MANAGEMENT OF PAEDIATRIC & ADOLESCENT WITH DIABETES MELLITUS

26.3.2016
by
D Leung
Outline

• Type 1 DM
  • Prevalence, pathogenesis and management strategy
  • Special issues in children and adolescents
  • Latest technologies and research

• Type 2 DM
  - Prevalence, pathogenesis and management strategy

• Paediatric DM service in QMH
TYPE 1 DIABETES MELLITUS
How common is type 1 DM?

- 90% of DM in childhood and adolescents
- Great variation in incidence world wide
  - Highest incidence: Finland
    - ~64/100 000/year
  - Lower incidence in Asia
    - China: 0.1/100 000 year
TYPE 1 DIABETES MELLITUS

How common is it in children?
Type 1 DM in HK

Table 2: Comparison of age-specific incidence rates of type 1 diabetes for Hong Kong Chinese/100,000 person/year (1984-1996 vs 1997-2007)

<table>
<thead>
<tr>
<th>Age-groups</th>
<th>1984-1996</th>
<th>1997-2007</th>
<th>Statistical significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-4 years</td>
<td>0.9</td>
<td>2.2</td>
<td>P&lt;0.001</td>
</tr>
<tr>
<td>5-9 years</td>
<td>1.5</td>
<td>2.4</td>
<td>P=0.518</td>
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<tr>
<td>10-14 years</td>
<td>1.7</td>
<td>2.4</td>
<td>P=0.663</td>
</tr>
<tr>
<td>Total 0-14 years</td>
<td>1.4</td>
<td>2.4</td>
<td>P&lt;0.001</td>
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</table>
# Type 1 DM in HK

<table>
<thead>
<tr>
<th>Year</th>
<th>Cases</th>
<th>Population &lt;15 years of age*</th>
<th>Incidence</th>
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<tbody>
<tr>
<td>1997</td>
<td>20</td>
<td>1,162,700</td>
<td>1.7201</td>
</tr>
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<td>1998</td>
<td>21</td>
<td>1,154,600</td>
<td>1.8188</td>
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<td>1999</td>
<td>24</td>
<td>1,137,400</td>
<td>2.1101</td>
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<tr>
<td>2000</td>
<td>26</td>
<td>1,114,800</td>
<td>2.3323</td>
</tr>
<tr>
<td>2001</td>
<td>28</td>
<td>1,083,400</td>
<td>2.5845</td>
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<td>2002</td>
<td>37</td>
<td>1,051,200</td>
<td>3.5198</td>
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<td>2003</td>
<td>32</td>
<td>1,023,300</td>
<td>3.1271</td>
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<td>2004</td>
<td>25</td>
<td>984,300</td>
<td>2.5399</td>
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<td>2005</td>
<td>33</td>
<td>948,500</td>
<td>3.4792</td>
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<tr>
<td>2006</td>
<td>24</td>
<td>935,800</td>
<td>2.5647</td>
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<td>2007</td>
<td>23</td>
<td>909,600</td>
<td>2.5286</td>
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</table>

*Population estimation based on 2001 census

HKJ Paediatr (New Series) 2009;14:252-259
Type 1 DM in HK

<table>
<thead>
<tr>
<th>Age groups</th>
<th>Cases (n)</th>
<th>Age-specific population*</th>
<th>Incidence#</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-4 years</td>
<td>65</td>
<td>261,800</td>
<td>2.2</td>
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<tr>
<td>5-9 years</td>
<td>110</td>
<td>391,700</td>
<td>2.4</td>
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<td>10-14 years</td>
<td>118</td>
<td>429,900</td>
<td>2.4</td>
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<tr>
<td>15-18 years</td>
<td>42</td>
<td>348,400</td>
<td>1.0</td>
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<tr>
<td>Total 0-14 years</td>
<td>293</td>
<td>1,083,400</td>
<td>2.4</td>
</tr>
<tr>
<td>Total 0-18 years</td>
<td>335</td>
<td>1,431,800</td>
<td>2.0</td>
</tr>
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</table>

* According to Hong Kong Resident Population as at End-2001
# Incidence rate was age-adjusted to the world's population of WHO World Standard (2000-2025)
Type 1 DM

- An absolute deficiency of insulin secretion
- Prone to ketoacidosis
- T-cell mediated pancreatic islet β-cell destruction
  - Occurs at a variable rate
TYPE 1 DIABETES MELLITUS

How do they present?
Type 1 DM: clinical presentation

- Clinical presentation
  - Polyuria, polydipsia, nocturia, enuresis, polyphagia…
  - Weight loss, failure to thrive…
  - Fatigue, irritability, decrease in school performance
  - Recurrent skin infection
  - Vaginal candidiasis
  - Severe dehydration, DKA…
Diabetic Ketoacidosis in Children

