New Diagnosis of Type 1 Diabetes

Hertfordshire GP Conference

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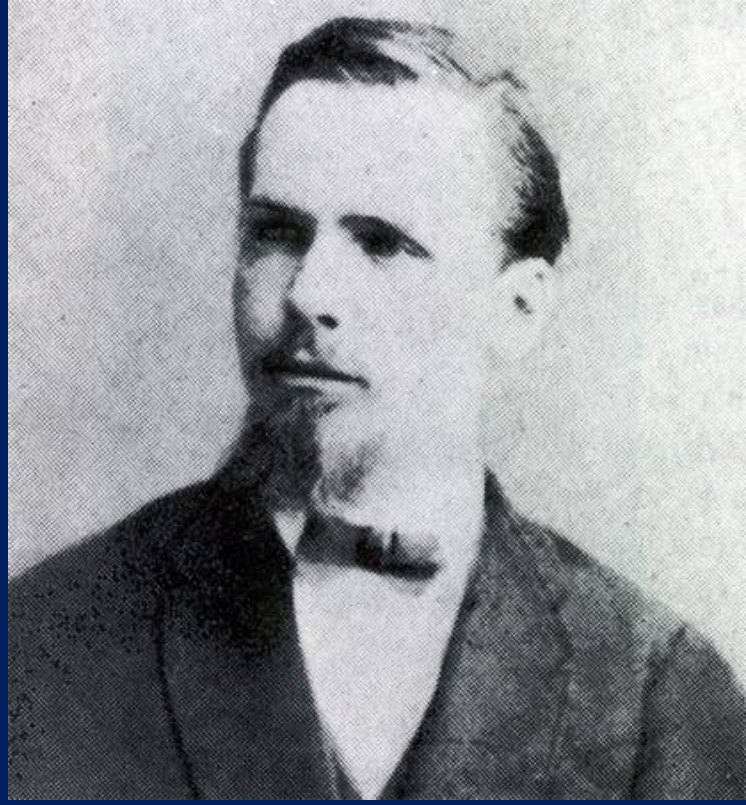
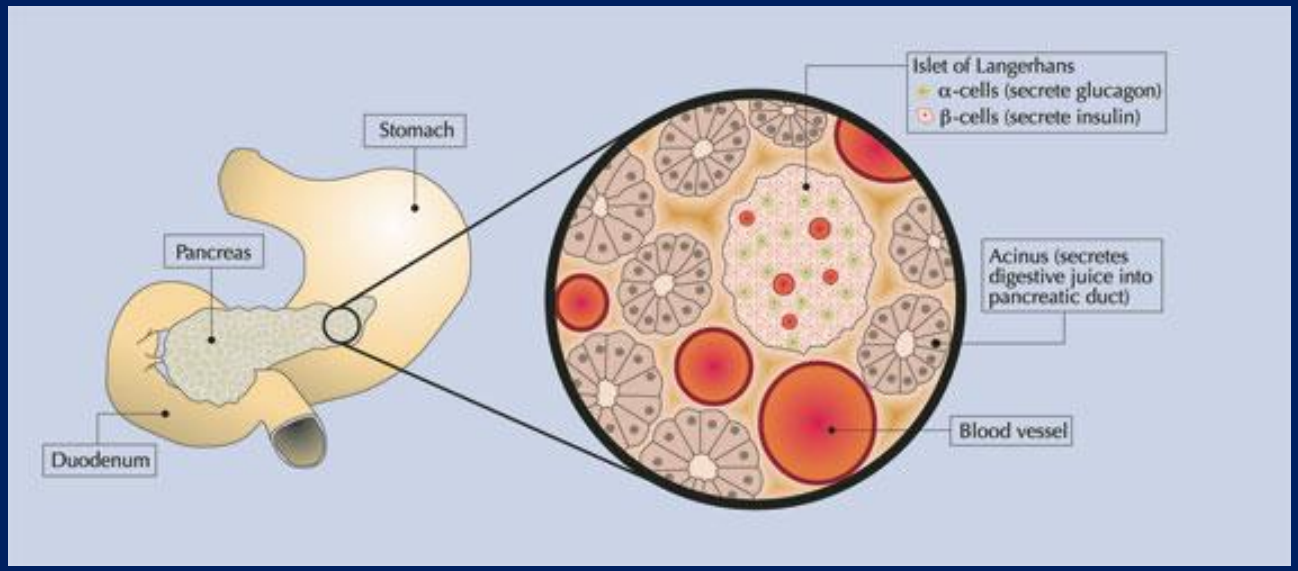
Scope

