POLYURIA

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Definition

- What is polyuria?
- What is frequency micturition?
- What is urgency micturition?
- What is nocturia?
- What is nocturnal enuresis?

Definition

- Polyuria is an excessive urine volume, usually > 900 ml/m/d

Case history (1)

- 9 years old boy presented with polyuria
- What is the differential diagnosis?

Differential diagnosis

- Diabetes mellitus
- Central Diabetes inspidus
- Nephrogenic Diabetes inspidus
- Wolfram syndrome
- Renal glucsuria(benign, Fanconi syndrome, renal tubular disorder)
- UTI
- Chronic renal failure
- Renal tubular acidosis
- Psychogenic polydipsia

History

- What are the clues from the history suggestive of different diagnoses?

History

- Volume of urine
- Frequency
- Urgency
- Enuresis
- Burning micturition
- Polydipsia, day and night
- Apetite
- Weight loss

History

- Failure to thrive
- Episodes of severe dehydration
- Vomiting, constipation, hyperthermia
- Headaches, visual disturbances, short stature
- Precocious puberty
- deafness
- Head injury, brain surgery
- Hx of meningitis, brain tumor
- Drug Hx: duiretics

Focused history:POLYURIA

1) History of polyphagia, polydipsia, and weight loss, may indicate diabetes mellitus.
2) Children with psychogenic polydipsia often drink more during the day.
3) Infants with polyuria due to diabetes insipidus (DI) often have failure to thrive and episodes of severe dehydration.

Focused history:POLYURIA

DI secondary to a CNS lesion may occur as visual changes, sexual precocity, growth failure, and short stature.

It is important to ask about a history of brain surgery or injury.

Physical Examination

- What are the physical signs suggestive of the diagnosis?

Physical Examination

- General condition of the patient, sick, well
- Growth assessment
- Blood pressure
- pallor
- Dehydration
- Fundoscopy
- Visual fields
- Skin

Physical Examination

- CVS
- CHEST
- Abdomen
- CNS
- Puberty assessment

1. Introduce self

2. Position patient
Initial inspection standing, then lying, adequately undressed

3. General inspection
Parameters
Weight
Height
Percentiles
Well or unwell
Hydration
Intravenous lines
Tanner staging

4. Hands
Fingertip pricks
Trophic changes
Cutaneous infections
Limitation of joint mobility
Pigmented palmar creases (Addison)

5. Blood pressure
Hypertension (nephropathy)
Hypotension (Addison)
Postural hypotension (autonomic neuropathy, dehydration)

6. Eyes
Inspection
Squint
Cataract
Contact lenses
Visual acuity
Eye movements
Pupillary reactions
Red reflex (cataracts)
Fundi
Retinopathy
Optic atrophy (DIDMOAD)

7. Mouth
Hydration
Ketotic breath
Oral candidiasis

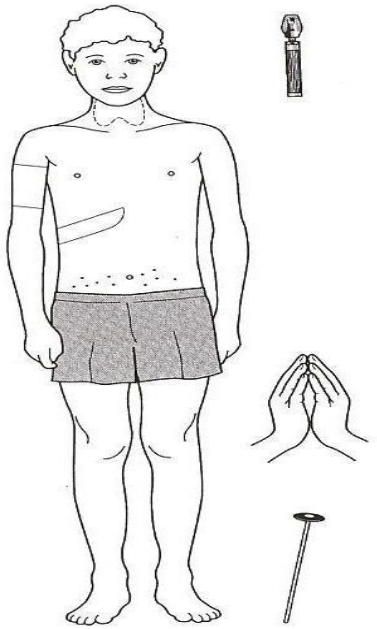
8. Thyroid
Inspect
Swallowing
Palpate
Auscultation

9. Abdomen
Injection sites
Fat atrophy, hypertrophy
Distension (coeliac disease)
Hepatomegaly
Tanner staging
Perineal candidiasis

10. Lower limbs
Injection sites
Fat atrophy, hypertrophy
Trophic changes
Candidiasis
Necrobiosis lipoidica
Reflexes
Sensation
Light touch
Vibration

11. Urinalysis
Glucose
Ketones
Protein
Blood

12. Other
Hearing (DIDMOAD)
ENT and chest (infection precipitating presentation)
Request insulin dosages and glucometer readings



Focused physical examination

- DM: findings
- DI: central, nephrogenic
- Psychogenic polydypsia
- Chronic renal failure

Investigations

- What investigations do you do to reach a diagnosis?

Investigations

- 24 HOUR URINE COLLECTION
- URINANALYSIS: NITRITE, LEUCOCYTE, PROTEIN, GLUCOSE, KETONES, MICROSCOPY
- URINE SPECIFIC GRAVITY>1.015 excludes DI
- URINE AND SERUM OSMOLALITY
- CBC
- RENAL FUNCTION
- GLUCOSE, HbA1c

Investigations

- Blood gas
- Serum calcium, phosphate
- Urine ca, po4, creatinine, protein, glucose
- Renal ultrasound
- MRI brain
- vsopressin
- Water deprivation test

Focused investigations

2) **UTI: Urinalysis revealing nitrite, white blood cells (WBC), and often bacteria**
3) **DM: hyperglycemia, glucosuria, ketonuria**
4) **Renal disease: impaired renal function, proteinuria, hematuria.**
5) **DI: high Na, serum osmolality, low urine osmolality & specific gravity.**

Urine specific gravity > 1.015m, DI unlikely.

6) Renal glucsuria

water deprivation test

Useful in differentiating DI from psychogenic polyuria and differenciate type of DI

DI is characterized by low urine specific gravity (usually < 1.005), low urine osmolality, and normal serum osmolality when hydration is adequate.

With water restriction or deprivation the serum sodium increases, as well as serum osmolality, whereas the patient remains unable to concentrate urine. The ratio of

- **This test should be conducted in a controlled setting and discontinues if the body weight decreases by more than 3%.**
- **In psychogenic , the serum sodium level is low normal but patients are able to concentrate urine. With water deprivation there is increased urine specific gravity and osmolality. The ratio of urine to serum osmolality is at least 2:1. There is no weight loss and the volume of urine decreases.**

Central DI

Caused by deficiency of ADH

Secretion of vasopressin is regulated at the paraventricular & supraoptic nuclei, which sense changes in osmolarity

Any lesion affecting the neurohypophyseal unit may cause central DI.

suprasellar and chiasmatic tumors (e.g. craniopahryngiomas, optic gliomas, germinomas

Infections (encephalitis) as well as infiltrative processes (leukemia, sarcoidosis, tuberculosis, histocytosis, actinomycosis) may also be causes.

