Sri Aurobindo College of Dentistry

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INDIA

Module plan

- Topic :DIABETES AND PERIODONTIUM
- Subject: Periodontics
- Target Group: Undergraduate Dentistry
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- Platform: Institutional LMS
- Presenter:Dr Kanteshwari IK

DIABETES AND PERIODONTIUM

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Contents

- Introduction
- Diabetes classification
- Diagnostic criteria
- Lab investigations
- Complications
- Association of diabetes and periodontal disease
- Signs of gingivitis and periodontitis in diabetic patients
- Mechanism of diabetes influence on Periodontitis
- How periodontitis affect diabetes (two way relationship)
- Dental management of patients with diabetes
- Conclusion
- References

Introduction

- Diabetes mellitus comprises a clinically and genetically heterogeneous group of metabolic disorders manifested by abnormally high levels of glucose in the blood.
- This abnormally high level of glucose in the blood is brought about :

- by insulin deficiency caused by pancreatic b-cell dysfunction,

- insulin resistance in the liver or muscle tissue,

- or a combination of both.

- Individuals with glucose levels more than normal but not meeting the diagnostic criteria of DM are termed as Prediabetics.

- Impaired fasting glucose (IFG) and impaired glucose tolerance (IGT).

- These patients are normoglycemic but demonstrate elevated blood glucose levels under certain conditions.

- Hyperglycemia limited to periods of fasting →impaired fasting glucose
- Hyperglycemia after a glucose load → impaired glucose tolerance
- Impaired fasting glucose and impaired glucose tolerance → strong predictors for future development of type 2 diabetes
- Patients with IFG/IGT → increased risk for CVS complications but not microvascular complications

Risk factors

- Family history of diabetes
- Overweight
- Unhealthy diet
- Physical inactivity
- Increasing age
- High blood pressure

Classification of Diabetes mellitus:

- American Diabetes Association Expert Committee on the Diagnosis and Classification of Diabetes Mellitus, 1999

Based on disease etiology :

I: Type 1 DM - formerly called insulin-dependent diabetes mellitus or IDDM

II: Type 2 DM - formerly called non-insulin-dependent diabetes mellitus or NIDDM

III: Other specific types of DM

IV: Gestational DM

i. Type 1 diabetes

- Destruction of beta cells of pancreatic islets
- Consequence: absolute deficit of insulin
  - A. subtype: induced by autoimmunity processes
  - B. subtype: idiopathic mechanism
- May be triggered by environmental factors like infections and diet.
- Constitutes 5 to 10 percent of DM cases

II. Type 2 diabetes

- Defect in insulin secretion and an impairment of insulin action in hepatic and peripheral tissues, especially muscle tissue and adipocytes.
- Caused primarily due to lifestyle and genetic factors
- Type 2 diabetes leads to hyperglycemia, hypertension, dyslipidemia (elevated triglycerides and/or decreased high-density lipoprotein) , central obesity (abdominal), and atherosclerosis
- "The insulin resistance syndrome"

Lab Investigations:

- Diagnostic criteria : plasma glucose level,
- Glycated Hb,
- Self monitoring devices ,
- Urine analysis,
- complete blood count,
- lipid profile,
- liver function testing, and
- measurement of serum electrolytes,
- creatinine,
- uric acid, and
- blood gases.

According to ADA Standards of medical care in diabetes (2019)

Table 2.2—Criteria for the diagnosis of diabetes

FPG ≥126 mg/dL (7.0 mmol/L). Fasting is defined as no caloric intake for at least 8 h.*
OR
2-h PG ≥200 mg/dL (11.1 mmol/L) during OGTT. The test should be performed as described by the WHO, using a glucose load containing the equivalent of 75-g anhydrous glucose dissolved in water.*
OR
A1C ≥6.5% (48 mmol/mol). The test should be performed in a laboratory using a method that is NGSP certified and standardized to the DCCT assay.*
OR
In a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose ≥200 mg/dL (11.1 mmol/L).

*In the absence of unequivocal hyperglycemia, diagnosis requires two abnormal test results from the same sample or in two separate test samples.

Table 2.3—Criteria for testing for diabetes or prediabetes in asymptomatic adults

1. Testing should be considered in overweight or obese (BMI ≥25 kg/m^2 or ≥23 kg/m^2 in Asian Americans) adults who have one or more of the following risk factors:
   - First-degree relative with diabetes
   - High-risk race/ethnicity (e.g., African American, Latino, Native American, Asian American, Pacific Islander)
   - History of CVD
   - Hypertension (≥140/90 mmHg or on therapy for hypertension)
   - HDL cholesterol level <35 mg/dL (0.90 mmol/L) and/or a triglyceride level >250 mg/dL (2.82 mmol/L)
   - Women with polycystic ovary syndrome
   - Physical inactivity
   - Other clinical conditions associated with insulin resistance (e.g., severe obesity, acanthosis nigricans)
2. Patients with prediabetes (A1C ≥5.7% [39 mmol/mol], IGT, or IFG) should be tested yearly.
3. Women who were diagnosed with GDM should have lifelong testing at least every 3 years.
4. For all other patients, testing should begin at age 45 years.
5. If results are normal, testing should be repeated at a minimum of 3-year intervals, with consideration of more frequent testing depending on initial results and risk status.

