DIABETES MELLITUS IN DENTISTRY

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UHS

Burden of Diabetes

- Diabetes has reached epidemic proportions worldwide.
- International Diabetes Federation (IDF) :
  - by 2025, 333 million diabetic patients
  - 90% of these people will have Type 2 diabetes.
- In most Western societies
  the overall prevalence = 4-8%,
  and among 60-70-year-old people= 10-12%
- In the GCC: it's catastrophic: 23.7% in Saudi Arabia (2004)
- The annual health costs caused by diabetes and its complications: estimated at around 14% of all health-care expenditure.

Diabetes

- Is a chronic disease, which occurs when
  - the pancreas does not produce enough insulin, or
  - the insulin produced cannot be effectively used, or
  - both
- This leads to an increased concentration of glucose in blood: HYPERGLYCEMIA.
- The chronic hyperglycemia is associated with long-term damage of various organs, especially the eyes, kidneys, nerves, heart and blood vessels.

CLASSIFICATION OF DIABETES

→ 4 TYPES

- Type 1 D M
- Type 2 D M
- Gestational Diabetes
- Other types:
  - ❖ LADA (latent autoimmune diabetes in adults)
  - ❖ MODY (maturity-onset diabetes of the young)
  - ❖ Secondary Diabetes Mellitus

CAUSES OF DM

GENETIC DEFECT

β CELL FUNCTION

the only cells that produce insulin

- Chromosome 12, HNF-1-alpha (MODY3)
- Chromosome 7, glucokinase (MODY2)
- Chromosome 20, HNF-4-alpha (MODY1)
- Chromosome 13, IPF-1 (MODY4)
- Chromosome 17, HNF-1-beta (MODY5)
- Chromosome 2, NeuroD1 (MODY6)
- Mitochondrial DNA
- Others

IN INSULIN ACTION

- Type A insulin resistance
- Leprechaunism
- Rabson-Mendenhall syndrome
- Lipoatrophic diabetes
- Others

EXOCRINE PANCREAS AFFECTIONS

- Pancreatitis
- Trauma/pancreatectomy
- Neoplasia, Cystic fibrosis, Hemochromatosis
- Others

ENDOCRINOPATHIES

- Acromegaly
- Cushing's syndrome
- Glucagonoma
- Pheochromocytoma
- Hyperthyroidism
- Others

DRUG OR CHEMICAL-INDUCED

- Vacor, Pentamidine
- Nicotinic acid, Diazoxide
- Glucocorticoids
- ImmunoSupp. drugs
- Thyroid hormone
- Beta-adrenergic agonists
- Thiazides, Dilantin
- Alpha-Interferon
- Others

INFECTIONS

- Congenital rubella
- Cytomegalovirus
- Others

IMMUNE-MEDIATED DM

- "Stiff man" syndrome
- Anti-insulin receptor Abs
- Others

Other genetic syndromes sometimes associated with DM

- Down's syndrome
- Klinefelter's syndrome
- Turner's syndrome
- Wolfram's syndrome
- Freiderich's ataxia
- Huntington's chorea
- Laurence-Moon-Biedl Σ
- Myotonic dystrophy
- Porphyria
- Prader-Willi syndrome
- Others

DIAGNOSIS OF D.M: Expert Committee

⟶ defined three categories

- **Normal** ►FPG <100 mg/dL (5.6 mmol/L).
  Fasting is defined as no caloric intake for at least eight hours.

- **Increased risk for diabetes ("pre-diabetes")**
  - **Impaired glucose tolerance (IGT)**
    - ► OGTT : 2h PG=140-199 mg/dL (7.8 11.0 mmol/L).
  - **Impaired fasting glucose (IFG)**
    - ► FPG 100 to 125 mg/dL (5.6 to 6.9 mmol/L).

- **Diabetes mellitus** – The diagnosis of diabetes must be confirmed on a subsequent day
  - ►FPG ≥126 mg/dL (7.0 mmol/L)
  - ►HbA1C ≥6.5 percent
  - ►Two-hour plasma glucose ≥200 mg/dL (11.1 mmol/L) in an OGTT
  - ►Random (or "casual") plasma glucose ≥200 mg/dL (11.1 mmol/L) in the presence of symptoms

ADA- Diabetes Care, 2011

Impaired fasting glucose

- Called sometimes prediabetes
- FPG= 100-125 mg/dl (5.6-7mmol/l)
- Increases the risk of developing type 2 diabetes
- Reversible

Type 1 diabetes

- Previously IDDM or juvenile-onset diabetes.
- >90% of the pancreatic beta cells are destroyed by the immune system
- ➔The pancreas produces no or little insulin.