Wolfram syndrome is associated with insulin-dependent diabetes mellitus, diabetes insipidus, optic atrophy, deafness

Diagnostic Studies

- Diagnosis should be suspected in any patient with sudden increased thirst & urination
- Laboratory examination will reveal very diluted urine,
- Examination of the blood will reveal very concentrated blood
  - The serum sodium may be as high as 170 mEq/L
  - Specific gravity of < 1.005 (low)
  - Urine osmolality of < 100 mOsm/kg (low)
  - Serum osmolality > 290 mOsm/kg (
  - water deprivation test)
  - MRI brain

Treatment

- Desmopressin
  - (DDAVP)
  - (desamino-desarginino-vasopressin)
  - Drug of choice in Diabetes insipidus
- Administration:
  - Oral, sub-cut, nasal spray

Nephrogenic DI: treat underline cause

Thaizide diuretics

Nephrogenic DI

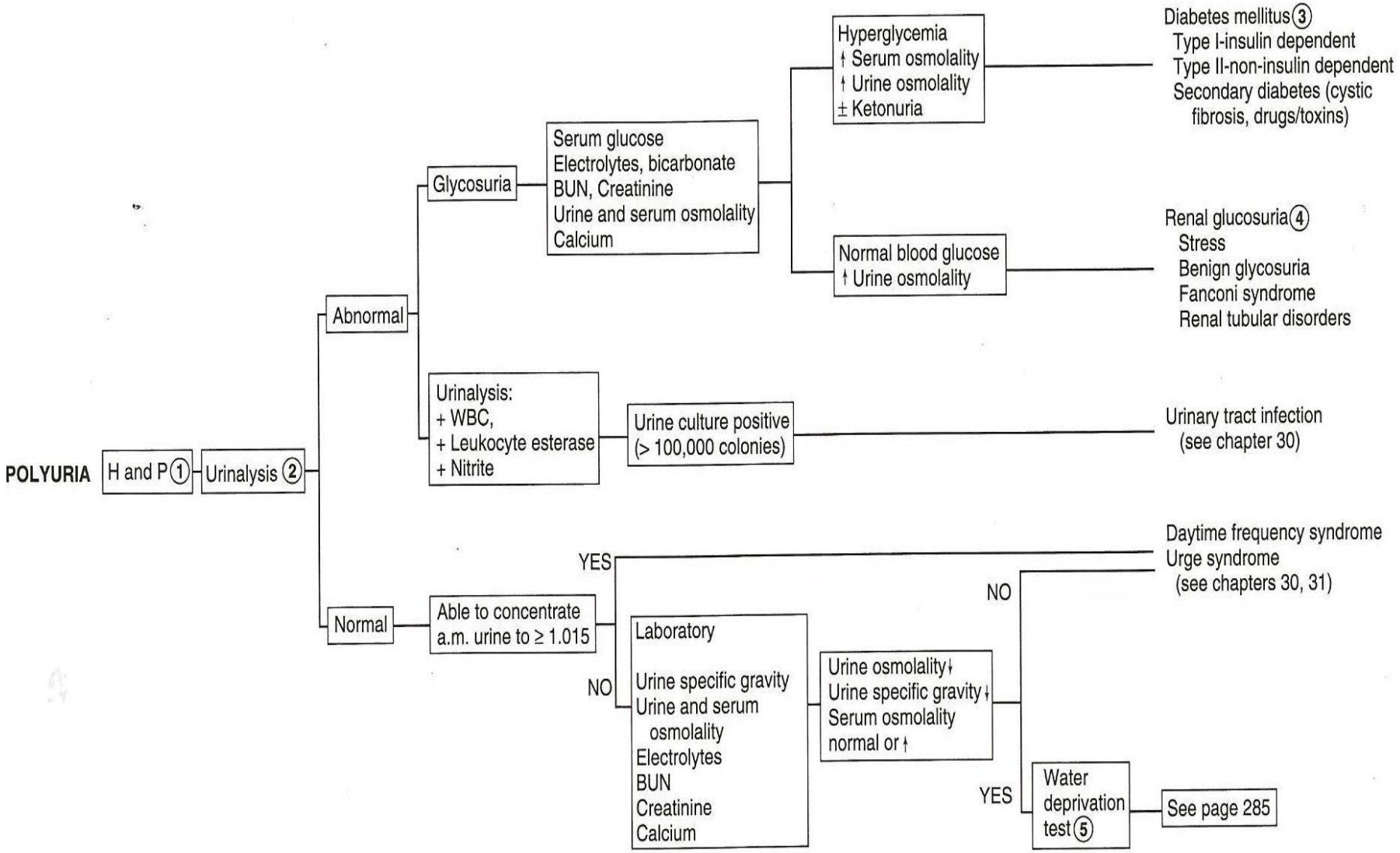
In nephrogenic DI, the kidney does not respond to antidiuretic hormone. It may be a primary condition (X-linked recessive), which usually appears in male infants as polyuria, polydipsia, and hypernatremic dehydration.

Secondary Nephrogenic DI may be seen in conditions causing a loss of medullary concentrating gradient, such as renal failure, tubular defects, and obstructive uropathy.

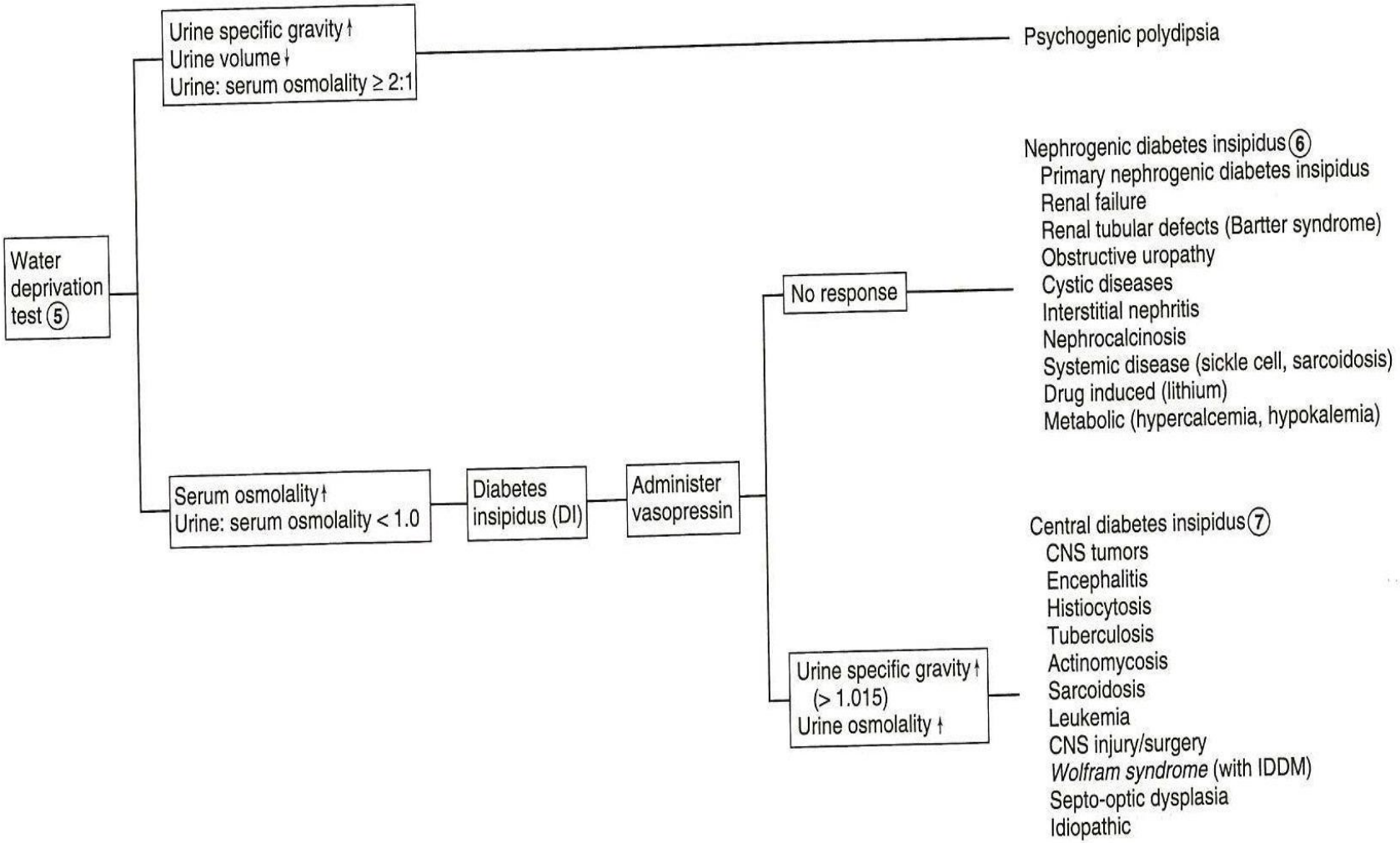
- Diseases such as sickle cell disease may cause renal damage and often may be associated with isosthenuria (urine specific gravity = 1.010).
- Drugs (e.g., lithium) or metabolic diseases (e.g. hypokalemia, hypercalcemia) may decrease the effect of antidiuretic hormone on the tubule causing DI.