- Vomiting and abdominal pain
- Hyperventilation (Kussmaul respiration)
  - High respiratory rate and large tidal volume of each breath, which gives it a sighing quality
- Disordered sensorium
- Decreased peripheral circulation with rapid pulse rate
- Hypotension and shock with peripheral cyanosis
  - A late sign and rare in children with diabetic ketoacidosis
Diagnostic Difficulties

• Very young children may present in severe ketoacidosis because of a more rapid onset of severe insulin deficiency

• **Wrong/delayed in diagnosis**
  • Hyperventilation → pneumonia or asthma
  • Abdominal pain → acute abdomen/mesenteric adenitis
  • Polyuria and enuresis → UTI
  • Polydipsia → psychogenic, anxious child
  • Vomiting → gastroenteritis or sepsis

• If a child is diagnosed with diabetes in the presence of symptoms: **immediate** referral is mandatory
  • Prevent rapid deterioration into ketoacidosis
Diagnosis of diabetes

1. Symptoms of diabetes plus casual plasma glucose concentration $\geq 11.1$ mmol/l (200 mg/dl)*.
   Casual is defined as any time of day without regard to time since last meal.

or

2. Fasting plasma glucose $\geq 7.0$ mmol/l (126 mg/dl) †.
   Fasting is defined as no caloric intake for at least 8 hours.

or

3. 2 hour postload glucose $\geq 11.1$ mmol/l (200 mg/dl) during an OGTT.
   The test should be performed as described by WHO (1), using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water or 1.75 g/kg of body weight to a maximum of 75 g (2).

4. HbA$_1c$ $\geq 6.5$.
   However, there are difficulties with assay standardisation and individual variation in the relationship between blood glucose and HbA$_1c$ which may outweigh the convenience of this test.

* Corresponding values are $\geq 10.0$ mmol/l for venous whole blood and $\geq 11.1$ mmol/l for capillary whole blood

† $\geq 6.3$ mmol/l for both venous and capillary whole blood

Prediabetes includes Impaired Glucose Tolerance (IGT) and Impaired Fasting Glycaemia (IFG)

- IGT: 2 hour postload plasma glucose 7.8-11.1 mmol/l (140-199 mg/dl)
- IFG: plasma glucose 5.6-6.9 mmol/l (100-125 mg/dl)
Diagnosis of type 1 DM

- Rarely by OGTT
- Already diagnostic if
  - Classical symptoms
  - RG $\geq 11.1$ mmol/L
  - +/- Ketosis (in urine/blood)
  - +/- Evidence of islet cell autoimmunity
    - Islet cell Ab markers (GAD, ICA, IAA Ab)
    - 85-90% in Caucasian
    - <20% in Chinese only
After diagnosis…

- Insulin therapy
  - Started as soon as the diagnosis to prevent development of life-threatening ketoacidosis
Break the news

- Not just fact telling
- Avoid too much information
- Acknowledge their feelings
- Encourage them to express the feelings
- Normal to feel shocked, depressed, helpless…
What so special with DM care?

• Requires **self-management** by patient/their carers/family in their **local environments**
  • Practical guidance and skilled training
  • Consistent and repeated education advice
  • Psychological needs
    • Emotional well-being strongly associated with positive diabetic outcomes
• Develop close links and communication with patient’s local environment, including carers, school and family doctors..etc
Principles of diabetic treatment

- Insulin therapy
- Dietary control
- Self blood glucose monitoring
- Exercise program
Principles of diabetic treatment

• Insulin therapy
• Dietary control
• Self blood glucose monitoring
• Exercise program
Normal insulin profile
Insulin therapy - principles

- **Bolus** to match glycaemic effect of meal
- **Constant basal** requirement throughout 24 hours
- **Usual dose**
  - Prepubertal: 0.7-1 u/kg/d
  - Partial remission phase: <0.5u/kg/d - 0u/kg/d
  - Puberty: 1-2u/kg/d
Commonly used insulin regimens in children

- 2 daily injections
  - Mixture of short and intermediate insulin before breakfast and before dinner
Commonly used insulin regimens in children

- 4 daily injections
  - Bolus short/ultra short acting insulin before main meals + intermediate/long acting basal insulin once a day
Various insulin and their profiles
### Various insulin and their profiles