Glycosylated Hb assay (Hb A1c)

Glucose binds to blood hemoglobin within the circulating erythrocytes during glycosylation

remains attached for the life cycle of the red blood cell (120 days) as this binding is highly stable

measures blood glucose levels over a period of **8 to 12 weeks**

HbA1c results

Percentage	Inference
4-6%	normal
< 7%	good diabetes control
7-8 %	moderate diabetes control
> 8%	physician intervention suggested

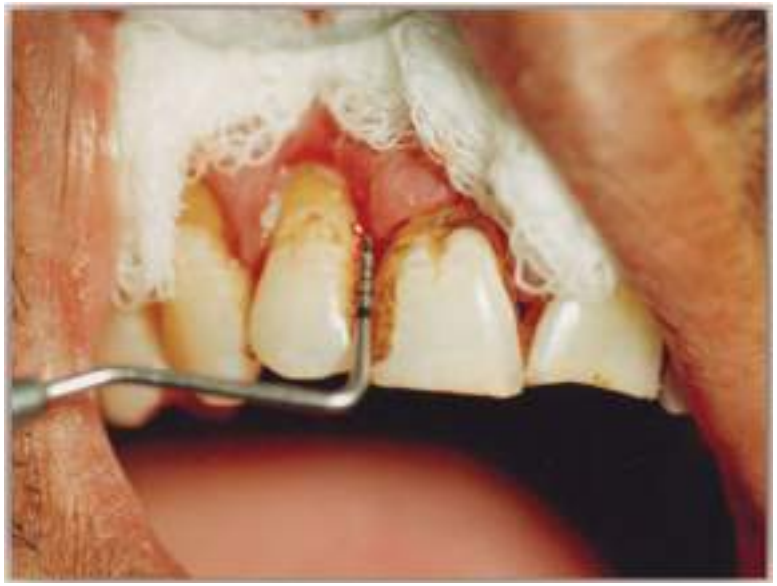
Correlation Between HbA1c Levels and Mean Plasma Glucose Levels

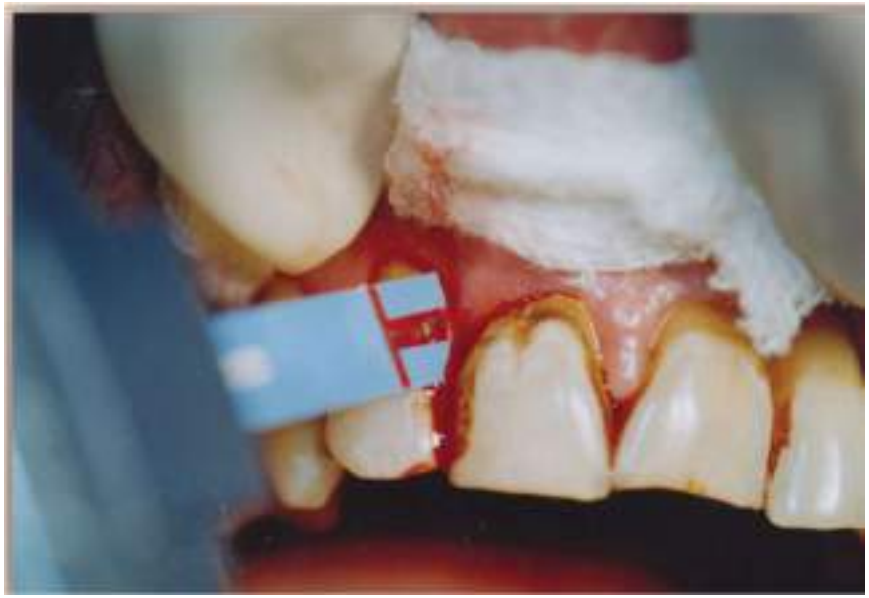
HbA1c (%)	Mean plasma glucose (mg/dl)
6	135
7	170
8	205
9	240
10	275
11	310
12	345

Self monitoring devices

- Glucometer for self blood glucose monitoring (SBGM)
- Small sterile lancet → puncture on the finger
- A drop of capillary blood drawn from the puncture site
- Blood placed on a strip placed in the glucometer
- Immediate reading

- For GCB, after probing, the site with profuse bleeding is selected and the device is introduced intraorally with the test strip in place and blood is allowed to flow onto its reactive area.
- The technique of Gingival Crevicular Blood described is more familiar and less traumatic to the patient than a finger puncture.
- This technique is safe, easy to perform and comfortable for the patient and might therefore help to increase the frequency of diabetes screening in dental offices.