water deprivation test

- How to differenciate central from nephrogenic DI


POLYURIA
H and P ①
Urinalysis ②
Abnormal
Glycosuria
Serum glucose
Electrolytes, bicarbonate
BUN, Creatinine
Urine and serum osmolality
Calcium
Hyperglycemia
↑ Serum osmolality
↑ Urine osmolality
± Ketonuria
Diabetes mellitus ③
Type I-insulin dependent
Type II-non-insulin dependent
Secondary diabetes (cystic fibrosis, drugs/toxins)
Normal blood glucose
↑ Urine osmolality
Renal glucosuria ④
Stress
Benign glycosuria
Fanconi syndrome
Renal tubular disorders
Urinalysis:
+ WBC,
+ Leukocyte esterase
+ Nitrite
Urine culture positive
(> 100,000 colonies)
Urinary tract infection
(see chapter 30)
Normal
Able to concentrate
a.m. urine to ≥ 1.015
YES
Daytime frequency syndrome
Urge syndrome
(see chapters 30, 31)
NO
Laboratory
Urine specific gravity
Urine and serum osmolality
Electrolytes
BUN
Creatinine
Calcium
Urine osmolality↓
Urine specific gravity↓
Serum osmolality normal or ↑
NO
YES
Water deprivation test ⑤
See page 285

POLYURIA (continued)



Treatment options

- DM: insulin, diet, education
- Central DI: DESMOPRESSIN, treat underline cause
- Nephrogenic DI: TREAT UNDERLINE CAUSE
- UTI: ANTIBIOTIC AND FOLLOW UP
- PSYCHOGENIC POLYDIPSIA: PSYCHOTHERAPY

Case 2: An 11-year-old boy presented with an 8-week history of polyuria and polydipsia. He was otherwise well apart from recent headaches. Investigations in clinic demonstrated the following:

- Serum sodium 142 mmol/L
- Serum potassium 3.7 mmol/L
- Serum urea 2.3 mmol/L
- Serum creatinine 52 μmol/L
- Plasma osmolality 305 mOsm/kg
- Plasma glucose 6.2 mmol/L
- Urine sodium 16 mmol/L
- Urine osmolality 78 mOsm/kg

QUESTIONS

1) **What further investigations required to clarify the diagnosis?**

ANSWERS

- Given that this child is spontaneously hyperosmolar, a formal water deprivation test is contraindicated.
- However, it is not clear whether this child has cranial or nephrogenic diabetes insipidus and the response to desmopressin needs evaluating.
- His urinary osmolality increased from 75 to 530 mOsm/kg and there was a dramtic reduction in his urine output suggesting that he has cranial diabetes insipidus.

- **Given diagnosis of cranial diabetes insipidus and a history of headaches, a full assessment of pituitary function and cranial imaging are indicated**

Case 3

- 12 y/o male presented with
  - Polyuria, polydipsia x 1 week
  - Wt loss
  - BG “high”, large urine ketones
  - What is the diagnosis?
- What is DD?
- What do you do next?
- How you investigate?
- How do you treat?

investigations

Serum glucose	497 mg/dl
Venous pH	7.396
Bicarb	27 mmol/l
UA	150 mg/dl ketones, + glucose
Serum acetone	Negative
Electrolytes	Na 133, K 4.2, Cl 94, BUN 14, creat 0.8

Diagnostic Criteria

- Symptoms of diabetes and a casual plasma glucose ≥200 mg/dl, OR
- Fasting plasma glucose ≥126 mg/dl, OR
- 2-hour plasma glucose ≥200 mg/dl during an oral glucose tolerance test.
- In the absence of unequivocal hyperglycemia, these criteria should be confirmed by repeat testing on a different day.

Classification of Different Forms of Diabetes Mellitus

I. Type 1 diabetes (beta cell destruction ultimately leading to complete insulin deficiency)
   A. Immune mediated
   B. Idiopathic
II. Type 2 diabetes (variable combinations of insulin resistance and insulin deficiency)
   A. Typical
   B. Atypical
III. Genetic defects of β cell function
   A. MODY syndromes
      1. MODY 1 Chromosome 20, HNF-4α
      2. MODY 2 Chromosome 7, glucokinase
      3. MODY 3 Chromosome 12, HNF-1α
      4. MODY 4 Chromosome 13, IPF-1
      5. MODY 5 Chromosome 17, HNF-1β, TCF-2
      6. MODY 6 Chromosome 2q32, Neuro-D1/Beta-2
   B. Mitochondrial DNA mutations (includes one form of Wolfram syndrome; Pearson syndrome; Kearns-Sayre, diabetes mellitus deafness)
   C. Wolfram syndrome—DIDMOAD (diabetes insipidus, diabetes mellitus, optic atrophy, deafness): *WFS1*-Wolfram—chromosome 4p
      1. Wolfram locus 2—chromosome 4q22-24
      2. Wolfram mitochondrial
   D. Thiamine responsive
IV. Drug or chemical induced
   A. Antirejection—cyclosporine
   B. Glucocorticoids (with impaired insulin secretion, e.g., cystic fibrosis)
   C. L-Asparaginase
   D. β-Adrenergic blockers
   E. Vacor (rodenticide)
   F. Phenytoin (Dilantin)
   G. alfa-Interferon
   H. Diazoxide
   I. Nicotinic acid
   J. Others
V. Diseases of exocrine pancreas
   A. Cystic fibrosis–related diabetes
   B. Trauma—pancreatectomy
   C. Pancreatitis—ionizing radiation
   D. Others
VI. Infections
   A. Congenital rubella
   B. Cytomegalovirus
   C. Hemolytic-uremic syndrome
VII. Variants of type 2 diabetes
   A. Genetic defects of insulin action
      1. Rabson-Mendenhall syndrome
      2. Leprechaunism
      3. Lipoatrophic diabetes syndromes
      4. Type A insulin resistance—acanthosis
   B. Acquired defects of insulin action
      1. Endocrine tumors—rare in childhood
         a. Pheochromocytoma
         b. Cushing
         c. Others
      2. Anti-insulin receptor antibodies
VIII. Genetic syndromes with diabetes and insulin resistance/insulin deficiency.
   A. Prader-Willi syndrome, chromosome 15
   B. Down syndrome, chromosome 21
   C. Turner syndrome
   D. Klinefelter syndrome
   E. Others
      1. Bardet-Biedel
      2. Alstrom
      3. Werner
IX. Gestational diabetes
X. Neonatal diabetes
   A. Transient—cyclic adenosine monophosphate maturation, chromosome 6q24
   B. Permanent—agenesis of pancreas
      —glucokinase deficiency, homozygous