<table>
<thead>
<tr>
<th>Insulin preparation</th>
<th>Brand name</th>
<th>Onset of action</th>
<th>Peak action</th>
<th>Effective duration</th>
<th>Maximum duration</th>
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</thead>
<tbody>
<tr>
<td><strong>Rapid-acting analogues</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insulin Lispro</td>
<td>Humalog</td>
<td>15-30min</td>
<td>30-75min</td>
<td>3-4hr</td>
<td>4-6hr</td>
</tr>
<tr>
<td>Insulin Aspart</td>
<td>Novorapid</td>
<td>15-30min</td>
<td>35-75min</td>
<td>3-4hr</td>
<td>4-6hr</td>
</tr>
<tr>
<td>Insulin Glulisine</td>
<td>Apidra</td>
<td>15-30min</td>
<td>30-75min</td>
<td>3-4hr</td>
<td>4-6hr</td>
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<tr>
<td><strong>Short-acting</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Regular insulin</td>
<td>Actrapid HM</td>
<td>30-60min</td>
<td>2-3hr</td>
<td>3-6hr</td>
<td>6-8hr</td>
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<tr>
<td><strong>Intermediate-acting</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NPH (isophane)</td>
<td>Protaphane HM</td>
<td>2-4hr</td>
<td>6-10hr</td>
<td>10-16hr</td>
<td>14-18hr</td>
</tr>
<tr>
<td><strong>Long-acting analogue</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insulin glargine</td>
<td>Lantus</td>
<td>3-4hr</td>
<td>8-16hr</td>
<td>18-20hr</td>
<td>20-24hr</td>
</tr>
<tr>
<td>Insulin detemir</td>
<td>Levemir</td>
<td>??3-4hr</td>
<td>6-8hr</td>
<td>14hr</td>
<td>Up to 20-24hr</td>
</tr>
</tbody>
</table>
Insulin therapy in paediatric patients

- Number of injection per day
  - Parents/carer’s availability and acceptance
  - Sites available
- Small dose of insulin
  - Use of special pen/needle with 0.5 unit markings
  - Use of diluent
- Use of fine needle
- Allow parents to try how it feels like to have insulin injection and finger prick
Factors affecting insulin action

- Subcutaneous blood flow
  - Increased by: heat, exercise
  - Decreased by: cold
- Injection depth
  - Faster after IM injection
- Injection site
  - Abdomen > buttock > thigh
- Massage
- Subcutaneous fat thickness
- Injection at lipohypertrophy site/fatty lumps
  - Slower and more erratic absorption
- Concentration of insulin
Principles of diabetic treatment

- Insulin therapy
- Dietary control
- Self blood glucose monitoring
- Exercise program
Dietary control

• Adequate energy and nutrition for optimal growth and development
• Healthy eating habits
• Aim at
  • Good glycaemic control
  • Ideal body weight
  • Prevent acute and long term complications
A typical DM diet order

- 1500 kcal DM diet
- CHO: 50/10/60/10/65/10 gram

55% total calories from CHO

= 825 kcal as CHO
= ~206 gram CHO

1 gram CHO = 4 kcal
10 gram = 1 portion CHO
Dietary control

• Carbohydrate counting
• Food label
• Glycaemic index
Glycaemic index

How fast does your food work?

Glucose drink
Glucose tablet
Glucose gel
Honey
Lemonade
Fruit syrup
**Milk**
Ice cream
Chocolate bar
Principles of diabetic treatment

- Insulin therapy
- Dietary control
- Self blood glucose monitoring
- Exercise program
Self blood glucose monitoring

- Good correlation between frequency of monitoring and glycaemic control
  - Allow patients to evaluate their individual response to therapy & whether glycaemic targets are achieved

- Four times daily if on multiple insulin injections or insulin pump
  - Different times in the day including nocturnal
  - Pre-meal (> 2 hrs) and post-meal (< 2 hrs)
  - To confirm hypoglycaemia and to monitor recovery
  - During inter-current illness to prevent DKA
  - In association with vigorous sports/↑activity
Choice of glucometer/prick in children

- Less blood required
- Finer needle
- Simple usage by kid
# Targets of DM control by age group

<table>
<thead>
<tr>
<th>Age Group</th>
<th>ADA Before meals (mmol/L)</th>
<th>ADA Post-meals (mmol/L)</th>
<th>ADA Bedtime (mmol/L)</th>
<th>ADA HbA1c (%)</th>
<th>ISPAD Before meals (mmol/L)</th>
<th>ISPAD Post-meals (mmol/L)</th>
<th>ISPAD Bedtime (mmol/L)</th>
<th>ISPAD HbA1c (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-6 yo</td>
<td>5.6-10</td>
<td>--</td>
<td>6.1-11.1</td>
<td>&lt;8.5</td>
<td>5-8</td>
<td>5-10</td>
<td>6.7-10</td>
<td>&lt;7.5</td>
</tr>
<tr>
<td>6-12 yo</td>
<td>5-10</td>
<td>--</td>
<td>5.6-10</td>
<td>&lt;8</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>13-19yo</td>
<td>5-7.2</td>
<td>--</td>
<td>5-8.3</td>
<td>&lt;7.5</td>
<td></td>
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<td></td>
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</tr>
</tbody>
</table>