Complications:

- **Acute :**
- Diabetic ketoacidosis
- Hyperglycemic Hyperosmolar State
- Hypoglycemia

Chronic

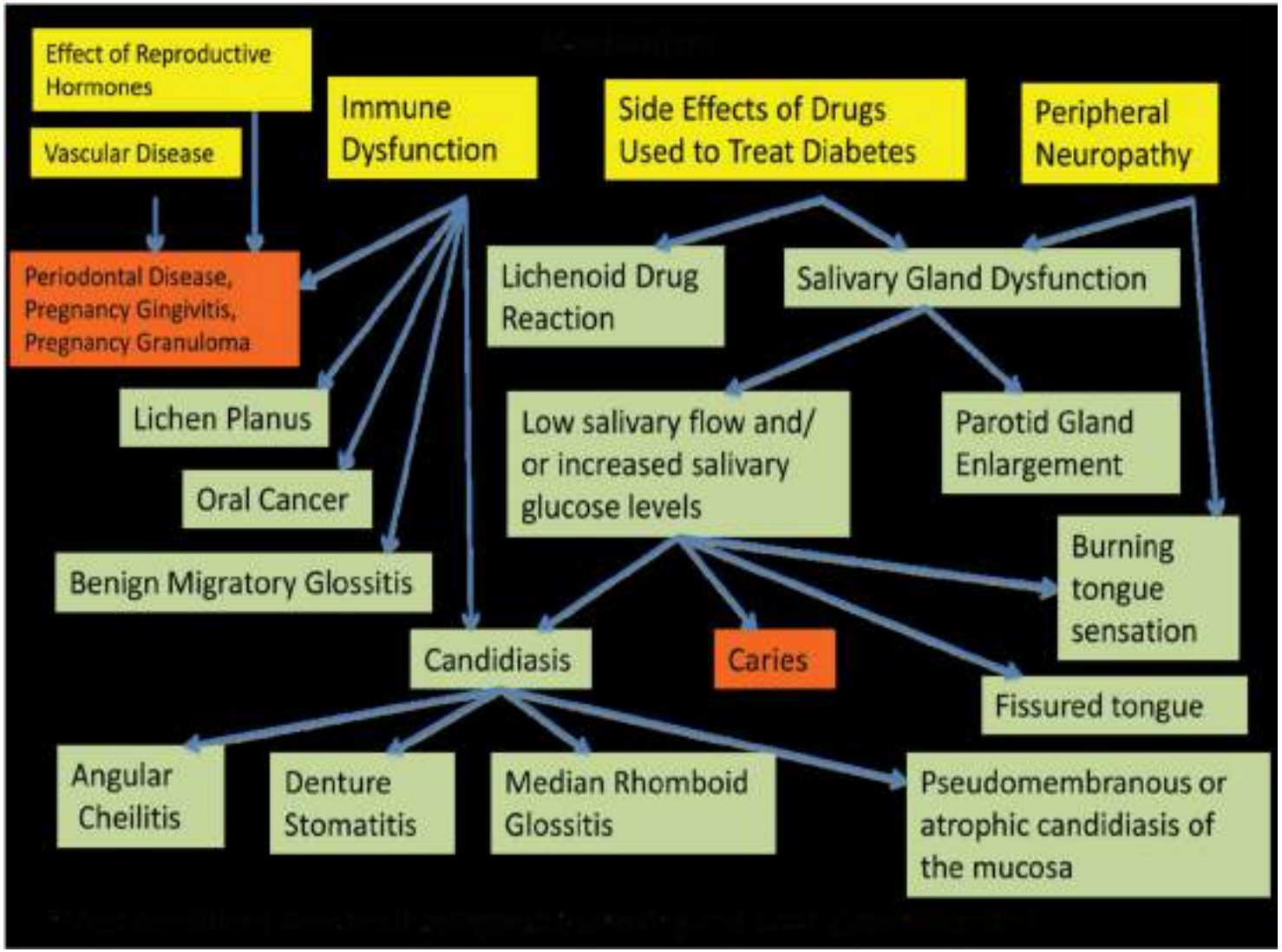
Microvascular:

-Retinopathy

-Nephropathy

-Neuropathy

Oral manifestation



Association between diabetes and periodontal disease

- Diabetes is a risk factor for periodontal disease
- sixth complication (Loe et al., 1993)
- Studies have clearly proven that diabetes increases the risk of both severity & incidence of periodontal disease progression.
- Increased gingival inflammation may be seen in diabetic subjects even though plaque levels are similar to non diabetic control.
- Further in addition , it has been shown that periodontal destruction was more severe in diabetic patients with greater bone loss & attachment loss.

Signs of gingivitis and periodontitis in diabetic patient

- Enlarged velvety red gingival tissues that bleed easily.
- Vascular changes that can give the gingiva a distinct purple/bluish hue.
- Multiple periodontal abscesses.
- Mobile teeth indicating bone loss.
- Proliferative tissue at the gingival margin.
- Inflammation spreading through the attached gingiva.
- Lack of resolution of gingival signs after conventional treatment.
- Severe, aggressive periodontitis relative to patient's age.
- Delayed wound healing following oral surgical procedures.

