italian data on patients who developed diabetes in the first year of life in the presupposition that if diabetes onset very early after the birth there were more

possibilities that the pathogenesis was not autoimmune because the autoimmune response needs time. A not autoimmune pathogenesis had been described in Permanent Neonatal Diabetes Mellitus (PNDM) (newborns with diabetes onset until 1 month of life) but the important research of dr Iafusco, published in 2002 (Iafusco D et al *Diabetologia* 45: 798-804: 2002), demonstrated, for the first time, that the most cases of Diabetes with onset before sixth months of life are not Autoimmune.

Immediately after this research he deepened the knowledge, with the contribute of Fabrizio Barbetti Lab, in University of Tor Vergata – Rome, on the genes involved in the insulin secretion from beta cells and in 2005 he typed all the DNA samples of Italian patients collected in 1990 demonstrating that about 50% had the mutation of gene KCNJ11 (KIR) (Massa O, Iafusco D et al) *Hum Mutat* 25(1): 22-27: 2005)

For this reason he noted that the diagnostic time limit for PNDM had changed over the years, ranging from onset within 30 days of birth to 3 months of age. However, as patients with the clinical phenotype caused by mutation in the KCNJ11 gene have been identified with onset up to 6 months of age, Massa O, Iafusco D et al. (2005) suggested that the term 'permanent diabetes mellitus of infancy'(PDMI) replaced PNDM as a more accurate description, and included those who presented up to 6 months of age. The authors suggested that the new acronym had to be linked to the gene product (e.g., GCK-PDMI, KCNJ11-PDMI) to avoid confusion with patients with early-onset, autoimmune type 1 diabetes.

In 2008 he demonstrated in a mouse model and in humans the pathogenetic mechanism of the mutation of insulin gene and contributed to characterise of this new form of early onset diabetes (Diabetes INS) (Colombo C, Iafusco D et al *J Clin Invest.* 118(6); 2148-56: 2008).

Subsequently he proposed that, because individuals with INS gene mutations may present with diabetes well beyond 6 months of age and cannot be distinguished from patients with type 1 diabetes except for the absence of type 1 diabetes autoantibodies, the term PNDM should be replaced with 'monogenic diabetes of infancy (MDI),' a broad definition including any form of diabetes, permanent or transient, with onset during the first years of life and caused by a single gene defect.

Personal contribution to the “weaning” of Italian children, adolescents and young adults with not autoimmune diabetes from insulin to sulphonylurea.

After the discovered of A. Hattersley of the possibility to care patients with KCNJ11-PDMI with oral sulphonylurea indeed of insulin, he began to travel throughout Italy to try to wean the patients signalled by the Pediatric Diabetologists referring of the Italian Society of Pediatric Endocrinology and Diabetology (ISPED). Thanks to this exciting experience Italy was the Country with the most number of patients with KCNJ11-PDMI in the world in treatment with oral drugs and the results were published in 2006 (G. Tonini, et al and D. Iafusco “Sulphonylurea treatment outweighs insulin therapy in short-term metabolic control of patients with permanent neonatal diabetes mellitus due to activating mutations of the KCNJ11 (KIR6.2) gene. Early-Onset Diabetes Study Group of the Italian Society of Pediatric Endocrinology and Diabetology. *Diabetologia*.49(9); 2210-3: 2006)

Very intriguing are the data on the long-term follow up of patients with neonatal diabetes due to KCNJ11 mutations published in 2018 on *Lancet Diabetes Endocrinol* (Bowman P, Sulen Å, Barbetti F, Beltrand J, Svalastoga P, Codner E, Tessmann

EH, Juliusson PB, Skrivarhaug T, Pearson ER, Flanagan SE, Babiker T, Thomas NJ, Shepherd MH, Ellard S, Klimes I, Szopa M, Polak M, Iafusco D, Hattersley AT, Njølstad PR; Neonatal Diabetes International Collaborative Group. Effectiveness

and safety of long-term treatment with sulphonylureas in patients with neonatal diabetes due to KCNJ11 mutations: an international cohort study. *Lancet Diabetes*