ADA, Diabetes Care 2011; 34: S39
ISPAD/IDF Clinical Practice Consensus Guidelines 2011
Target of DM control

- Individualized based on benefit-risk assessment
  - No DKA
  - Minimal hypoglycaemia
- ADA and ISPAD/IDF recommendation 2011
  - HbA1c targets < 7.5%
    - Each 1% reduction leads to 15 to 30% reduction in long term health risks
    - HbA1c < 7% reduce your risk dramatically
    - Lower goal (< 7%) is reasonable if it could be achieved without excessive hypoglycaemia
Principles of diabetic treatment

• Insulin therapy
• Dietary control
• Self blood glucose monitoring
• Exercise program
Exercise

• Measure blood glucose before exercise, and prn during exercise
• Insulin dose prior to exercise may often need to be decreased
• ~ 1-1.5 g CHO/kg body weight/hour during strenuous exercise if no insulin reduction
• Hypoglycaemia may be anticipated during or shortly after exercise but also up to 24 hours afterwards
• Post-exercise nocturnal hypoglycaemia
  Particularly if bedtime blood glucose < 7.0mmol/L
• Unaccustomed exercise e.g. at a diabetes camp
  • A significant reduction in total daily dose of insulin (20-50%) may be necessary to avoid hypoglycaemia
Potential acute problems in type 1 DM

- Sick days
- Hypoglycaemia
- Diabetic ketoacidosis
Sick days in DM

- Increased blood glucose
  - Higher levels of stress hormones, gluconeogenesis and insulin resistance

- Decreased blood glucose
  - Poor oral intake and vomiting
    - Give insulin after meal

- Never stop insulin

- More frequent BG monitoring and urinary ketone test

- Replace meals with easily digestable food and sugar-containing fluids

- Adequate hydration

- Flu vaccine every year
Hypoglycaemia

- A mismatch between insulin, oral intake and exercise
- Usually defined as blood glucose < 4 mmol/L
- Symptomatic hypoglycaemia resulting from autonomic activation or neuroglycopenia
  - Autonomic: hunger, trembling, palpitations, pallor, sweating
  - Neuroglycopenic: Dizziness, headache, change in mood, confusion, convulsion
- Blood glucose for cognitive impairment usually at 2.6-3.5 mmol/L

http://www.diabetesinfo.org.au/
Hypoglycaemic unawareness

• Develops if frequent hypoglycaemia
  • Body’s defense mechanisms against hypoglycaemia reset their level for symptoms
  • Defective glucagon, hydrocortisone and catecholamine counter-regulation

• Could be reverted with avoiding hypoglycaemia for 2 weeks
Nocturnal hypoglycaemia

- Usually asymptomatic
  - Counter-regulatory responses may be impaired during sleep

- Suspect when
  - Pre-breakfast BG fluctuates (Somogyi effect)
  - Headache, nightmares, sweating at night
  - Urine ketone +ve in early morning

- Confirmed by
  - Blood glucose at 2-3 am
  - CGMS
Somogyi effect

• Somogyi effect
  • Rebound of blood glucose in morning after nocturnal hypoglycaemia by counter-regulatory mechanisms
  • Suspect if
    • High blood glucose in morning despite progressive increase long acting insulin at night
    • Morning urine ketone
Dawn phenomenon

• Blood glucose tends to increase in early morning
  • Increase nocturnal growth hormone
  • Increase insulin resistance
  • Increase hepatic glucose production
  • +/- waning effect of intermediate insulin
Exercise related hypoglycaemia

- Can occur during, immediately after or up to 24 hrs after exercise
- Change in insulin resistance
- Prevented by
  - Extra snacks before exercise
    - Small rapidly absorbed carbohydrate for light exercise
    - Slowly absorbed carbohydrate for strenuous and prolonged exercise
  - Extra snack before bed for strenuous exercise in the afternoon or evening
  - Reduce insulin dose
  - Monitor BG before exercise
Management of hypoglycemia

- **Document**
- **If fully conscious**
  - 10 g glucose orally (or 0.3 g/kg)
  - Further 10 g glucose if no improvement by 3-5 minutes
  - Complex carbohydrate afterwards if far from meal times
- **If unconscious**
  - Glucagon injection
    - < 12 years: 0.5 mg
    - > 12 years: 1 mg
- **Find out the cause**
  - Too much insulin/increased exercise/decreased intake?
HYPOGLYCAEMIA MANAGEMENT

HYPOGLYCAEMIA

Hypoglycaemia: d’stix <4mmol/L
Ask for contributing factors (see table in appendix D)

Unconscious or confused?

