Clinical Practice Consensus Guidelines

A Rosenbloom et al.

Pediatric Diabetes 2009

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GLOBAL IDF/ISPAD GUIDELINE FOR
DIABETES IN CHILDHOOD
AND ADOLESCENCE

www.ispad.org
Patients characteristics T2DM

- Europe/US  obesity (>85%)
- Japan 30% NON obese
- Asian Indian children 50% normal weight
- Taiwan 50% normal weight
• Initial treatment: clinical symptoms dependent → insulin
  → lifestyle: diet-exercise
• Once metabolically ok (1-2 wks post diagnosis)
  Start Metformin (250mg),
  Progressive increase 2x/day till 2x 1000 mg
  transition time for insulin weaning in 2-6w
• Glucose measurements (min) 2x/day
Figure 1. Management of type 2 diabetes mellitus in children and adolescents

**DIAGNOSIS**

- **Random glucose > 250 mg/dL with symptoms and ketosis or ketosis acidosis**
  - Insulin, diet, and exercise, metformin
  - Premeal glucose 90-130 mg/dL
  - Peak postprandial < 180 mg/dL
  - Attempt to wean off insulin

- **Midly symptomatic without ketosis**
  - Asymptomatic
  - Diet and exercise
    - Monthly review
    - Blood glucose < 130/180
    - HbA1c < 7%

- **HbA1c > 7%
  - Blood glucose > 130/180**
  - Metformin
    - Monthly review
    - HbA1c < 7%
  - Blood glucose < 130/180

- **HbA1c > 7%
  - Blood glucose > 130/180**
  - Check compliance
  - Add sulfonylurea or change to insulin glargine + meglitinide

- **HbA1c > 7%
  - Blood glucose > 130/180**
  - Check compliance
  - Add low-dose metformin if on glargine/meglitinide
  - Change to glargine/meglitinide if on metformin/sulfonylurea
  - Consider adding glitazone

* Blood glucose values > 130/180 (7.2/10 mmol/L) refer to self-monitoring of plasma blood glucose values of 90-130 mg/dL (5.0-7.2 mmol/L fasting or preprandial and peak postprandial values of > 180 mg/dL/110 mmol/L).
**Fig. 1.** Treatment decision tree for type 2 diabetes in children and adolescents.
Conclusion ISPAD
IDF-ISPAD

• Diagnostic criteria

• Treatment regimens
  - insulin, metformin, D/E → and ???

• Complication screening in both: high priority

• ISPAD GUIDELINES: revision 2013
Type 2 diabetes: Prevalence and Management in Europe

Professor David Dunger
Professor Tim Barrett
Professor Reinhard Holl

EnprEMA meeting
European Medicines Agency, London 25th February 2013
European Diabetes Registers

• EuroDIAB  Existing diabetes registers

• EnprEMA  Survey

• German Diabetes Register

• UK JUMP Study
<table>
<thead>
<tr>
<th>Country</th>
<th>Name</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>FRANCE</td>
<td>Jean-Jacques Robert</td>
<td>No existing T2D register but plans to establish a Register with the support of the association Aide aux Jeunes Diabetiques</td>
</tr>
<tr>
<td>POLAND</td>
<td>Przemyslawwa Jarosz-Chobot</td>
<td>No existing T2D register. Numbers of patients likely to be very low</td>
</tr>
<tr>
<td>ITALY</td>
<td>Francesco Chiarelli</td>
<td>Network established to collect robust data on T2D in children</td>
</tr>
<tr>
<td>UK</td>
<td>Timothy Barrett</td>
<td>National study of subjects with T2D funded by the MRC has characterised 192 out of an estimated 240 in the UK.</td>
</tr>
<tr>
<td>DENMARK</td>
<td>Henrik Mortensen</td>
<td>All diabetic subjects are registered in the Danish Registry for Childhood and Adolescent Diabetes. 27 subjects have been identified nationally</td>
</tr>
<tr>
<td>GERMANY</td>
<td>Reinhard Holl Olaf Hiort</td>
<td>DPV initiative provides an excellent national register of all paediatric diabetes patients including 860 type 2 patients. Population well characterised and potentially available for data exchange and collaborative studies</td>
</tr>
<tr>
<td>SPAIN</td>
<td>Lourdes Ibanez</td>
<td>4-5 centres doing clinical trials. Investigate possible networks through Spanish Paediatric society.</td>
</tr>
<tr>
<td>SLOVENIA</td>
<td>Tadej Battelino</td>
<td>A national T2D registry for the paediatric age group (0-end of 18y) – not many patients; also impaired glucose tolerance registry (more patients, screened with an OGTT obese children with BMI SDS more</td>
</tr>
<tr>
<td>Country</td>
<td>Name</td>
<td>Information</td>
</tr>
<tr>
<td>--------------</td>
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<td>--------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>LUXEMBOURG</td>
<td>Carine de Beaufort</td>
<td>Currently seeing 2-4 cases aged under 18 years at CB’s clinic. More statistics to follow.</td>
</tr>
<tr>
<td>AUSTRIA</td>
<td>Thomas Pieber</td>
<td>Paediatricians (Austrian Diabetes Incidence Study Group) have a prospective registry for all types of DM including T2 DM since 1999 for the age group &lt; 18 years. The majority of the paediatric diabetes centres participate in DPV.</td>
</tr>
<tr>
<td>FINLAND</td>
<td>Mikael Knip</td>
<td>Finland has a national register for all cases with diabetes diagnosed in pediatric units in. That register started in 2002 and currently they have 5419 registered patients, out of whom 37 (0.7%) have been diagnosed with type 2 diabetes. The number of patients with T2D varies from one to six per year.</td>
</tr>
</tbody>
</table>
## Metabolic outcome - type 2 diabetes