1. Diabetes - History
2. Symptoms – sometimes can be non-specific
3. Referring to Hospital – EARLY!
4. Patient Story

History…

- Egyptian papyrus 1550 BC – treatment was a boiled assortment of bones, wheat, grain and earth for four days
- 2nd Century AD - Aretaeus of Cappadocia, term “diabetes” after the Greek word for “sieve”
- 5th Century, Indian physician noted urine of diabetic patients tasted sweet, like honey (“mellitus”)
- 18th century - Matthew Dobson (Englishman) - sticky substance found in diabetic urine was sugar
- 1856 Claude Bernard, “Father of Physiology” postulated pancreas as role of disease – confirmed 1889 by 2 German physicians




Islet of Langerhans
α-cells (secrete glucagon)
β-cells (secrete insulin)
Stomach
Pancreas
Acinus (secretes digestive juice into pancreatic duct)
Blood vessel
Duodenum

History…

- 1869 - Paul Langerhans – described cluster of cells he separated
- 1889 – Edouard Laguesse - named Islet of Langerhans and suggested they lower blood glucose levels
- Jean de Meyer (Belgium) named the mysterious pancreatic substance “insulin” from the Latin word for island
- 1914-1922 – Dr Frederick Allen era of diabetes – “starvation treatment”

Case 2 H.

(1)

Female age 15 years. Admitted Aug. 16, 1922.

Present Illness.

During the autumn of 1918 patient had frequent colds, felt weak, and had occasional polydipsia and polyuria. During the winter she had, in addition, pains in legs & back and insomnia.

In march 1919 there was an exacerbation of these conditions & all the active symptoms of diabetes were present — polyuria, polyphagia, polydipsia, dry skin, pruritis, loss of wt. (75 lbs. — to 62 lbs)

Banting and Best – Canada 1921

100 years ago... first children treated with insulin

Diabetes - Definition

- Diabetes: Group of metabolic conditions characterized by hyperglycaemia, resulting from defects in insulin secretion, insulin action or both

- Chronic hyperglycaemia – associated with long term damage, dysfunction and failure of various organs (eyes, kidneys, nerves, heart, blood vessels)

Type 1 - Definition Criteria

1. Classic symptoms of diabetes or hyperglycemic crisis, with plasma glucose concentration ≥ 11.1 mmol/L(200 mg/dL) or

2. Fasting plasma glucose ≥ 7.0 mmol/L (126 mg/dL)

- Fasting Blood Glucose is NOT REQUIRED – Lab Blood test delays referral

NB HbA1c – IS NOT THE WAY TO MAKE A DIAGNOSIS OF TYPE 1 Diabetes

Type 1 Diabetes - statistics

- Most frequent endocrine disease in children
- Incidence 17-24/100,000 CYP in the UK
- Peaks @ 5-7 years and adolescence
- Presentation of CYP with new onset T1DM relatively uncommon for General Practitioners

- At diagnosis – DKA rate 27%/year national (12% in our Trust, in last year raised to 27.5%)

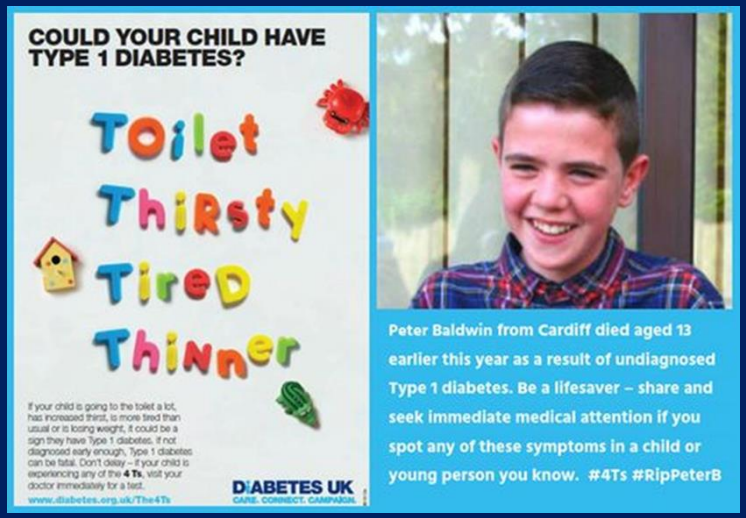
- DKA – mortality of 0.15-0.3%
- DKA – 83% cause of death in Type 1 diabetes