Yes

Give glucagon IM:
- <6y: 0.5mg (0.5 vial)
- >6y: 1mg (1 vial)

- Recovery position
- Call ambulance

No

Give 10gram high GI CHO (e.g. juice)
Give extra 10gram complex CHO (e.g. biscuits) if d’stix <3mmol/L & not before regular meal time
Repeat d’stix in 30min

D’stix still <4mmol/L

Give additional 10gram high GI CHO (e.g. juice)
Repeat d’stix in 30min

D’stix >4mmol/L

Continue with usual management

D’stix still <4mmol/L

Inform endocrine/general on-call MO (dect phone: 1279)
Consider giving glucagon as above

HYPOGLYCAEMIA MANAGEMENT (DM HOTLINE)
Diabetic ketoacidosis

- Potentially fatal
- Death from cerebral oedema
- Can usually be prevented except in newly diagnosed patients
  - Appropriate management during inter-current illness
  - Avoid insulin omission and poor control

- Diagnosis
  - Hyperglycaemia (usually BS > 11 mmol/L)
  - Ketosis
  - pH < 7.3
  - Bicarbonate < 15 mmol/L and
Management of DKA

- Fluid resuscitation and rehydration
- Insulin (IV)
- Look out for complications
- Treat occult infection
Hyponatraemia: D’stix > 15mmol/L
Encourage clear fluid if child can tolerate
Ask for contributing factors (see table in appendix D)

Impaired consciousness or severe vomiting?

Yes

Call an ambulance and bring to hospital

No

Urine ketones +ve

Yes

Give 10% total daily dose as short acting insulin (in addition to usual insulin)

No

Observe and repeat d’stix in 2 hrs

Repeat d’stix and urine ketones in 2 hours

No improvement in d’stix & urine ketones still +ve

Give further 10% of total daily dose as short acting insulin +/- advise to come to hospital

Some improvements in D’stix (but still >15mmol/L) & ketones -ve/decrease

Continue monitoring and repeat d’stix in 2 hours

D’stix <15mmol/L

Observe

HYPERGLYCAEMIA MANAGEMENT (DM HOTLINE)
Upon discharge of a newly diagnose DM…

- Completed DM education
  - Knowledge on DM
  - Insulin injection and SBGM technique
  - CHO counting/reading food label
  - Basic insulin adjustment
  - Hypoglycaemia management
  - Sick day management
- Letter/education pack +/- visit to school
- DM hotline
- Referral to clinical psychology service
- Referral to patient support group
Our smart but cunning kids…

- Recurrent hypoglycaemia
  - Genuine vs. tricks for sweets
- High HbA1c with weight loss
- Perfect readings on record book but high HbA1c
  - Glucometer history, average readings etc.
- Skipping insulin
  - Fear of letting others know – fear of being abnormal
  - Acceptance of condition
Adolescents with diabetes

- Respect the young adults
  - Confidentiality
  - Avoid direct confrontation
  - Understand their concern
  - Listen and feed back
  - Empowerment
- Encourage appropriate involvement but not excessive control by parents
NEWER TECHNOLOGIES/RESEARCH IN TYPE 1 DIABETES MELLITUS.

Newer technologies/research in type 1 diabetes mellitus.
Continuous subcutaneous insulin infusion (CSII or insulin pump)

- Constant, continuous infusion of a short acting insulin
- Allow a close to physiologic insulin delivery
  - Basal rates programmed over 24 hours with circadian rhythms
- Delivery of extremely small amounts of insulin in very young children
Continuous subcutaneous insulin infusion

- Basal rates
  - 4-6 basal rates/day
  - Depends on age and time of day
  - Usually not exceed 30-40% of total daily insulin

- CHO insulin ratio
  - Depends on circadian variation in insulin sensitivity

- Correction bolus

- 3 different ways of bolus delivery
  - Standard shot bolus, square wave over extended period, dual-wave
Benefits of CSII

- Significant reduction of severe hypoglycemia, especially nocturnal hypoglycemia
- Reduction of HbA1c and an improvement of metabolic control has been reported in short term and in some but not all long term studies
- Ketoacidosis rate did not increase in insulin pump therapy
Potential problems of CSII

- Local infections and dermatological changes
- DKA if blocked tubing/machine failure
- Technical support
- Requires patients and carers understanding on diabetes e.g. CHO counting
- Magical thinking: “pump control is less work”
- Omitted or forgotten insulin boluses
- Cost (machine $60,000; Accessory $2,000 per month; 5-6 pt, >12 yrs, mostly Caucasian)
How effective is CSII?

- **PedPump study** Average HbA1c 8.0 ± 1.3% in 1041 children
  - Preschool: 7.5 ± 0.9%
  - Pre-adolescent: 7.7 ± 1.0%
- Historical controls of MDI in 2780 patients in Hvidore Study = 8.6 ± 1.6% (1995)
- Rate of severe hypoglycaemia 10x lower

  *Diabetologia 2008; 51: 1594-601*

- **Multicentre, matched-pair cohort analysis over 3-year**
  - Similar glycaemic control
  - Significantly reduced rates of hypoglycaemia and DKA
  - Lower insulin requirement
  - Rapid decrease in HBA1c in first months up to 1 year, followed by rebound

  *Diabet Med 2008; 25: 80-5*
How effective is CSII?