<table>
<thead>
<tr>
<th>Number of centres:</th>
<th>12</th>
</tr>
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<tbody>
<tr>
<td>Number of patients (overall):</td>
<td>57</td>
</tr>
<tr>
<td>Number of visits (overall):</td>
<td>118</td>
</tr>
<tr>
<td>Data status:</td>
<td>2013-01-13, 13:52:09 CET</td>
</tr>
</tbody>
</table>

### HbA1c (type 2 diabetes)

<table>
<thead>
<tr>
<th>HbA1c</th>
<th>Number of patients</th>
<th>Median</th>
<th>&lt; 7.0% percentage and number of patients</th>
<th>7.0% - 7.5% percentage and number of patients</th>
<th>7.5% - 9.0% percentage and number of patients</th>
<th>&gt; 9.0% percentage and number of patients</th>
<th>Patients with at least 4 measurements</th>
</tr>
</thead>
<tbody>
<tr>
<td>all patients</td>
<td>57</td>
<td>6,42</td>
<td>59,65% (34)</td>
<td>10,53% (6)</td>
<td>12,28% (7)</td>
<td>17,54% (10)</td>
<td>15,09%</td>
</tr>
<tr>
<td>&lt; 1 year since diabetes manifestation</td>
<td>6</td>
<td>6,29</td>
<td>83,33% (5)</td>
<td>0,00% (0)</td>
<td>16,67% (1)</td>
<td>0,00% (0)</td>
<td>11,11%</td>
</tr>
<tr>
<td>&gt; 1 year since diabetes manifestation</td>
<td>43</td>
<td>6,80</td>
<td>53,49% (23)</td>
<td>13,95% (6)</td>
<td>13,95% (6)</td>
<td>18,60% (8)</td>
<td>13,33%</td>
</tr>
<tr>
<td>age 0 - &lt;6</td>
<td>1</td>
<td>6,20</td>
<td>100,00% (1)</td>
<td>0,00% (0)</td>
<td>0,00% (0)</td>
<td>0,00% (0)</td>
<td>0,00%</td>
</tr>
<tr>
<td>age 6 - &lt;12</td>
<td>1</td>
<td>8,90</td>
<td>0,00% (0)</td>
<td>0,00% (0)</td>
<td>100,00% (1)</td>
<td>0,00% (0)</td>
<td>100,00%</td>
</tr>
<tr>
<td>age 12 - &lt;18</td>
<td>39</td>
<td>6,20</td>
<td>64,10% (25)</td>
<td>10,26% (4)</td>
<td>10,26% (4)</td>
<td>15,38% (6)</td>
<td>13,89%</td>
</tr>
<tr>
<td>age &gt;= 18</td>
<td>16</td>
<td>7,45</td>
<td>50,00% (8)</td>
<td>12,50% (2)</td>
<td>12,50% (2)</td>
<td>25,00% (4)</td>
<td>6,25%</td>
</tr>
</tbody>
</table>
Type-2-Diabetes in Adolescents – German Data

Dr. med. Dipl.Math Joachim Rosenbauer
German Diabetes Center, Epidemiology
Düsseldorf

Reinhard Holl, MD
DPV coordinator / pediatric endocrinologist / diabetologist,
University of Ulm, Germany
Pediatric Diabetes Incidence registry Northrhine-Westfalia
The number of type-2-DM-patients 5-19 years in Germany is still low.