- Type 1 diabetes = 5-10% of all cases of diabetes.
- Age of onset of type 1 DM mostly < 30 but can happen anytime
- Risk factors for type 1 DM include autoimmune, genetic, and environmental factors.

Type 2 diabetes

- Previously NIDDM or adult-onset diabetes .
- 90-95% of all cases of DM
- In type 2 DM the pancreas continues to produce insulin. However the body develops resistance to the effect of insulin, ➔there is not enough insulin to meet the body's needs.
- Type 2 DM is associated with
    - older age > 30,
    - obesity (80-90% overweight or obese),
    - family history of diabetes,
    - history of gestational diabetes,
    - physical inactivity,
    - race/ethnicity: African Americans, Hispanic Americans, American Indians

Gestational diabetes (GDM)

World Health Organization (WHO) thresholds for positive two-hour 75-gram oral GTT

Fasting	92 to 125 mg/dL (5.1 to 6.9 mmol/L)
OR	
One-hour	≥180 mg/dL (10.0 mmol/L)
OR	
Two-hour	153 to 199 mg/dL (8.5 to 11.0 mmol/L)

A diagnosis of "gestational diabetes" is made when one or more of the above glucose thresholds are met. In contrast, a diagnosis of "diabetes in pregnancy" is made if one or more of the following criteria are met: fasting plasma glucose ≥126 mg/dL (7.0 mmol/L), two hour plasma glucose ≥200 mg/dL (11.1 mmol/L) following a 75 gram oral glucose load, random blood glucose ≥200 mg/dL (11.1 mmol/L) in the presence of diabetes symptoms.

Risk factors for diabetes

Identifying risk factors for diabetes may help to target specific patient groups for screening

- **Age ≥45 years.**
- **Overweight (BMI≥25 kg/m2) and Obesity**
- **Fat distribution = central or abdominal obesity**
- **DM in any first degree relative ➔3 fold, in both parents ➔6 fold**
- **Sedentary lifestyle**
- **Sleep duration: short (<5h) and long (>8h)**
- **High-risk ethnic or racial group (African-American, Hispanic,…)**
- **History of delivering a baby weighing >4.1 kg or of gestational DM**
- **Hyperuricemia**
- **Dyslipidemia**
- **HbA1c ≥5.7 percent, impaired fasting glucose.**
- **Polycystic ovary syndrome.**
- **Hypertension >140/90**
- **Cardiovascular Disease= MI or Heart Failure**

Symptoms

The 2 types have similar symptoms

- Frequent urination of large volume (polyuria),
- thirst (polydipsia),
- hunger (polyphagia),
- and unexplained weight loss.
- numbness in extremities, pain in feet (disesthesias), fatigue, and blurred vision.
- recurrent or severe infections.

Symptoms in Type 1

Often the symptoms begin abruptly and dramatically.
→diabetic ketoacidosis.

The initial symptoms of diabetic ketoacidosis include

- ♦ excessive thirst and urination,
- ♦ weight loss, nausea, vomiting,
- ♦ fatigue, abdominal pain
- ♦ Kussmaul respiration: breathing deep and rapid.

The breath smells like nail polish remover
(smell of the ketones escaping into the breath.)

Without treatment, diabetic ketoacidosis can progress to coma and death, sometimes very quickly.

Symptoms in Type 2

♦ No symptoms for years or decades.

♦ Symptoms may be subtle.

mild polyuria and polydipsia at first with gradual worsening Eventually; fatigue, blurred vision, and may become dehydrated.

♦ Hypoglycemia: sometimes during the early stages of diabetes.

♦ Ketoacidosis: unusual because DM2 pts still produce some insulin.

♦ Severe hyperglycemia:

→ people may develop severe dehydration, mental confusion, drowsiness, and seizures,

► nonketotic hyperglycemic-hyperosmolar syndrome.