Endocrinol. 2018 Aug;6(8):637-646. doi: 10.1016/S2213-8587(18)30106-2. Epub 2018

Jun 4. Erratum in: *Lancet Diabetes Endocrinol.* 2018 Sep;6(9):e17. PubMed PMID:

Also Autoimmune Diabetes was an Area of interest of dr Dario Iafusco

Personal contribution to the individuation of best insulin schemes for children and adolescents with type 1 diabetes and to the use of technologies for the therapies of diabetes

Dario Iafusco dedicated many time to study the insulin treatment for pediatric patients and was persuaded that the therapy has to be “tailored” on the patients: the therapy has to be adapted to the life style of the patients rather than the opposite. In Italy he was a “pioneer” and, at the same time, a “revolutionary” in this field and his contributes were followed by many others pediatric diabetologists especially after the publication of two reviews: D. Iafusco : Insulin therapy regimens in pediatric age. *Acta Biomed.* 76 Suppl 3:39-43: 2005 Review and D. Iafusco: Diet and physical activity in patients with type 1 diabetes. *Acta Biomed.* 77 Suppl 1;41-6: 2006 Review.

Very intriguing was the demonstration that is better to use human regular instead of analogue as premeal insulin treatment during basal bolus regimen. (V Cherubini, D Iafusco et al Premeal insulin treatment during basal-bolus regimen in young children with type 1 diabetes. *Diabetes Care.* 29(10); 2311-2: 2006). This study was considered “countertrend” despite the fact that the world pharmacological research is addressed to new analogues and new insulins.

A noteworthy experience was in the field of Technologies applied to Diabetes Care and, after two papers dedicated to the compliance of patients using subcutaneous pump with insulin (D Iafusco et al The egg or the chicken? Should good compliance to multi-injection insulin therapy be a criterion for insulin pump therapy, or does insulin pump therapy improve compliance? *J Pediatr.* 148(3); 421-2: 2006 and Lombardo F, Iafusco D, et al The egg or the chicken? Further data on whether good compliance to multi-injection insulin therapy should be a criterion for insulin pump therapy, or does insulin pump therapy improve compliance? *J Pediatr.* 151(6); e23-4: 2007), his collaboration with the Italian Society of Pediatric Endocrinology and Diabetology (ISPED) conducted to elaborate the Italian guidelines for the use of insulin pumps in children and adolescents with diabetes. (Pinelli L, Iafusco D, et al and Italian Study Group on Diabetes of ISPED: Insulin Pump Therapy in Children and Adolescents with Type 1 Diabetes. The Italian Viewpoint; *Acta Biomed* 79; 57-64: 2008). Very interesting is the fact that after these national guidelines, was described an “Italian viewpoint” in this subject.

Very intriguing are the experiences of Dr Iafusco in the evaluation of the effect of pump insulin in lowering postprandial glycaemia in children after Italian Pizza Margherita (A De Palma, D Iafusco et al Lowering Postprandial Glycemia in Children with Type 1 Diabetes After Italian Pizza "Margherita" (TyBoDi2 Study). *Diabetes Technol Ther.* 2; 28: 2011), the effect of timing of boluses (AE Scaramuzza, D Iafusco, et al Timing of bolus in children with type 1 diabetes using continuous subcutaneous insulin infusion (TiBoDi Study). *Diabetes Technol Ther.* 12(2):149-52: 2010 and the effect of reducing boluses in very young children (I. Rabbone, D Iafusco et al Insulin pump therapy management in very young children with type 1 diabetes using continuous subcutaneous insulin infusion. *Diabetes Technol Ther.* 11(11); 707-9: 2009

Dario Iafusco has published data on the use of insulin pump in children and adolescent. Very interesting is the paper on the best place where insert the niddle (Zanfardino A and Iafusco D “Butt or tummy. *Diabetes Technology and Therapeutics* 2014).