No increase between 2002 and 2010

Estimated new cases per year in Germany: 130 – 160 (1.0-1.3 per 100,000)

Estimated total number of pediatric type-2 patients in Germany: 580 – 780 (6.0-6.5 per 100,000)
Other population-based data from Germany:

Type-2-diabetes in children and adolescents in Baden-Württemberg

• 56 patients identified

• prevalence: 2.3 per 100,000 (age 0-20 y.)

• mean age at onset: 15.8 years

• extrapolated for Germany: 390 cases

Neu et al., Pediatric Diabetes 2009; 20: 468-473
DPV-Initiative 1995 – 2011

Patient visits: 2,432,466
  outpatient: 2,116,426
  inpatient: 316,040

Patients: 272,657
  pre-DM: 1,761
  type-1-DM: 78,551
  type-2-DM: 172,856
  type-3-DM: 10,019
  gest.-DM: 9,470

Age at onset
  < 18 y.: 63,716
  > 18 y.: 207,180

Participating centers: 370
  pediatric
  internal medicine
Pediatric type-2-patients (0-20 years) available in DPV Database

Cumulative 1995 to 2012
1432 patients
38 % males, 62 % females
14.5 years age at onset
32.3 kg/m² BMI
+2.4 BMI-SDS
33 % migration background

As of January 1st, 2012
517 patients
We are sorry for not being able to join this EnprEMA meeting today,

But we are both happy to cooperate with the initiative in the future

Joachim Rosenbauer
Reinhard Holl
Homepage:  http://www.d-p-v.eu

Funding of DPV-Initiative
JUMP

TYPE 2 DIABETES IN CHILDHOOD: BUILDING A PLATFORM FOR INTERVENTIONS TO PREVENT THE PROGRESSION TO CARDIOVASCULAR DISEASE

Gray Z¹, Ilsley E², Cotter C¹, Ford A³, Turner K⁴, Heywood J⁴, Barnett A², Dunger D⁴, Hamilton-Shield J⁵, Wales J⁶, Barrett T².

¹Birmingham Children’s Hospital NHS Foundation Trust, ²University of Birmingham, ³Sheffield Children’s Hospital NHS Foundation Trust, ⁴University of Cambridge, ⁵University of Bristol, ⁶University of Sheffield
**Introduction**

- Type 2 diabetes reported in children since 1979
- First UK reports 2000
- USA SEARCH, TODAY studies
- Little phenotypic data on UK patients
- UK ethnic minority population from Pakistan, India, Bangladesh, West Indies

RCPCH/DUK ‘snapshot’ 2009
328 ‘paediatrician diagnoses’

Vs ~23,000 Type 1 diabetes
UK childhood T2DM

• UK paediatric type 2 diabetes cohort
  – Characterized by anthropometry, biomarkers, and co-morbidities
  – Other diagnoses (type 1, monogenic) excluded
    • Autoantibody testing University of Bristol
    • Monogenic diabetes testing University of Exeter
  – Chart natural history, co-morbidities
  – Characterise insulin secretory reserve, resistance
  – Cohort for recruitment to clinical trials
Results

- Notified of 256 children with paediatrician diagnosis
- Recruited to end Jan 2013: 175
- Exclusions: 7 secondary diabetes
- Exclusions: 17 pancreatic autoimmunity
- Results showing data for first 156 patients
- M:F ratio 1 : 2.39
- Ethnic origin: 42% white UK, 15% black, 33% S. Asian, 9.0% other, 1% unknown
- Median age at diagnosis 13.4 yrs (range 7.9-17.5)
- 66% osmotic symptoms at presentation, 23% asymptomatic, 4% DKA
- Median diabetes duration 3.25 yrs
Treatment:

- Diet / lifestyle only 8%
- Metformin only 55%
- Metformin and insulin 32%

- UK practice to add insulin:
  - At diagnosis if osmotic symptoms, then wean off
  - if HbA1c persistently greater than 7.5% despite maximal tolerated dose metformin

- Other agents: small numbers only
Conclusions

- T2DM still ~1% of childhood diabetes in UK
- White UK children older at diagnosis than non-white children, more obese
- Trend to ethnic differences in fasting C-peptide, BMI-SDS at diagnosis.
- African-Caribbean UK children have poorer metabolic control, signs of cardiovascular dysfunction compared to White UK and South Asian children.
Acknowledgements

Medicines for Children Research Network nurses

Diabetes research network

Local Principle Investigators round UK

Diabetes UK