♦Currently, many people with type 2 diabetes are diagnosed by routine blood glucose testing.

Complications of Diabetes Mellitus

- Mortality: ↑3-4 fold
- Prevalence of CVD: ↑ 3-fold
- Retinopathy in 40-50%
- Neuropathy in 50%
- Nephropathy in 10%
- *foot ulcer* in any year : 5%
- *Amputation* rates are often around 0.5% per year.

Lipid abnormalities

Hyperlipidemia ** Common in DM II, increases CV risk

Baseline problem:

Insulin Resistance

Hyperinsulinemia →high TG.
→low HDL.
→high VLDL
→high LDL and high IDL

Vascular Complications

1- MICROVASCULAR : small blood vessels

2- MACROVASCULAR : larger blood vessels.

- **MICROVASCULAR COMPLICATIONS : include damage to**
  - ♦ **eyes (retinopathy) leading to blindness,**
  - ♦ **kidneys (nephropathy) leading to renal failure**
  - ♦ **nerves (neuropathy) leading to impotence and diabetic foot**

- **MACROVASCULAR COMPLICATIONS : include**
  - ♦ **cardiovascular diseases such as Myocardial Infarct.**
  - ♦ **strokes**
  - ♦ **insufficiency in blood flow to legs.**

► **Large randomized-controlled trials**

→good metabolic control in both type 1 and 2 diabetes can delay the onset and progression of these complications.

Long term complications

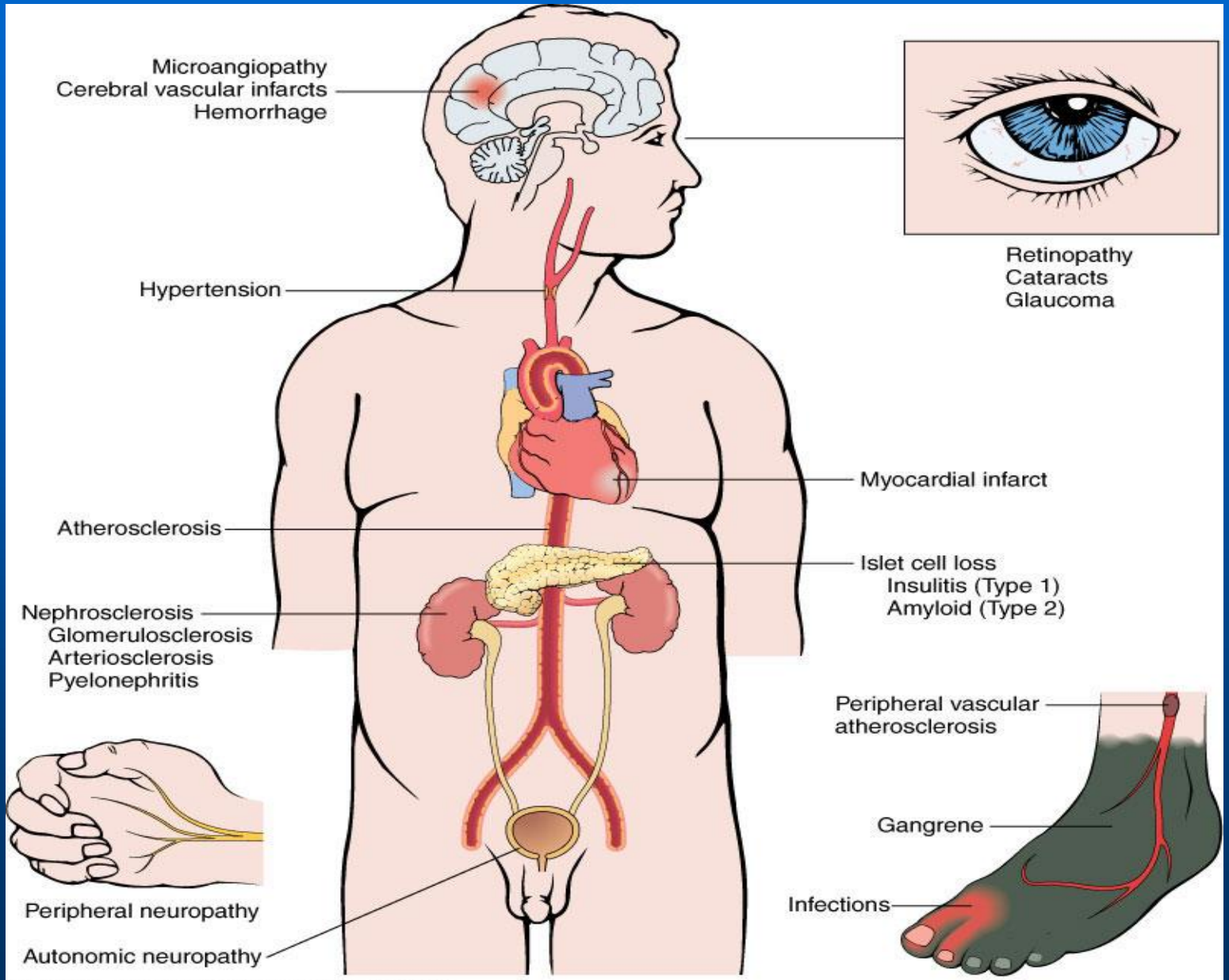
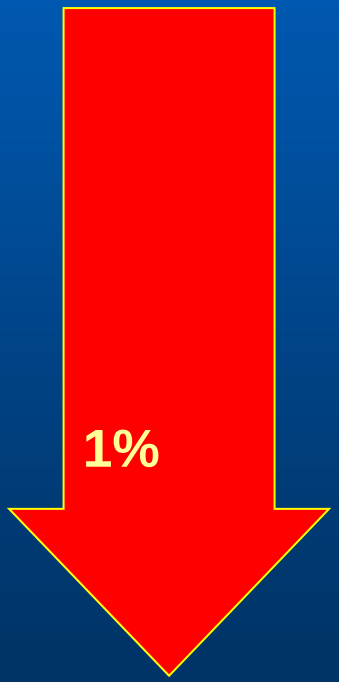