Another experience of dr Iafusco was the invention of a new educational tool for adolescents with type 1 diabetes: the use of a chatline moderated by him and with a psychologist who records all the meeting. This experience began in 2000 (D Iafusco et al The chatline as a communication and educational tool in adolescents with insulin-dependent diabetes:

preliminary observations. Diabetes Care 23(12); 1853: 2000) and it is ongoing (D Iafusco et al Chat line for adolescents with type 1 diabetes. A useful tool to improve coping with diabetes Diabetes Technol Ther 2011). The chat is ongoing and new data are in press on Diabetes Technol Ther. Dario Iafusco participated to the first experience of the use of artificial pancreas (PEDarPAN PEDiatric artificial PANcreas) in little children with type 1, autoimmune, diabetes of 5-9 years during a school camp in Bardonecchia (Turin) in July and September 2015. The results of this experience have been submitted and are in press in Diabetes Care 2016.

Dr Dario Iafusco is the Principal Investigator of the following studies:

- Protocol ID PZ_2018 ClinicalTrials.gov NCT03748251 “Management of Glycemia following Pizza Meal”
- Protocol ID inCamp ClinicalTrials.gov NCT03725657 “Correlation Between Exercise and Insulin Dose in Camp for Pediatric Type 1 patients (inCamp)”
- Study in Phase 3: “Studio in Fase 3, multicentrico, randomizzato, controllato con placebo, in doppio cieco, a gruppi paralleli, della durata di 26 settimane, con un periodo di estensione di sicurezza di 26 settimane, volto a valutare la sicurezza e l’efficacia di dapagliflozin da 5 a 10 mg e saxagliptin da 2,5 e 5 mg in pazienti pediatrici con diabete mellito di tipo 2, di età compresa tra 10 e 18 anni”.
- Observational Study on patients in insulin therapy by I-Port Advance From Jul 2016 to 2017
- Nov 2012 to 2017. Observational Study: “Glycemic control and quality of life in children, adolescents and Young adults with type-1 diabetes mellitus described in a worl-wide cross-sectional study in 2012: impact of age-patient-related, behaviour and structure of care-related variables"-study TEENs (DIREG_C_05444)
- Jul-Dec 2015. National Multicentric Project PEDarPAN Pediatric Artificial Pancreas "Uso del pancreas artificiale in età pediatrica. Studio di fattibilità, sicurezza ed efficacia del controllo automatico della glicemia 24h/24 in ambiente extraospedaliero", Clinical trial reg. no. NCT02620878, clinical tials.gov; first experiment of the use of artificial pancreas in children. Coordinator University of Padoa (Principal Investigator Prof. Daniela Bruttomesso), with the participation of pediatric diabetology teams from Naples (Second University of Naples), Rome, Turin, Veron, Milan
- Feb 2012- Oct 2015. Clinic Sperimentation: BI trial n. 1218.56 : “A randomized double-blind, placebo-controlled parallel group dose-finding study of linagliptin (1 mg or 5 mg administered orally once daily) over 12 weeks in children and adolescents, from 10 to 17 years of age, with type 2 diabetes and insufficient glycaemic control despite treatment with diet and exercise alone”. COD EudraCT: 2009-017004-91
- Jul 2006-Gen 2015. Study IMITA (Indagine sul Microinfusore in ITAlia), survey on the use of insulin pump in Italy in Pediatrics and in Adults.
- Jul 2012- Gen 2014. Study IBGStar - iNEWTREND - Study IBGST_L_05971
- PRIN-2018 (submitted) “Italian Network Prevention and TPrediction of Type 1 Diabetes in Children (NIPPED)” Principal Coordinator Prof Francesco Chiarelli (University of Chieti); Local Principal Investigator Dr Dario Iafusco University of Campania “Luigi Vanvitelli”

Dr Dario Iafusco was invited speaker in 288 National and International Conferences and his Scientific Production is composed by 408 publications: **212** cited by www.Pubmed.org and **160** original articles cited by www.scopus.com with **2460** citations with an h-index of **25** and **45** publications as Correspondent Author, first or last name.

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Dr Dario Iafusco