Symptomatic diabetes

- Polydipsia (98%)
- Polyuria (84%)
- Tiredness (76%)
- Weight loss (65%)

- Progress over weeks/sometimes days
- DKA – can develop very quickly
- Known association between DKA at diagnosis and worse long term prognosis
- Blood glucose ≥ 11.1 mmol/l confirms diagnosis
- SAME DAY REFERRAL to Hospital – can avoid deterioration (Referral Pathway)

Importance to avoid delayed diagnosis



GP Referral Pathway

- https://www.enherts-tr.nhs.uk/gps-professionals/key-documents/

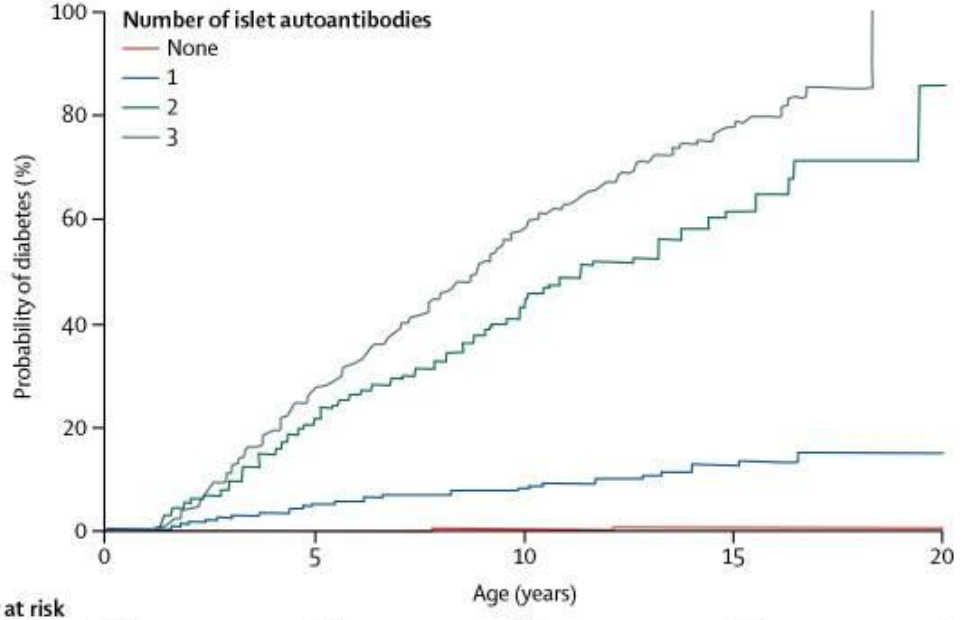
Pathogenesis

- Environmental factors – microbiome – genome - metabolism and immune systems that vary between individual cases

- >90% have al least 1 present antibody: insulin (IAA), glutamate decarboxylase (GADA), islet antigen 2 (IA2), Zinc transporter 8 (ZnT8A)

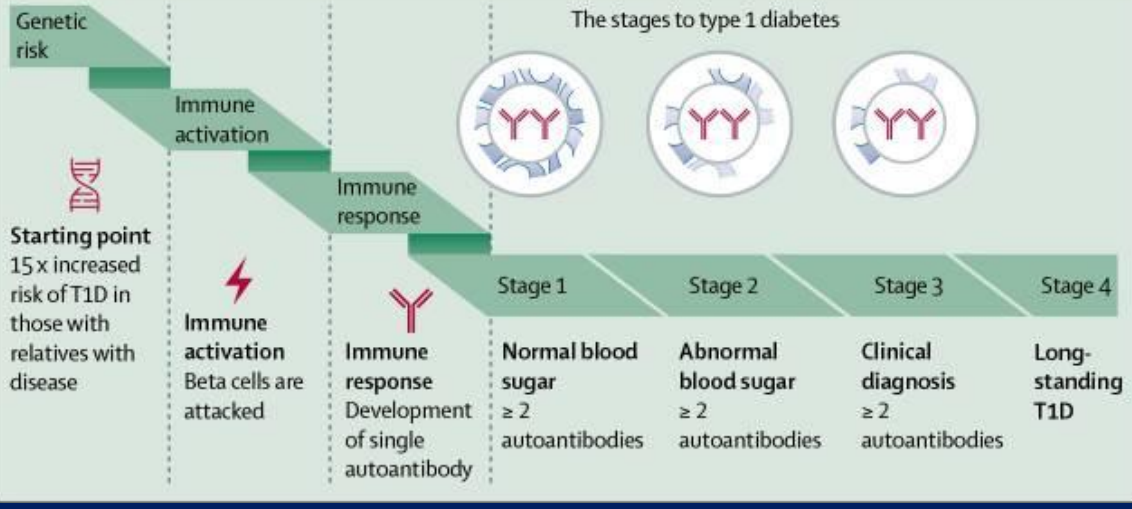
- Peak antibody production < 2 years of age
- 2 or more antibodies – 84% to develop T1DM by the age 18