Fig. 24-34. Long-term complications of diabetes.

Lowering HbA_{1C} Reduces Risk of Complications

Treatment Target

Every 1% ↘HbA_{1C}



REDUCED RISK

-21%	Death from diabetes
-14%	Cardiovasc.disease
-37%	Microvascular complications over 10y.
-43%	Peripheral vascular disorders

UKPDS 35. BMJ 2000; 321: 405-12.

Why not lower than 6.5% ?

- Type 2 DM

  No beneficial effect on CV outcomes

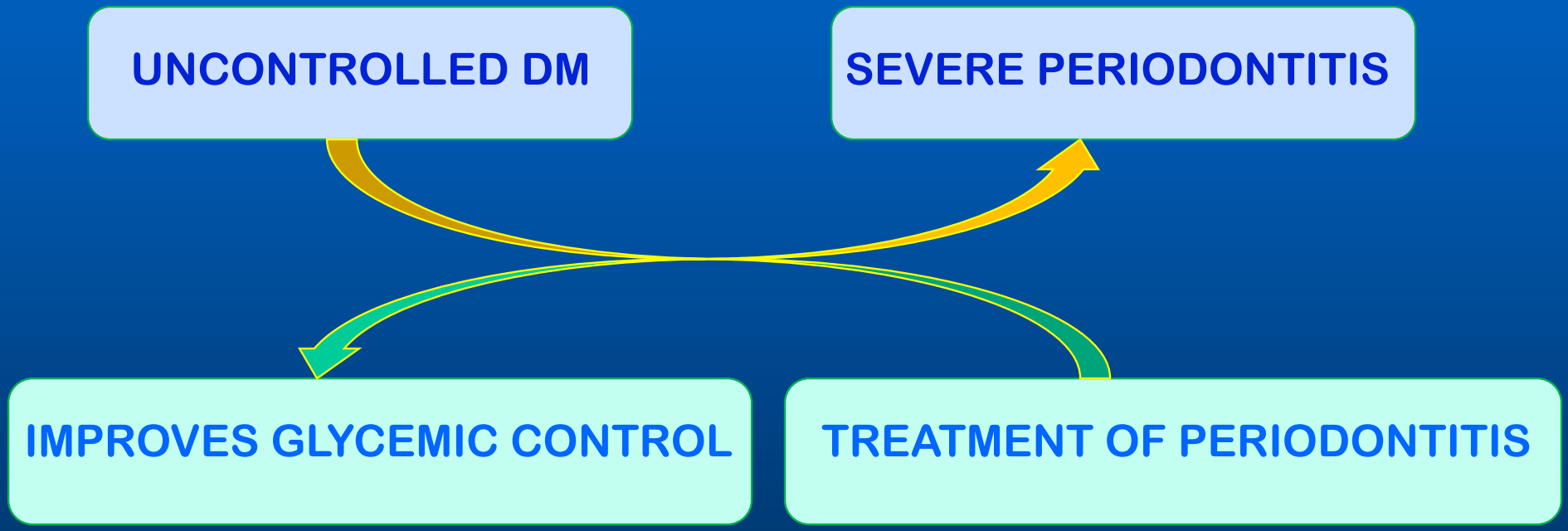
- Increased risk of hypoglycemia
- ACCORD and ADVANCE
  - HbA1c of 6.4 %
    - less nephropathy
    - but no change in macrovascular events
    - increased risk of death by 20%
  - Reasons unclear – but ? related to intensive insulin regimen