MECHANISM OF DIABETIC INFLUENCE ON PERIODONTITIS

- Changes in subgingival microbiota
- Increase in GCF glucose level and decreased wound healing
- Peripheral vasculature
- Formation of ADVANCED GLYCATION END PRODUCTS
- Altered host immune response (defects in PMN adherence, chemotaxis, phagocytosis)

Effect on periodontal flora

- In the diabetic patient, the abnormal host defence mechanism in addition to hyperglycemia state can lead to the growth of particular fastidious organism.
- The most frequently isolated microrganism are Prevotella intermedia followed by Camphylobacter rectus.
- The association of AA & capnocytophaga is similar to periodontitis in healthy patient & periodontitis in diabetic patient.
- Differences in the subgingival bacterial flora in people with diabetes, known to consists of Capnocytophaga, Vibrios & Actinomyces, P gingivalis, P.intermedia, Aacomitans. (Mushimo et al 1987)

Gingival crevicular fluid glucose level

- Increased blood glucose levels in diabetes are reflected in increased levels of GCF glucose.
- In vitro studies show decreased chemotaxis of periodontal ligament fibroblast to PDGF when placed in hyperglycemic environment compared to normoglycemic condition.
- Thus, elevated glucose levels in diabetes adversely affect periodontal wound healing & local host respose to microbial challenge.(Levin et al. 1989)

Periodontal Vasculature

- Increased thickening of gingival capillary endothelial basement membrane & the walls of small blood vessels seen in diabetes.
- This thickening may impair oxygen diffusion & nutrient provision across the basement membrane.
- Which alters normal tissue homeostasis leading to increased severity and progression of periodontal disease. (Frantzis et al, 1971; Listgarten et al, 1974; Seppälä et al, 1997).