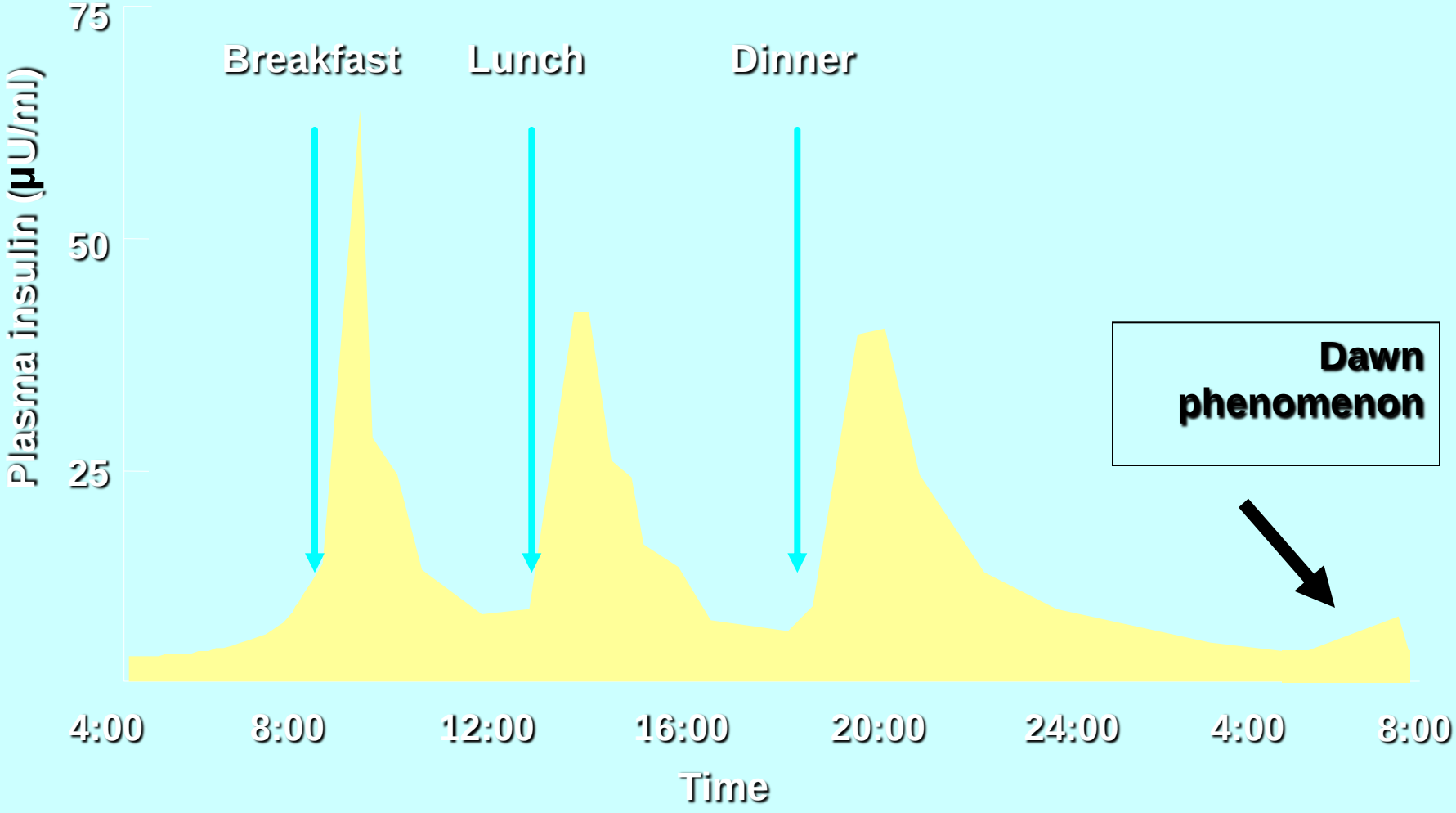
Management

- Diabetes team
- Insulin
- Diet
- Exercise
- Psychological support

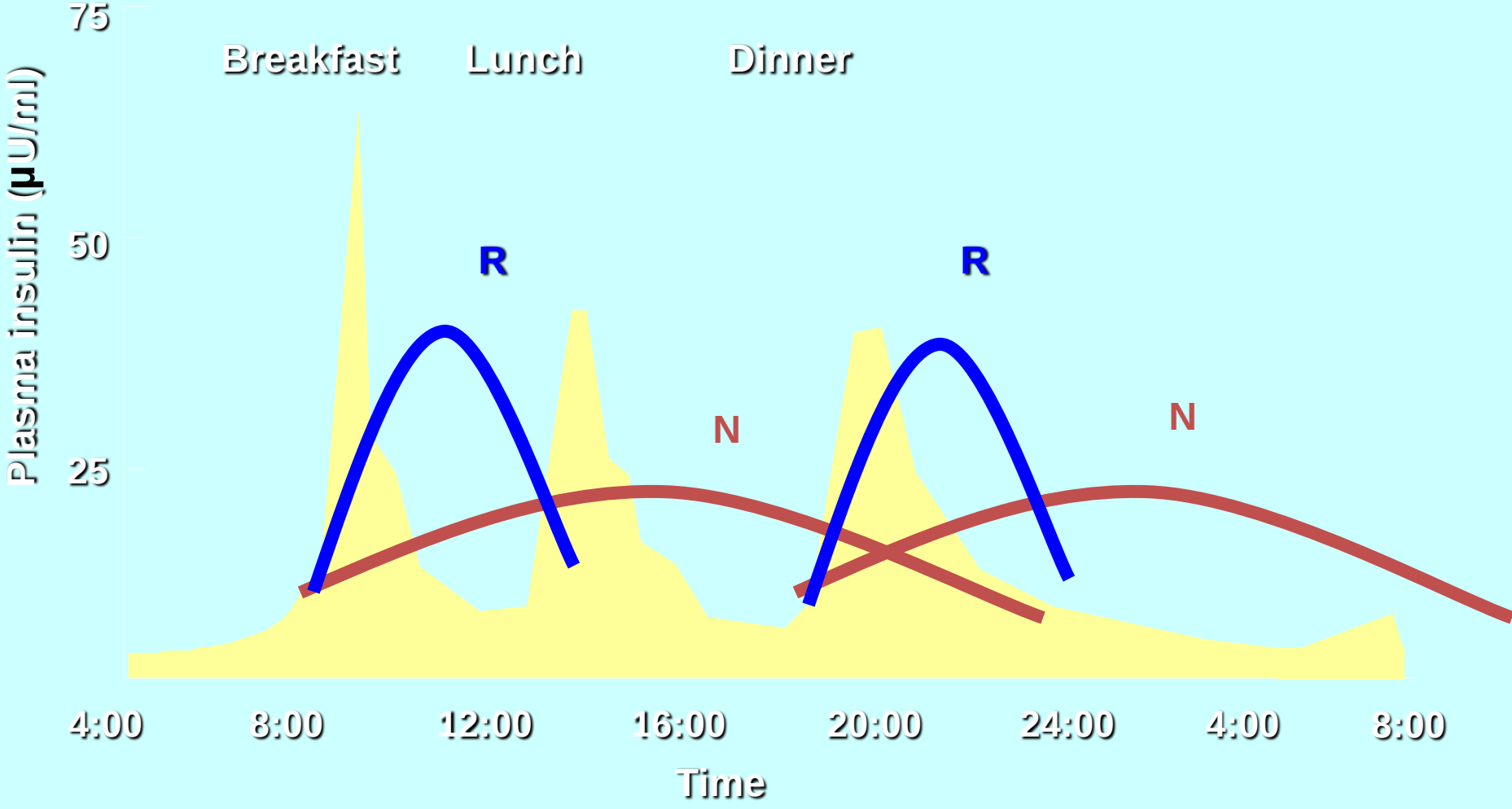
Banting and Best

1923 Nobel Prize for discovery and use of insulin in the treatment of IDDM

Physiological Serum Insulin Secretion Profile



NPH and Regular



NPH and Regular

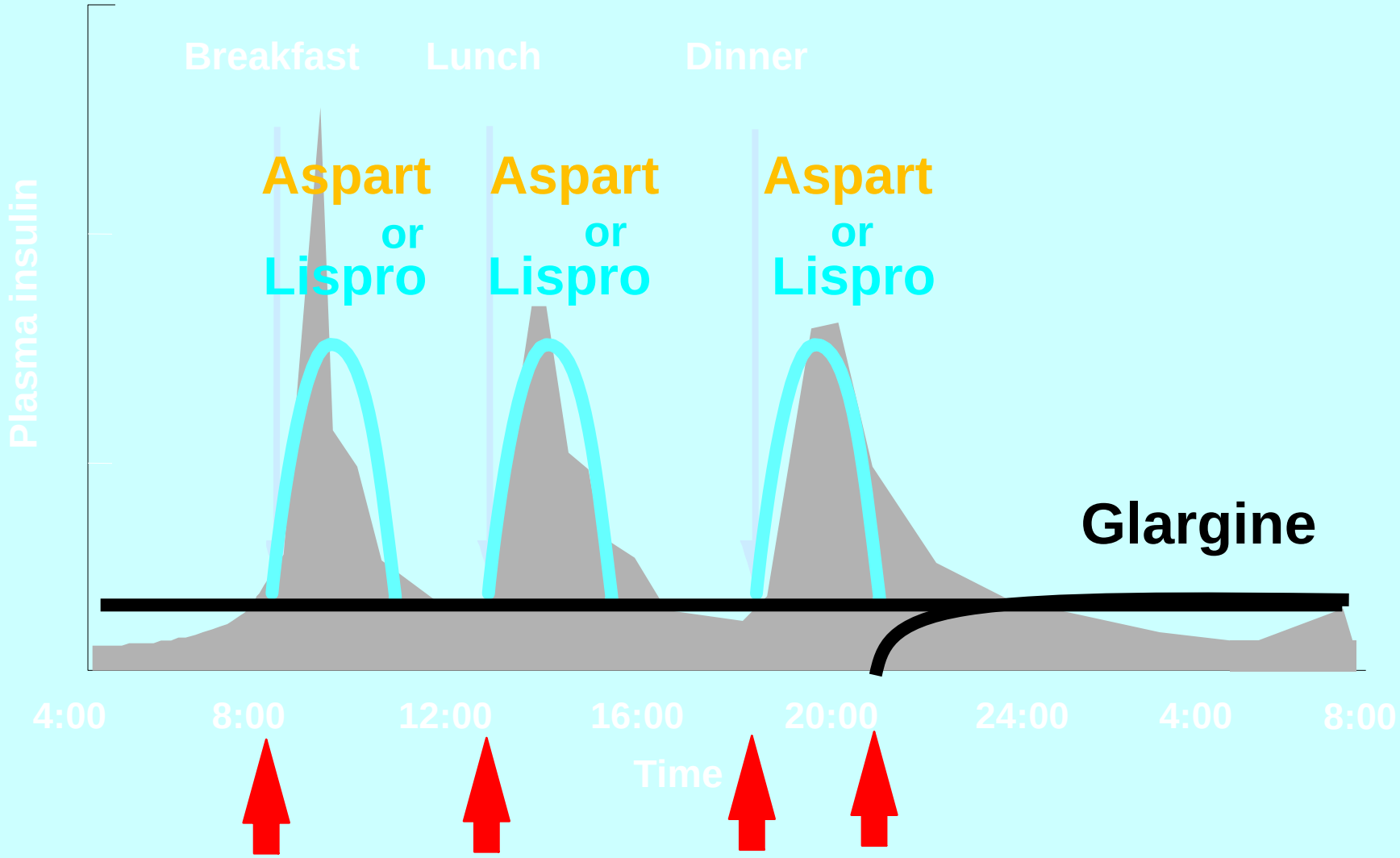
AM 2/3

- 2/3 NPH
- 1/3 Regular

PM 1/3

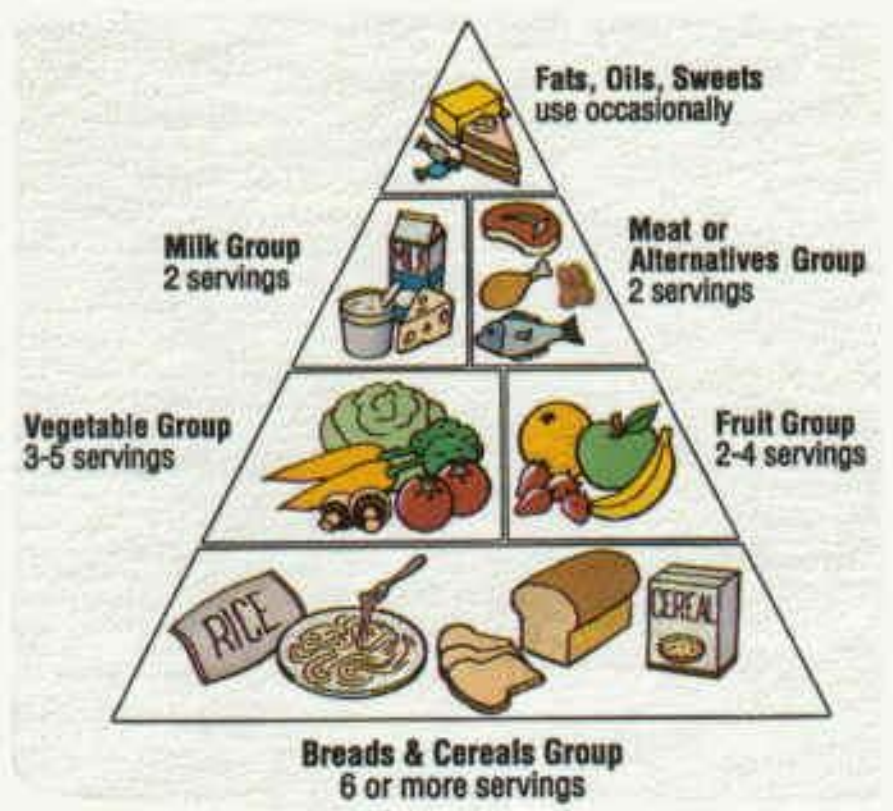
- ½ NPH (2/3)
- ½ Regular (1/3)

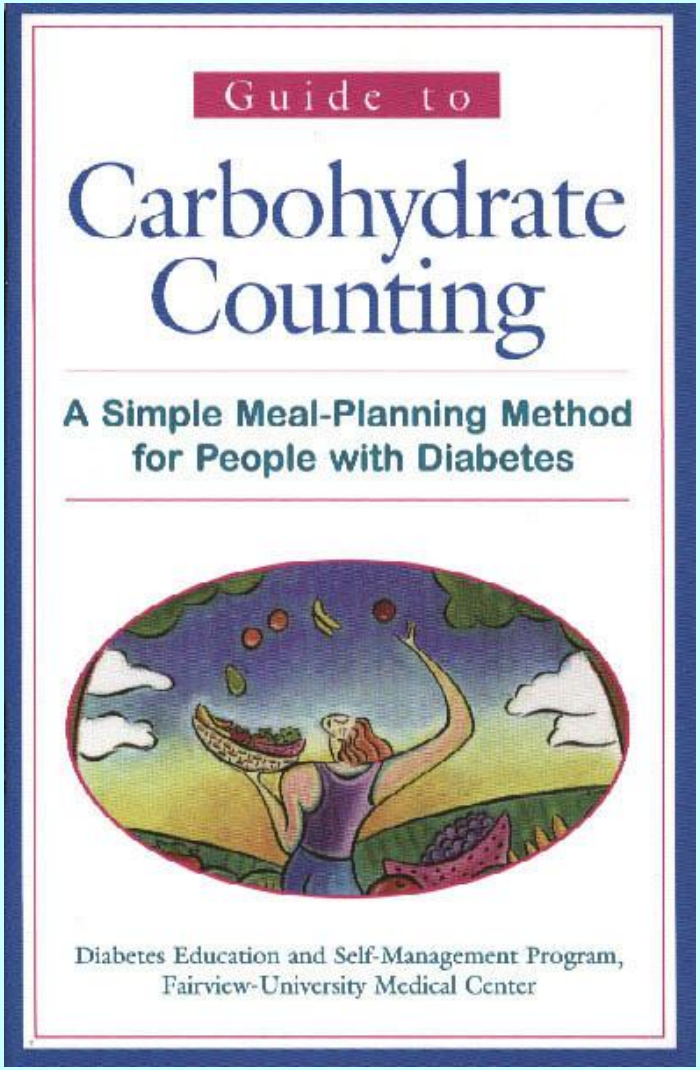
Basal/Bolus


Breakfast
Lunch
Dinner
Aspart or Lispro
Aspart or Lispro
Aspart or Lispro
Glargine
Plasma insulin
4:00
8:00
12:00
16:00
20:00
24:00
4:00
8:00
Time

Diet

- **Healthy, balanced diet**
  - **50-60% total calories from carbohydrate**
  - **<30% fat**
  - **10-20% protein**
- **Carbohydrate counting**
- **No forbidden foods - moderation**


Fats, Oils, Sweets