Diabetes complications affect also the teeth!

Diabetic patients :

- 3x more periodontal disease that the normal population.
- Displays greater severity
- Periodontitis: 6th complication of DM

Bidirectional relationship between periodontal disease and DM



Antibiotic: amoxicillin or
Doxicyclin

study

Periodontal regeneration compared with access-flap surgery in human intra-bony defects, 20-year follow-up of a randomised clinical trial: tooth retention, periodontitis recurrence and costs

Pierpaolo Cortellini, Jacopo Buti, Giovanpaolo Pini Prato, Maurizio S. Tonetti

J Clin Periodontol 2017: 44: 58-66.

SUB-ANALYSIS OF THE DATA BY A FRENCH GROUP AND PUBLISHED IN THE SAME JOURNAL SHOWED:

PERIODONTITIS: RISK FACTOR FOR DEVELOPING DM

Other Complications

- **Fungal Infections**
  - Manifestations of Oral Candidiasis including:
    Rhomboid Glossitis,
    Denture Stomatitis,
    Angular Cheilitis.

- Mucormycosis:
  rare and serious
  systemic fungal infection

Oral involvement:
→Palatal ulceration
or necrosis

Other Complications

- **Oral Burning and Taste disturbances**
  Can lead to diagnose DM
  (In one study from Jordan:
  37% of patients C/O mouth or tongue burning were diagnosed DM.)

- **Dental Caries**

- **Traumatic Ulcers and Irritation Fibromas**

3 main causes responsible for Dental diseases in diabetic pts:

1- Dental calculus: More important in DM pts because they produce less saliva= Xerostomia.

! Many anti diabetic drugs cause bucal drought

2- Hyperglycemia: saliva contains more glucose which modifies the composition of the dental plaque and favors microorganisms growth

3- Microangiopathy (with long term uncontrolled DM)

can also affect the capillaries of the oral cavity.

►Therefore gingival nutrition can be affected

►and the healing of the lesions can be affected.