- Cochrane Metabolic & Endocrine disorders group
  - 23 RCTs, 976 patients
  - Weighted mean difference in HbA1c -0.3%
  - Reduced severe hypoglycaemia

  *Cochrane Database Syst Rev 2010;1:CD 005103*

- Meta-analyses of RCTs in children
  - Pooled weighted mean HbA1c reduction -0.24%

  *Pediatr Diabetes 2009; 10: 52-8*

- HbA1c changing from split mix insulin to basal-bolus insulin to CSII
  - No difference in HbA1c up to 1 year
  - Burn out effect at 1 year

  *J Pediatr Endocrinol Metab 2011; 24: 369-71*
Continuous glucose monitoring system (CGMS)

- Measurement of subcutaneous/interstitial glucose concentration every 1-5 mins
  - Lag time: 7-15 min
  - Info on trend of glucose excursions
  - Alarms for values exceeding preset levels
  - FDA – not ‘stand alone’ device for insulin adjustment decisions
  - RT-CGMS CANNOT replace fingerpick!!
Sensor-Augmented Insulin Pump Therapy

- 2 components
  - RT-CGMS
  - Insulin Pump

- Potential candidate
  - Frequent SMBG
  - Motivated to improve glycemic control
  - Adherence
  - Family support
  - Carbohydrate counting
  - Diabetes Knowledge
  - Insurance Coverage
**Pancreatic islets transplant**

- Minimal invasive procedure

- US Collaboration islet transplant registry
  - Insulin independence at 3 years
    - 1999-2002 (n = 214): 27%
    - 2003-2006 (n = 255): 37%
    - 2007-2010 (n = 208): 44%

- Risks/problems
  - Procedure-related
  - Immunosuppressive drugs
  - Shortage of islets

National Diabetes Information Clearinghouse
# Table 1. Recent trials of immunotherapy in Type 1 diabetes.

<table>
<thead>
<tr>
<th>Immunotherapy</th>
<th>Type of immunotherapy</th>
<th>Participants (n)</th>
<th>Dosing</th>
<th>Duration (time of evaluation after end of treatment)</th>
<th>Main outcome</th>
<th>Preservation of C-peptide secretion</th>
<th>Decrease in insulin requirements/secondary outcomes</th>
<th>Adverse events</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>GAD vaccine</td>
<td>Autoantigen-based therapy</td>
<td>334 (1:1:1)</td>
<td>Group 1: four injections of 20 µg; Group 2: two injections of 20 µg on days 1, 30, 90 and 270</td>
<td>15 months (6 months after end of treatment)</td>
<td>Change in stimulated C-peptide (MMTT)</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>GAD vaccine</td>
<td>Autoantigen-based therapy</td>
<td>145 (1:1:1)</td>
<td>Group 1: three injections of 20 µg; Group 2: two injections of 20 µg on day 1, week 4 and 12</td>
<td>1 year (9 months after end of treatment)</td>
<td>C-peptide AUC (MMTT)</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>Teplizumab</td>
<td>Anti-CD3 monoclonal antibody</td>
<td>516 (2:1:1:1)</td>
<td>Group 1: 14 days, ~9 mg/m² total dose; Group 2: 14 days, ~3 mg/m² total dose; Group 3: 6 days, ~2.4 mg/m² total dose</td>
<td>1 year (11.5 months after end of treatment)</td>
<td>HbA1c &lt;6.5% and insulin; dose &lt;0.5 U/kg/day at 1 year</td>
<td>Yes</td>
<td>Decrease in insulin requirements</td>
<td>Rash, leukopenia and cytokine-release syndrome (rare)</td>
<td></td>
</tr>
<tr>
<td>Otleixumab</td>
<td>Anti-CD3 monoclonal antibody</td>
<td>208 (2:1)</td>
<td>8 days, 3.1 mg total dose</td>
<td>1 year (11.7 months after end of treatment)</td>
<td>C-peptide AUC (MMTT)</td>
<td>No</td>
<td>No</td>
<td>Constitutional symptoms</td>
<td></td>
</tr>
<tr>
<td>Abatacept</td>
<td>CTL44-Ig fusion protein</td>
<td>112 (2:1)</td>
<td>10 mg/kg on day 1, 14, 28 and then monthly over 2 years</td>
<td>2 years (end of treatment)</td>
<td>C-peptide AUC (MMTT)</td>
<td>Yes</td>
<td>Lower insulin dose at 6 months and 1 year but not at 2 years</td>
<td>Constitutional symptoms</td>
<td></td>
</tr>
<tr>
<td>DiaPep277®</td>
<td>Autoantigen-based therapy/T-cell modulator</td>
<td>457 (1:1)</td>
<td>Nine injections of 1 mg on day 0, month 1, month 3, then every 3 months</td>
<td>2 years (3 months after end of treatment)</td>
<td>Glucagon-stimulated C-peptide</td>
<td>Yes</td>
<td>Higher number of subjects with treat-to-target HbA1c &lt;7%</td>
<td>No</td>
<td></td>
</tr>
</tbody>
</table>
Autologous nonmyeloablative hematopoietic stem cell transplantation