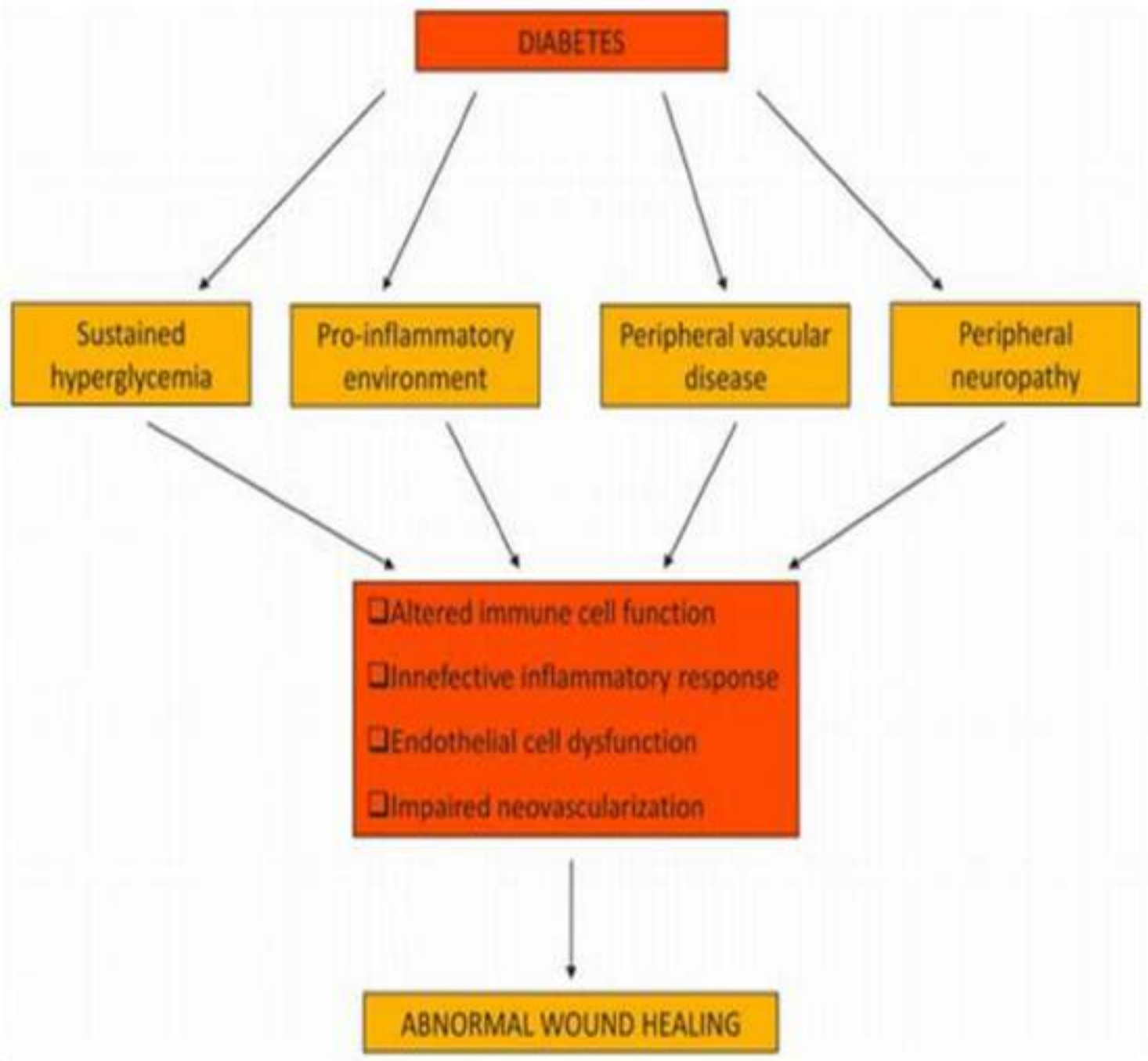
Collagen Metabolism

- Increased collagen breakdown through stimulation of collagenase activity has been observed in periodontium of diabetic individuals.
- Sustained hyperglycemia results in AGE modification of existing collagen with increased cross linking.
- This results in rapid degradation of recently synthesized collagen by host collagenase and predominance of older highly cross linked modified collagen.

Impaired wound healing

Table 1. Key events in wound healing

Repair phase	Key mediators	Defect in diabetes
Inflammation	Platelets, neutrophils, macrophages	Limited vasodilation Poor leucocyte infiltration Cell basement membrane thickening Glycosylation and aggregation of blood cells Increased viscosity of blood
Destruction	Neutrophils, monocytes	Poor chemotaxis Decreased phagocytosis Reduced bactericidal activity Endothelial damage by free radicals Poor tissue oxygenation Increased risk of infections
Proliferation	Fibroblasts, platelets	Reduced fibroblast numbers Decreased growth factors Low collagen content in granulation tissue Absence of cross-linking in collagen fibres
Maturation	Myofibroblasts, epithelial cells	Reduced contraction Prolonged granulation


DIABETES
Sustained hyperglycemia
Pro-inflammatory environment
Peripheral vascular disease
Peripheral neuropathy
❑Altered immune cell function
❑Innefective inflammatory response
❑Endothelial cell dysfunction
❑Impaired neovascularization
ABNORMAL WOUND HEALING

Altered host response

- Altered host response has long been considered in the pathogenesis of periodontitis.
- Defects in polymorphonuclear leucocyte adherence, chemotaxis, phagocytosis have been observed in some individuals with diabetes.
- Altered neutrophil chemotaxis may contribute to severity of periodontitis.
- These defects in diabetes may relate to insulin dysregulation.

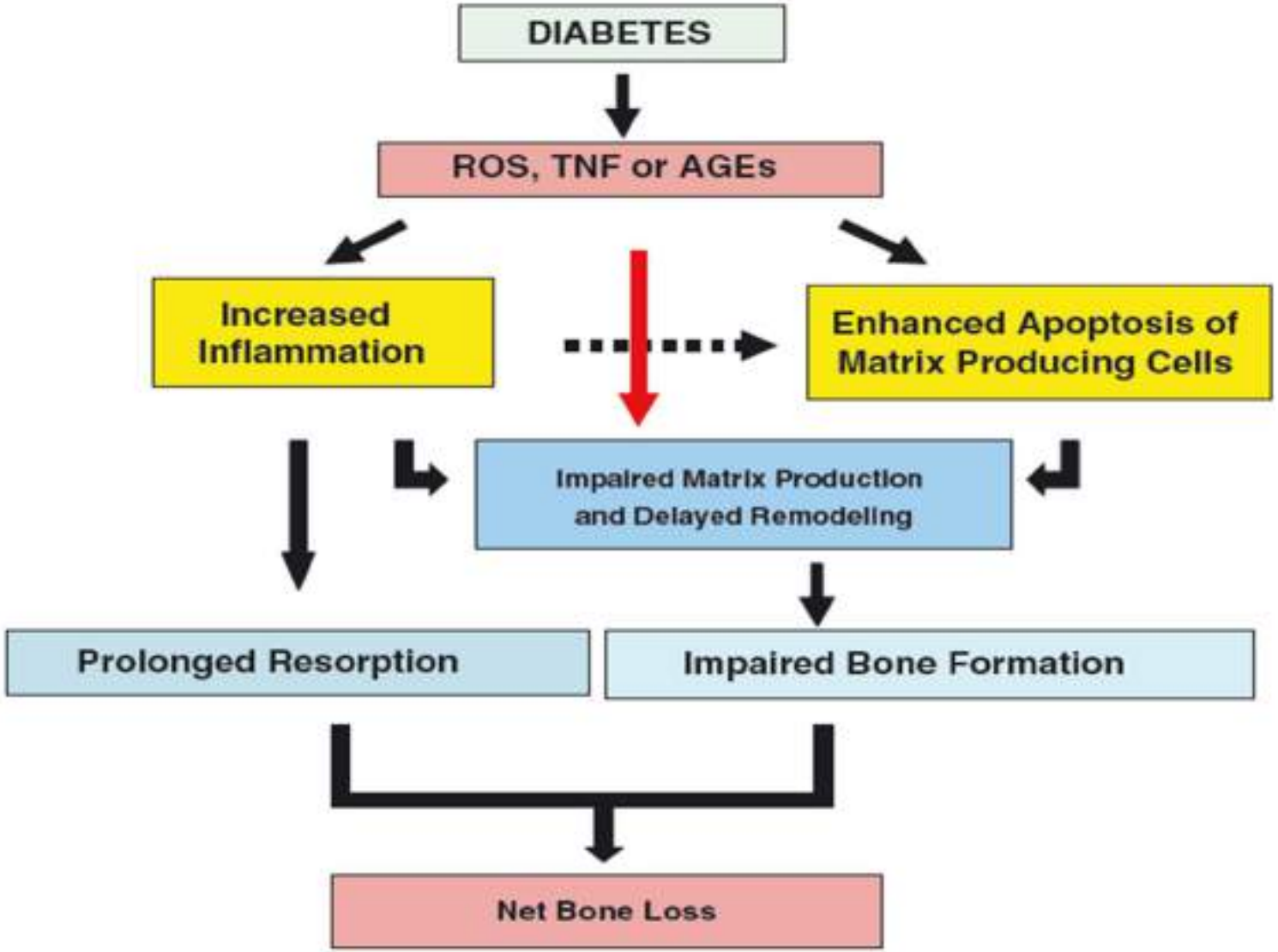
- **Impaired Neutrophil Function : (Gillman et al 1978)**
- Diabetes leads to impaired polymorphonuclear leukocyte adherence, chemotaxis and phagocytosis which decreases bacterial killing.
- This leads to proliferation of pathogenic bacteria and increased periodontal destruction.