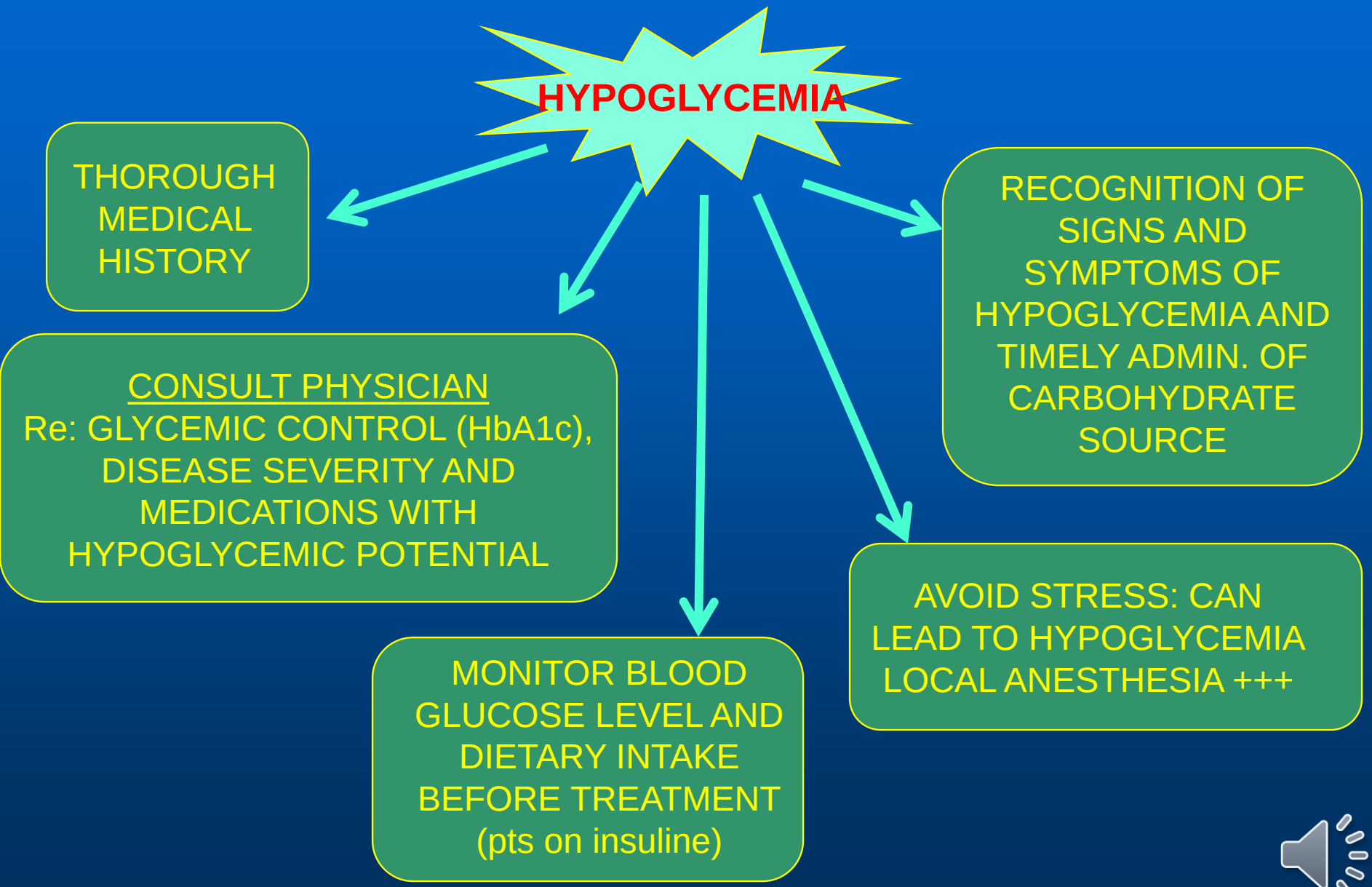
This important relationship between periodontal disease and DM leads to adopt:

1- Effective behaviors to prevent and control PD (brushing, flossing,..)

2- Routine dental visits: integral part of diabetic patients' health (recommended every 6m)

3- if we have difficulties in controlling a diabetic patient, we should look for a silent infection: Gingivitis? Periodontitis?

Dental Management of the diabetic patient



Hypoglycemia

- Mainly seen in pts on Insulin or sulfonylurea
- NOT with Metformin, TZD, DPP4, GLP-1, SGLT2
- Diagnosis: low blood sugar and symptoms
  * Glucose level < 0.6 g/l (3.3 mmol/l)
  * Symptoms:
    - sudden intense hunger
    - sweating
    - trembling, nervousness
    - weakness, palpitations
    - often have trouble speaking
    - confusion, drowsiness, convulsions and coma

How to manage hypoglycemia ?

►rapid delivery of a source of easily absorbed sugar
soft drinks, juice, lifesaver candies, table sugar,

►In general, 15 grams of glucose is given,
followed by an assessment of symptoms
and a blood glucose check if possible.

►If after 10 minutes there is no improvement,
give another 10-15 g.
→→ This can be repeated up to 3 times.

►At that point, the patient should be considered as not responding to the therapy and an ambulance should be called.