A



Number at risk					
3 islet autoantibodies	358	250	112	20	0
2 islet autoantibodies	227	168	82	19	1
1 islet autoantibodies	474	430	272	118	9
No islet autoantibodies	12318	8875	5253	1161	44

B



Environmental factors – may contribute to onset

- Enterovirus infections
- In at risk children protective – possibly: breast milk, omega 3, Vitamin D

- On going research studies at Stage1 and Stage 2 diabetes
- Programmes of universal screening for antibodies – Germany/USA
- Trying to stop exposure to environmental factors that trigger the immune response in genetically prone individuals (Primary prevention)
- Immunotherapies – trying to stop progression from stage 1 to stage 2 (Secondary prevention)
- Preserving residual βcell function (Tertiary prevention)

Diabetes Classification

- Type 1 – absolute insulin deficiency, most common in children, 5-10% of all cases; can occur in adults even 8th or 9th decade
- Type 2 – Insulin resistance and a relative inadequate compensatory insulin secretion, 90-95% of all cases
- Monogenic Diabetes – defects in β cell function – MODY

- HNF1α(3), Glucokinase deficiency(2), HNF4α(1), HNF 1β(5)

www.diabetesgenes.org

- Exocrine pancreas: pancreatitis, trauma, CF (CFRD)
- Endocrinopathies (Excess of GH, cortisol, Glucagon, epinephrine) can cause diabetes – resolves when hormone excess resolved

Diabetes Classification

- Genetic Syndromes associated with DM
  (Down's and Turner – higher risk of autoimmune disease)

- Impaired Fasting Glucose (Blood glucose 5.6-6.9mmol/l)

- Impaired Glucose Tolerance (2h OGTT 7.8-11.1mmol/l)

Diagnostic difficulties that may delay referral / diagnosis

- Polyuria and enuresis may be misdiagnosed as a urinary tract infection
- Polydipsia may be thought to be psychogenic
- Vomiting may be misdiagnosed as gastroenteritis or sepsis
- Hyperventilation of ketoacidosis- misdiagnosed as pneumonia / asthma (cough and breathlessness distinguish these); asthma treated with glucocorticoids - exacerbates hyperglycaemia
- Abdominal pain - ketoacidosis may simulate an acute abdomen - referral to a surgeon

DKA at Diagnosis

- Vary worldwide (11-80%) – 59,000 children from 13 countries
- Study over 11 years
- Overall mean prevalence 29.9%
- Younger and ethnic minority groups – increased prevalence

- Burden of DKA remains high
- Education campaigns have not demonstrated uniform results
- Universal screening (antibodies) has not been cosidered cost-effective
- Data – worrying and requires collaboration
- Call for ACTION!

American Diabetes Association. Diabetes Care

Original Research

Impact of Early Diabetic Ketoacidosis on the Developing Brain

Tandy Aye, Paul K. Mazaika, Nelly Mauras, Matthew J. Marzelli, Hanyang Shen, Tamara Hershey, Allison Cato, Stuart A. Weinzimer, Neil H. White, Eva Tsalikian, Booil Jo and Allan L. Reiss, for the Diabetes Research in Children Network (DirecNet) Study Group