- In newly diagnosed T1 DM
  - Stop autoimmune destruction of B-cells with immunosuppressant
    - Residual B-cell function
  - Reset the immune system
    - Hematopoietic stem cells mobilized GCSF → collected from peripheral blood by leukapheresis and cryopreserved → injected intravenously after conditioning

- Different conditioning regimen
  - Cyclophosphamide
  - Antithymocyte globulin
TYPE 2 DIABETES MELLITUS
TYPE 2 DIABETES MELLITUS

How do they present?
Type 2 DM in children and adolescent

- Uncommon in the past → more common now
- Parallel increase with emergence of childhood obesity
Type 2 DM in HK

Figure 3  Time trends in incidence of type 2 diabetes for 0-18 year-old in Hong Kong from 1997 to 2007.
Type 2 DM in HK

<table>
<thead>
<tr>
<th>Year</th>
<th>Cases</th>
<th>Population &lt;19 years of age*</th>
<th>Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>1997</td>
<td>3</td>
<td>1,537,100</td>
<td>0.1952</td>
</tr>
<tr>
<td>1998</td>
<td>4</td>
<td>1,530,800</td>
<td>0.2613</td>
</tr>
<tr>
<td>1999</td>
<td>6</td>
<td>1,505,500</td>
<td>0.3985</td>
</tr>
<tr>
<td>2000</td>
<td>8</td>
<td>1,477,800</td>
<td>0.5413</td>
</tr>
<tr>
<td>2001</td>
<td>12</td>
<td>1,431,800</td>
<td>0.8381</td>
</tr>
<tr>
<td>2002</td>
<td>14</td>
<td>1,392,300</td>
<td>1.0055</td>
</tr>
<tr>
<td>2003</td>
<td>13</td>
<td>1,368,700</td>
<td>0.9498</td>
</tr>
<tr>
<td>2004</td>
<td>17</td>
<td>1,329,000</td>
<td>1.2792</td>
</tr>
<tr>
<td>2005</td>
<td>52</td>
<td>1,300,700</td>
<td>3.9978</td>
</tr>
<tr>
<td>2006</td>
<td>36</td>
<td>1,290,800</td>
<td>2.7890</td>
</tr>
<tr>
<td>2007</td>
<td>33</td>
<td>1,260,300</td>
<td>2.6184</td>
</tr>
</tbody>
</table>

*Population estimation based on 2001 census
Type 2 DM in HK

<table>
<thead>
<tr>
<th>Age-groups</th>
<th>Cases (n)</th>
<th>Age-specific population*</th>
<th>Incidence#</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-4 years</td>
<td>0</td>
<td>261,800</td>
<td>0</td>
</tr>
<tr>
<td>5-9 years</td>
<td>3</td>
<td>391,700</td>
<td>0.1</td>
</tr>
<tr>
<td>10-14 years</td>
<td>114</td>
<td>429,900</td>
<td>2.3</td>
</tr>
<tr>
<td>15-18 years</td>
<td>81</td>
<td>348,400</td>
<td>2.0</td>
</tr>
<tr>
<td>Total 0-14 years</td>
<td>117</td>
<td>1,083,400</td>
<td>0.9</td>
</tr>
<tr>
<td>Total 0-18 years</td>
<td>198</td>
<td>1,431,800</td>
<td>1.2</td>
</tr>
</tbody>
</table>

* According to Hong Kong Resident Population as at End-2001
# Incidence rate was age-adjusted to the world’s population of WHO World Standard (2000-2025)
Pathogenesis of type 2 DM

1. The stomach changes food into glucose.
2. Glucose enters the bloodstream.
3. The pancreas makes insulin.
4. Insulin enters the bloodstream.
5. Glucose can’t get into the cells of the body. Glucose builds up in the blood vessels.
Clinical presentation of Type 2 DM

- Wide range of presentation
  - Insulin deficiency (DKA) to mild incidental hyperglycaemia
  - Incidental finding on health screening (targeted vs. routine)
  - Obesity → fasting blood/OGTT
  - Weight loss in an obese kid
- Mean age at diagnosis: 13.5y, majority in mid-puberty
- Most associated with obesity and peripheral insulin resistance in ethnic minority groups with a family history of type 2 DM
- Absence to 15-40% of autoimmunity
  - Antibody +ve patients are significantly less overweight, younger, have higher HbA1c and earlier need for insulin
- Female : male = 1.6:1 to 3:1