The equivalency of 10-15 grams of glucose:

- ♦ 4 lifesavers
- ♦ 4 teaspoons of sugar
- ♦ 1/2 can of regular soda or juice

Treatment

Lifestyle intervention

Treatment recommendation for individuals with IFG, IGT, or elevated A1C

Population	Treatment
IFG, IGT, or A1C (5.7 to 6.4 percent)*	Lifestyle modification (ie, 5 to 10 percent weight loss and moderate intensity physical activity ~30 min/day)
Individuals with IFG, IGT, or A1C 5.7 to 6.4 percent, especially for those:	Lifestyle modification (as above) and/or metformin•
<60 years of age	
BMI ≥35 kg/m^2	
Women with prior gestational diabetes	

Smoking cessation may also be important

IFG: impaired fasting glucose; IGT: impaired glucose tolerance; A1C: glycated hemoglobin; BMI: body mass index.
* Updated information from American Diabetes Association. Standards of medical care in diabetes—2013. Diabetes Care 2013; 36 Suppl 1:S11.
• Metformin 850 mg twice per day.

ANTIDIABETIC DRUGS

DRUG CLASS	DRUG NAME	BRAND NAME	MODE OF ACTION
BIGUANIDES	METFORMINE	**GLUCOPHAGE**	Inh.G.prod/liver
Sulfonylureas	Glimiperide Gliclazide	**AMARYL** **DIAMICRON**	↗Insulin secretion by β cells
Thiazolidinedines TZDs	Pioglitazone Rosiglitazone	**ACTOS** **AVANDIA**	↗G.intake by skeletal muscle
DPP 4- Inhibitors	Sitagliptin, Vildagliptin, Saxagliptin, Linagliptin	**JANUVIA** **GALVUS** **ONGLYZA** **TRAJENTA**	Incretin (H): ↗Insulin prod when needed↘G.prod/liver Destroyed/dpp4enzyme
GLP1- analogues	Exenatide, Liraglutide Dulaglutide	**BYETTA** **VICTOZA** **TRULICITY**	↗insulin secretion when G. level is high
SGLT2- inhibitors	Empagliflozine Canagliflozine Dapagliflozine	**JARDIANCE** **INVOKANA** **FARXIGA**	Inh.G.reabsorption in the proximal tubule

INSULINS

Type of Insulin & Brand Names	Onset	Peak	Duration	Role in Blood Sugar Management
Rapid-Acting				
Lispro (Humalog)	15-30 min.	30-90 min	3-5 hours	Rapid-acting insulin covers insulin needs for meals eaten at the same time as the injection. This type of insulin is often used with longer-acting insulin.
Aspart (Novolog)	10-20 min.	40-50 min.	3-5 hours	
Glulisine (Apidra)	20-30 min.	30-90 min.	1-2½ hours	
Short-Acting				
Regular (R) humulinor novolin	30 min. -1 hour	2-5 hours	5-8 hours	Short-acting insulin covers insulin needs for meals eaten within 30-60 minutes.
Velosulin (for use in the insulin pump)	30 min.-1 hour	2-3 hours	2-3 hours	
Intermediate-Acting				
NPH (N)	1-2 hours	4-12 hours	18-24 hours	Intermediate-acting insulin covers insulin needs for about half the day or overnight. This type of insulin is often combined with a rapid- or short-acting type.

Long-Acting				
Long-acting insulin covers insulin needs for about one full day. This type is often combined, when needed, with rapid- or short-acting insulin.	Insulin glargine (Lantus,Toujeo)	1-1½ hour	No peak time. Insulin is delivered at a steady level.	20-24 hours
	Insulin detemir (Levemir)	1-2 hours	6-8 hours	Up to 24 hours
Pre-Mixed*				
Humulin 70/30	30 min.	2-4 hours	14-24 hours	These products are generally taken two or three times a day before mealtime.
Novolin 70/30	30 min.	2-12 hours	Up to 24 hours	
Novolog 70/30	10-20 min.	1-4 hours	Up to 24 hours	
Humulin 50/50	30 min.	2-5 hours	18-24 hours	
Humalog mix 75/25	15 min.	30 min.-2½ hours	16-20 hours	

*Premixed insulins combine intermediate and short-acting insulin (in specific percentage of each type of insulin.)