use occasionally
Milk Group
2 servings
Meat or
Alternatives Group
2 servings
Vegetable Group
3-5 servings
Fruit Group
2-4 servings
RICE
CEREAL
Breads & Cereals Group
6 or more servings


Guide to
Carbohydrate Counting
A Simple Meal-Planning Method for People with Diabetes
Diabetes Education and Self-Management Program,
Fairview-University Medical Center

Case 3: Results

- Hemoglobin A1c - 6.0%
- Ophthalmology exam – no retinopathy
- TSH, FT4 – normal
- Lipids – cholesterol 143
- Urine microalbumin - negative

Case 3

- Discharged after teaching complete on
  - insulin
  - 0.7 units/kg/day
- 3 weeks after diagnosis blood sugars begin going low frequently
- Insulin requirement 0.2 u/kg/d
- What is going on?

Honeymoon Phase

- Educate that it may happen
- Diabetes is not cured!
- Occurs within first 3 months of diagnosis
- Insulin requirements <0.5 units/kg/day
- Lasts weeks to up to 2 years
- Resolution of glucotoxicity, recovery of residual β-cell function

Case 3 OPD evaluation

- Two month later Patient was back on 0.7 u/kg
- Returned to OPD for F/U
- What are important findings on examination you elicit?
- What investigations you request on routine follow up?

Physical Exam

- Height, weight, BP
- Pubertal progression
- Thyroid
- Abdomen
- Shot sites - lipohypertrophy
- Feet

Monitoring

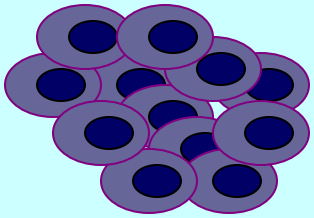
- Hemoglobin A1c – every 3 months
- Celiac screen – at diagnosis and if indicated
- Annually
  - TSH
  - Ophthalmology exam - after 10 and 3-5 yrs disease
  - Urine microalbumin - after 10 and 5 yrs disease
  - Lipid panel - puberty, unless fam hx, q5 years if normal
  - Influenza vaccine

Case 3

- 6 month later presented with incresing polyuria, polydipsia, tachypnea, vomiting, abdominal pain.
- O/E dehydrated, drowzy
- Glucose 500
- Urine glucose and ketones
- What is the Diagnosis?