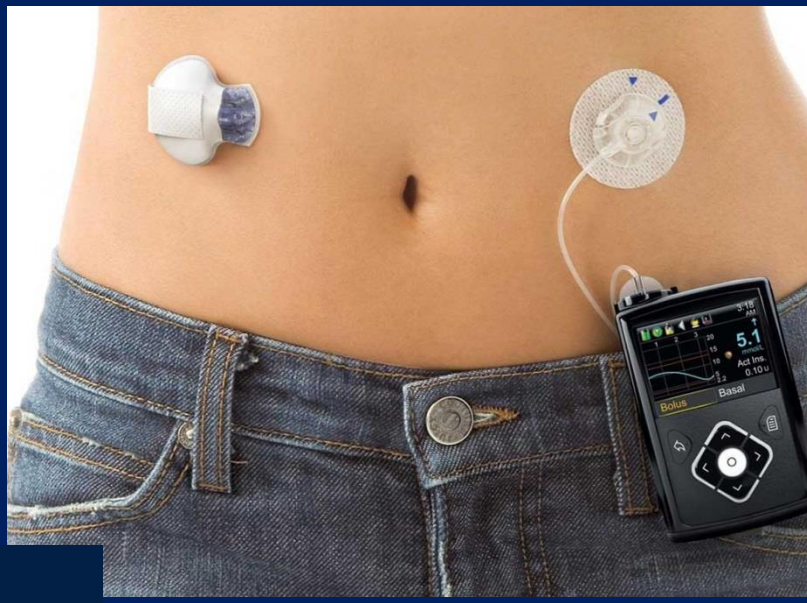
Diabetes Care 2018 Dec; dc181405.
https://doi.org/10.2337/dc18-1405

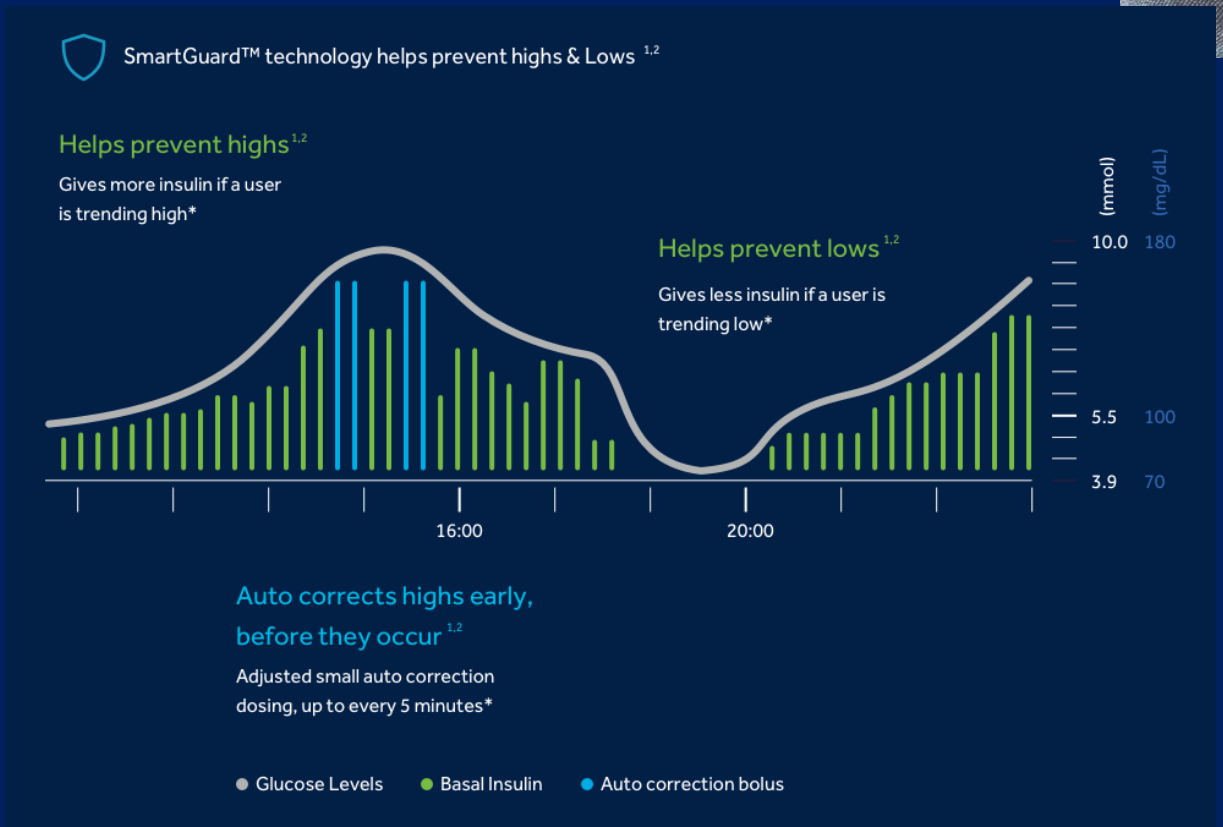
CONCLUSIONS A single episode of moderate/severe DKA in young children at diagnosis is associated with lower cognitive scores and altered brain growth. Further studies are needed to assess whether earlier diagnosis of type 1 diabetes and prevention of DKA may reduce the long-term effect of ketoacidosis on the developing brain.