- Accumulation of AGE in the periodontium causes influx of monocytes.
- Once in the tissue AGEs interact with the RAGE induces proinflammatory cytokine production.
- Monocytes from patients with T1DM have a hyper-inflammatory phenotype and these cells respond to LPS from periodontal bacteria to produce significantly higher levels of IL-1b, TNF-a and PGE2 than cells from patients without diabetes. (Salvi et al. 1997)

Effect of AGEs on Periodontium:

- AGEs accumulate two fold in diabetic periodontium as compared to other tissues.
- Increased accumulation of AGEs and their interaction with RAGE in diabetic gingiva leads to
  - vascular dysfunction and hyper permeability,
  - loss of effective tissue integrity and barrier function,
  - alteration, immobilization and activation of mononuclear phagocytes,
- critical mediators in generation of proinflammatory cytokines and matrix metalloproteinase's (MMP's). (Lalla et al., 2000)

Diabetes and alveolar bone destruction



Mechanisms through which diabetes may affect periodontal disease progression. (Graves et al., 2007)

- Diabetes-induced production of reactive oxygen species, tumor necrosis factor or advanced glycation end products can have direct effects on bone including increased osteoclast formation and resorption as well as inhibition of collagen production by osteoblasts.
- However, they could also have indirect effects by enhancing apoptosis of osteoblasts or their precursors.