DEFINITION of DKA

- An acute complication of diabetes mellitus characterised by :
  - Hyperglycaemia
  - Ketonuria
  - Metabolic acidosis
  - Dehydration



Islets of Langerhans

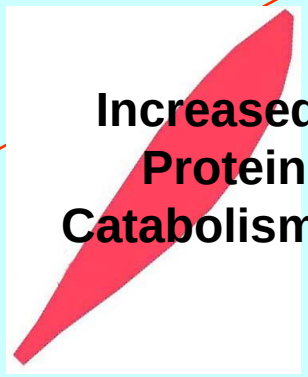
β-cell destruction

Insulin Deficiency

Decreased Glucose Utilization

Glucagon Excess

Muscle

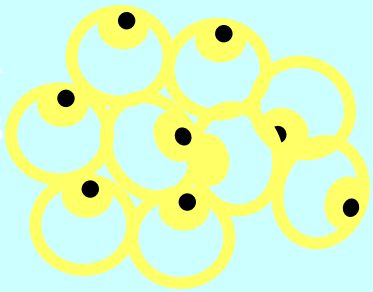


Increased Protein Catabolism

Liver

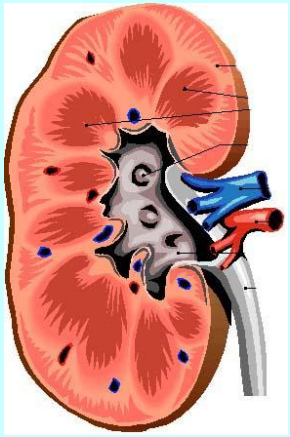
Increased Ketogenesis Gluconeogenesis

Adipo-cytes



IncreasedLipolysis

Hyperglycemia Ketoacidosis



Polyuria Volume Depletion Ketonuria

Case 3 Results

- Blood glucose >15 mmol/l
- Urinary ketones +2
- PH <7.3
- HCO3<15 mmol/l
- How do you manage? (assess, investigate, treat)

INITIAL ASSESSMENT

- Assess consciousness level
- Fundoscopy
- Assess degree of dehydration
- Precipitating factors
  - Missing insulin
  - infection

INVESTIGATIONS

- Blood glucose –in lab
- Blood glucose –using glucometer
- Blood gas-use heparinsed syring
- U/E
- CBC
- Blood culture
- Urine samples
  - Dipstick for glucose & ketones
  - Urgent microscopy
  - C & S
- Others as indicated

FLUID CALCULATION

- Volume required=deficit +maintenance
- Deficit =degree of dehydration X WT X 10
- Maintenance fluids
  - 0-10 kg 100 ml/kg/d
  - 10-20 kg 50 ml/kg/d
  - 21-30 kg 20 ml/kg/d
  - >30 kg 10 ml/kg/d
- Correct dehydration in 48 hours

Fluid management

- Type of fluid: normal saline
- Bolus 10 ml/kg if indicated, may repeat
- Subtract resuscitation fluid
- K can be given in the first fluid bag unless anuric
- Add dextrose when glucose < 15 mmol/l

INSULIN

- Commence insulin infusion one hour after start of resuscitation
- Use regular insulin infusion 0.1 unit/kg/hr

BICARBONATE

- Rarely indicated
- Use only if severely acidotic ,PH<6.9

ON-GOING CLINICAL MANAGEMENT

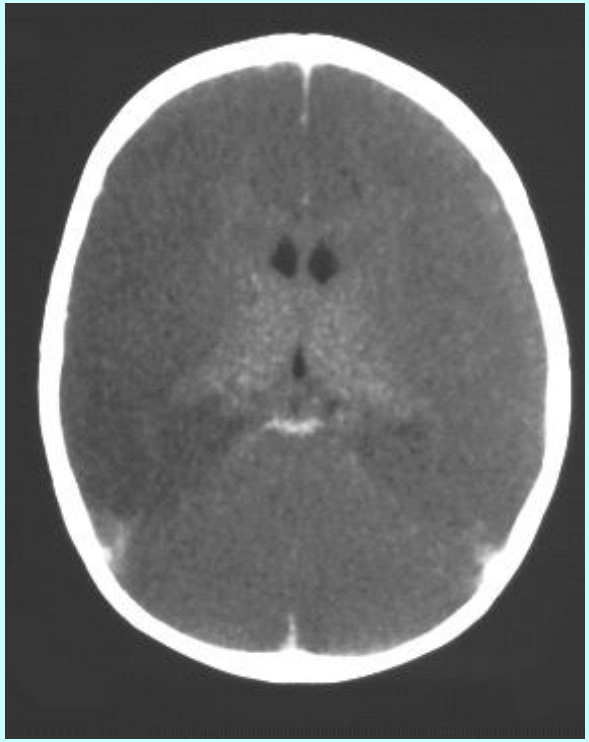
- DKA continues to be a medical emergency up to 24 hours after treatment has started
- Hourly r/v of the clinical status,BG,fluid & electrolytes
- Record all results,insulin & fluid on flow sheet

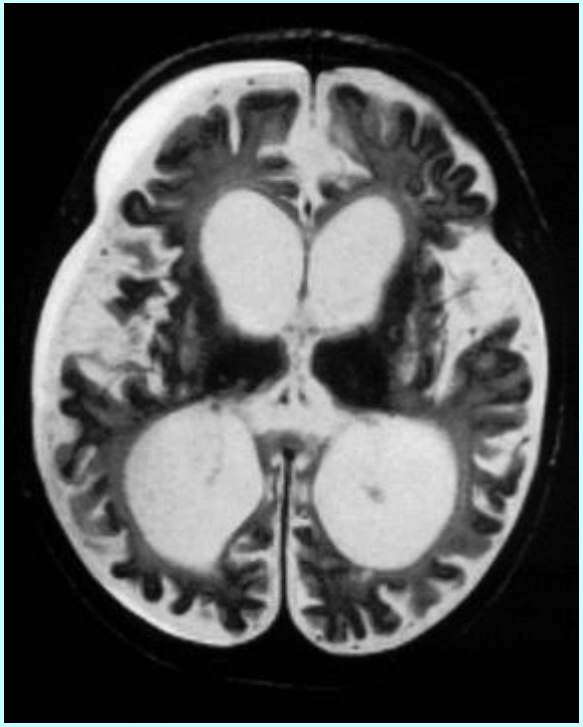
COMPLICATIONS

- Cerebral oedema
- Fluid overload
- Electrolyte imbalance
- Hypoglycemia
- Persistance of acidosis

CEREBRAL OEDEMA

- The most common cause of death in DKA
- Incidence is 0.7% in DKA
- Sudden deterioration in the level of consc
- Papilloedema ,focal or generalized seizures
- Treatment :manitol 1g/kg IV repeat prn
- Alternative 3% saline
- Restrict fluid to 50%





Case 3: follow up

- 1 year after diagnosis, remains diligent about sending blood sugars
- Insulin requirements 0.5 units/kg/day
- A1c 5.9%
- One morning he c/o sweating and tiredness.
- Glucose was 50 mg/dl
- What is the diagnosis and how you treat?