J Pediatr Endocrinol Metab 2002; 15: 525-30
Type 2 DM

- Comorbidities of insulin resistance (cardiovascular risks) commonly seen at diagnosis or appear early in course of T2DM
  - These should be tested for earlier than in T1DM!!
- Insidious onset, unknown duration of IGT and lipid dysmetabolism of T2DM → may be associated with micro- and macro-vascular disease at diagnosis
  - Importance of treating of comorbidities
Risk factors associated with type 2 DM in children

- Ethnicity
- Obesity
- Family history of type 2 DM
- Acanthosis nigricans
- Small for gestational age

Management of type 2 DM in children

• Life style modification
  • Diet control and exercises
  • Weight reduction

• Medical treatment
  • OHA
    • Biguanides (Metformin), sulphonylureas, glucosidase inhibitors (Acarbose), thiazolidinediones
  • Insulin
  • Incretin-based therapies - ? In children
Initial medical treatment in type 2 DM

- Determined by symptoms, severity of hyperglycaemia, and presence or absence of ketosis/ketoacidosis
- Those with symptoms, particularly vomiting, can deteriorate rapidly and need urgent assessment and appropriate treatment.
  - Insulin may be required for initial metabolic stabilization if significant hyperglycaemia and ketosis is present, even in the absence of ketoacidosis
Management of type 2 diabetes mellitus in children and adolescents

Global IDF/ISPAD Guideline for Diabetes in Childhood and Adolescence 2011
Complication testing specific to type 2 diabetes in young people

• Microalbuminuria or macroalbuminurina
  • At diagnosis → annually
  • Elevated levels of urine albumin should be confirmed on two of three samples.
• Blood pressure every visit
• Lipids screening
  • Soon after diagnosis when blood glucose control has been achieved and annually thereafter
• Non-alcoholic fatty liver disease (NAFLD)
  • At diagnosis and annually thereafter
• Retinopathy
  • At diagnosis and annually thereafter
• History for PCOS, OSA
PAEDIATRIC DM SERVICES IN QMH
Paediatric DM Services in QMH

- DM education
- 24hour diabetes hotline and E-mail
- Annually diabetes complication screening
- Outpatient diabetic clinic:
  - Endocrinologist clinic
  - DM nurse clinic
Aim:

- Encourage and empower patients to take more responsibilities for their own optimal diabetic care.
DM Education(2)

• **Essential elements** for looking after children with diabetes from day to day and in special situations (e.g., illness, travel).

• Provided by the diabetes team (Pediatric endocrinologists, diabetes nurses, dietitian and clinical psychologist).

• To newly diagnosed diabetic patients and current diabetic patients.

• Type 1 and Type 2 DM patients.
DM Education (3)

- Provide both inpatient and outpatient education
- To diabetes children, their parents and the main caretakers.
- School teachers or staff from institution
- Focus on knowledge and management on diabetes and practical skills for day to day diabetic care.
24 hour Diabetic Telephone Hotline and E-mail services

Objective: To provide medical and nursing support, counselling and advise to DM patients and their family, to minimize the need of readmission and frequent follow up

• 24hours DM hotline service was initiated in December, 1997 (annual call number: 700-800)
• The E-mail service was established since 2014 (annual number: 300-400)
Annual Diabetic Complication Screening

- Perform annual assessment of diabetic complication of our patients
- All type 2 DM patients (approx no: 40 patients)
- For type 1 who are 9 years old and has had diabetes for 5 years
- Also 11 years old and over and has had diabetes for 2 years
Outpatient DM Clinic(1)

Endocrinologist clinic:
• Review patients by pediatric endocrinologist approximately every 2 to 3 months or sometimes more often
Outpatient DM Clinic (2)

DM nurse clinic:
• Provide continual DM assessment and education by DM nurse once a month in OPD
• Review problematic cases frequently in OPD
• Refer to other disciplines if needed (eg dietitian, podiatrist or clinical psychologist
• Transition care
Transition Care

- Transition to adult services needs to be planned at the appropriate time for preparation and adaptation
- Starts at 16 years of age
- Allow to have enough time for reviewing the knowledge and skills of our adolescents as to provide them with reinforcement and relevant information
- Follow up by contact through phone half yearly since transferred to medical diabetic service
Messages

• Diabetes mellitus in children
  • No longer a rare problems
  • More and more type 2 DM coming up

• Largely a self-manage illness supported by medical TEAM
  • DM educators/nurses
  • Dietitian
  • Paediatrician/paediatric endocrinologist
  • Support from CP, support group
THE END

But there is always tomorrow!!!
THANK YOU