How periodontitis affects diabetes

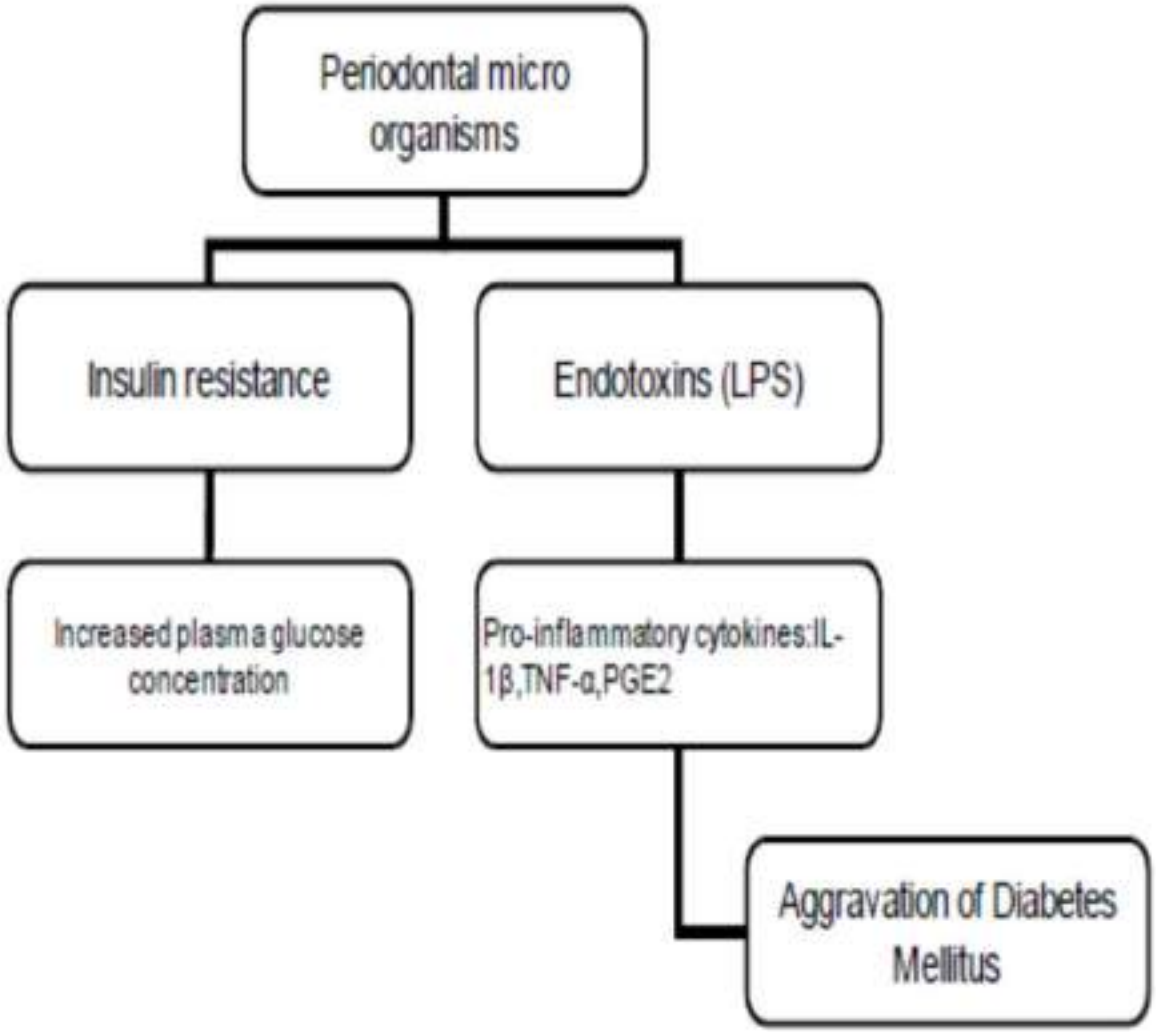
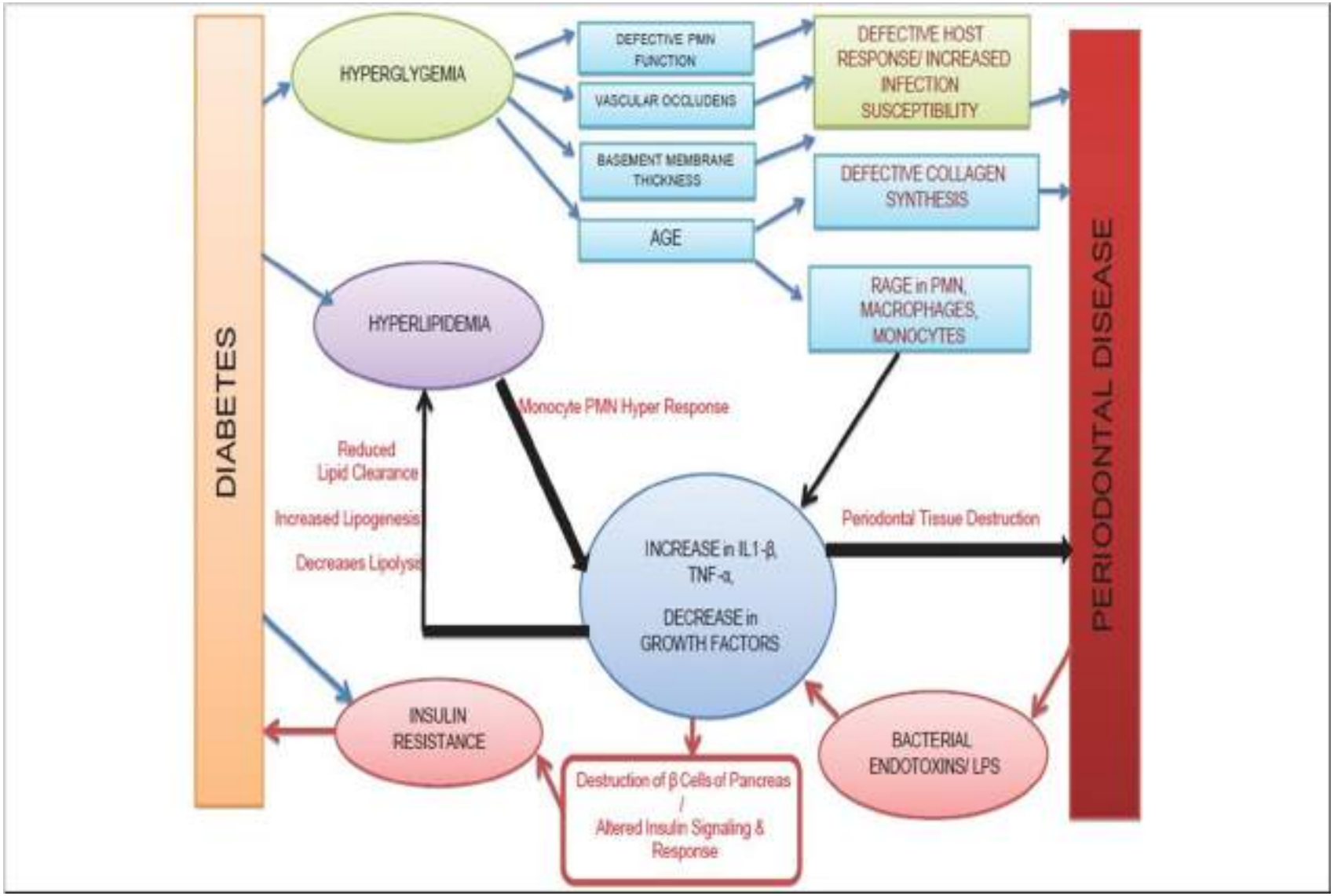