HYPOGLYCAEMIA

- AIM
  - To maintain BG between 4-8 mmol/l after hypoglycemia
- SYMPTOMS
  - Sweating,coldness,nausea,irritability,abdominal pain,headache,faintness,drowsiness and blurred vision.
- Treatment
  - Oral CHO: juice
  - If severe im glucagon
  - 2ml/kg Dex 10%

Case 3

- **Developed morning hyperglycemia, cause?**
  - **Dawn phenomenon**
    - **To correct: Move evening NPH to bedtime**
  - **Somogyi phenomenon – rebound hyperglycemia after hypoglycemia**
    - **Treatment: decrease evening NPH**

Case 3:Sick Day Management

- Developed tonsilitis with hyperglycemia
- Test blood sugars every 2-4 hours
- Check urine ketones
- Drink plenty of fluids (1 cup per hour)
- Need extra insulin to clear ketones
- Never omit insulin
- Hypoglycemia may be a problem, especially in younger children

Long Term Complications

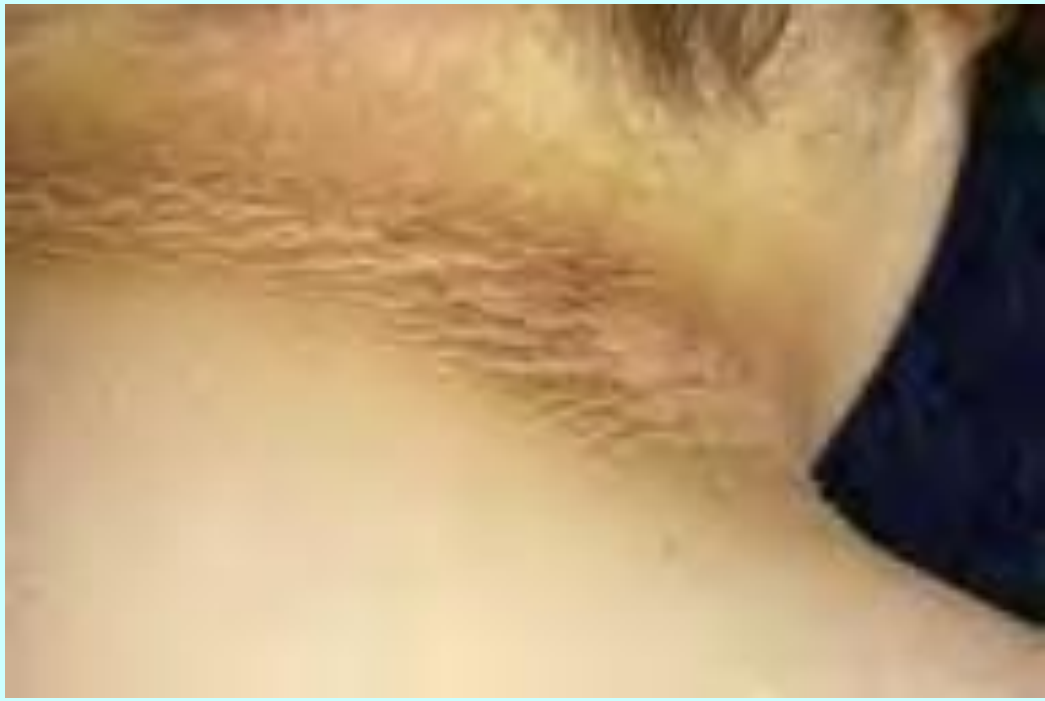
- Retinopathy
- Nephropathy
- Neuropathy
- Cardiovascular disease

- Prevention by optimal glucose control

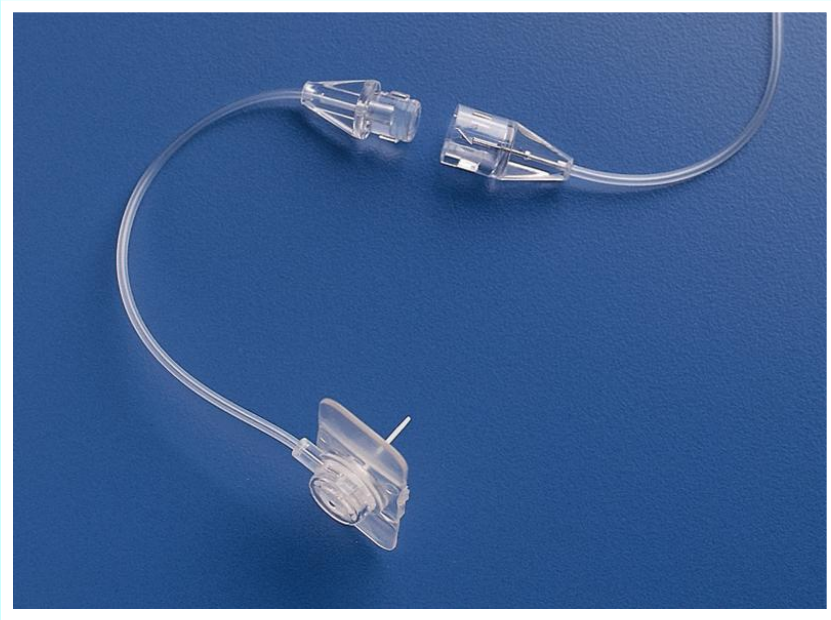
Risk Factors for Type 2

- Obesity
- Acanthosis nigricans
- Family history

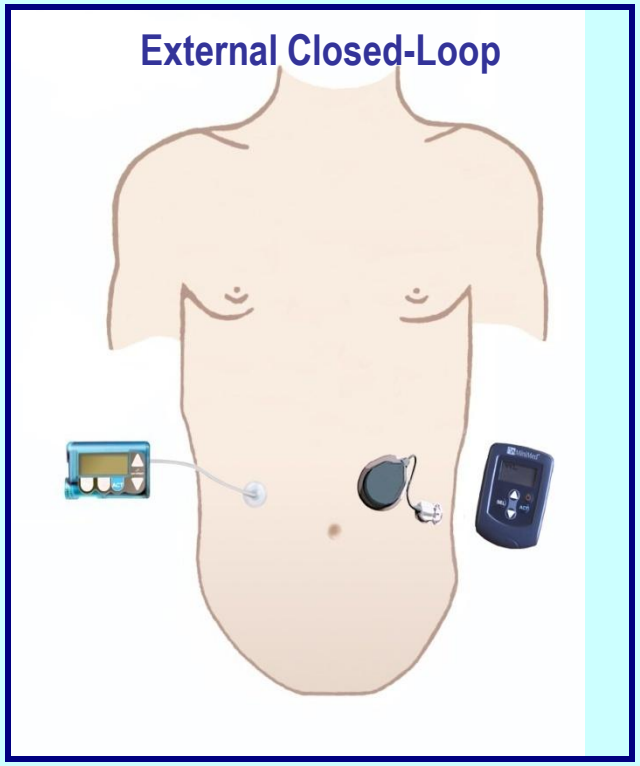
- Maternal gestational diabetes




108
ACT
80



Islet transplant & Artificial Pancreas



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