Technology progress

CSII (Insulin Pumps)

Hybrid loop system





Research – on going

- Early intervention – public health screening for Genetic risk/T cell divergence - train body tolerance to insulin – oral insulin (A Ziegler – Germany) – 0-4 months screened 36509, enrolled 83 (need 1,000)
- TrailNet – presence of autoantibodies in relatives – in those with positive antibodies DKA reduced to 3% when developed T1DM
- INNODIA – Newly diagnosed/Relatives – We are a recruiting centre
- Therapeutics trials trying to modify the immune response – Hydroxychloroquine prevention Study

Take home message

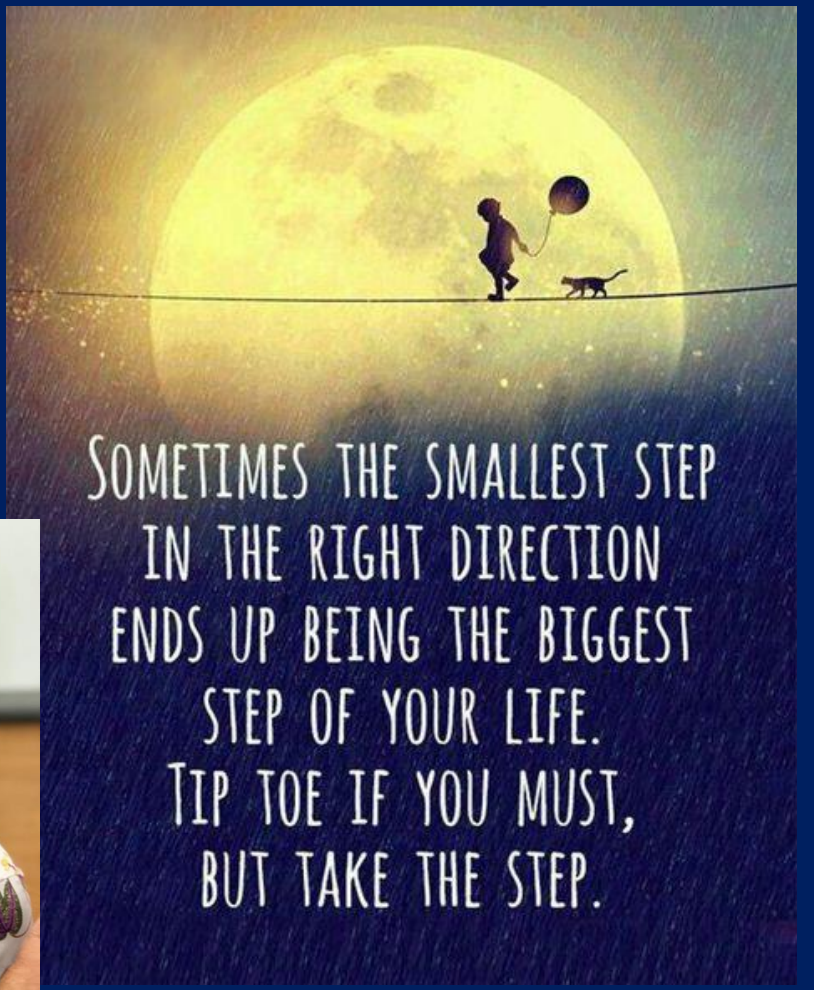
- Research continues….to find a prevention or “Cure”
- Our job is to treat each individual patient - clinical presentation in the complex psycho-social network of family
- Use the most recent available pathways
- Do Not Delay making a diagnosis of Type 1 Diabetes – Please!

Parent Story

Sarah Stockley


9am
5.30pm
2
HOUSEHOLD
KITCHENWARE
LINENS

Questions?


SOMETIMES THE SMALLEST STEP
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TIP TOE IF YOU MUST,
BUT TAKE THE STEP.

References

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