Fig. I: Mechanisms by which periodontitis may influence diabetes mellitus



Molecular mechanisms involved in the bidirectional relationship between diabetes mellitus and periodontal disease.(Grover HS et al., 2013)

Oxidative stress

- Oxidative stress is inextricably linked with chronic inflammation.
- Biochemical markers of systemic oxidative stress are elevated in both diabetes and periodontitis (Bullon et al. 2009) and are positively correlated with CRP in periodontitis patients as compared to healthy controls (D'Aiuto et al. 2010)

Effects of diabetes on the response to periodontal therapy

- Well-controlled diabetics →the clinical and microbiologic response to SRP similar to that in non-diabetic individuals. (Christgau et al, 1998; Tervonen et al, 1991)

- Patients with poorer glycemic control → more rapid recurrence of deep pockets and a less favorable long-term response. (Tervonen, 1997)

Management of diabetic patients

- Periodontal infection may worsen glycemic control and should be managed aggressively.
- Diabetic patients with periodontitis should receive oral hygiene instructions, mechanical debridement to remove local factors, and regular maintenance.
- When possible, an HbA1c of less than 7.5% should be established before surgical treatment is performed.

Systemic anti-infective therapy

- Systemic antibiotics are not needed routinely, although recent evidence indicate that tetracycline antibiotics in combination with scaling and root planing may positively influence glycemic control.
- If the patient has poor glycemic control and surgery is **absolutely** needed, prophylactic antibiotics may be given; penicillins are most often used for this purpose. **(Rees TD, 2000)**

- Doxycycline (DOX) 100mg: Is one of tetracycline (TCN) family it is the most potent family member as an anticollagenase drug besides its potent antimicrobial effects on most periodontal microorganism (bacteriostatic activity).
- It has the ability to concentrate in periodontal tissues with less side effects (nephrotoxic) comparing with TCN as it is not metabolized in the kidney. **(Rees TD, 2000)**

Management of known diabetic patients

- The patient should be questioned regarding the type of diabetes, the age at onset and duration of the disease; any current medications and their method of administration.
- Review any previous history of diabetic complications, determine the most recent laboratory results and record the name and address of the patient's physician.
- Under most circumstances, it would be prudent to obtain medical clearance prior to performing any extensive periodontal therapy, especially if surgery is indicated. **(Rees TD , 2000)**

- Periodontal surgical procedures can be performed, although it must be assured that the patient can maintain a normal diet post-surgically.
- If the treatment procedure modifies the patient's dietary habits, dietary supplements should be recommended.
- Supportive periodontal therapy should be provided at relatively close intervals (2 to 3 months) since some studies indicate a slight but persistent tendency to progressive periodontal destruction despite effective metabolic diabetes mellitus control. **(Rees TD , 2000)**

- In most instances a nonsurgical approach to periodontal therapy is preferred, with or without the use of appropriate antibiotic therapy.
- In the event that antibiotic therapy is anticipated, microbiological testing to identify putative periodontal pathogens is suggested.

Management of uncontrolled or poorly controlled diabetic patients

- Should not receive elective dental treatment until the condition is stabilized or medical clearance obtained.
- Consult the patient's physician.
- Analyze laboratory tests such as fasting blood glucose and casual glucose.
- Rule out acute orofacial infection or severe dental infection; if present, provide emergency care immediately.
- Establish best possible oral health through nonsurgical debridement of plaque and calculus; institute oral hygiene instruction. **(Carranza, 13th edition)**

Management of hypoglycemia

Causes of hypoglycemia includes: (Wray L et al., 2011)

- Excess insulin
- Stress
- Missed / Delayed meals
- Excess oral hypoglycemics (Sulphonylureas)

Identification and Treatment of Hypoglycemia	
Identification	
Symptoms	**Signs**
• Shakiness • Anxiety • Increased sweating • Hunger	• Tremors • Tachycardia • Altered consciousness (lethargy and obtundation or personality change) • Blood glucose level: < 60 mg/dl
Treatment	
Conscious patient	**Unconscious patient**
• Administer 15 mg of simple carbohydrates • Repeat finger- stick glucose test in 15 minutes: • Blood glucose level > 60 mg/dl: patient should be asked to eat or drink (for example, a sugar-sweetened beverage) • Blood glucose level < 60 mg/dl: repeat treat- ment of 15 g of simple carbohydrates and check blood glucose in 15 minutes. Continue until achieving a blood gluco- se level > 60mg/ dl Ask the patient to notify his/ her physician.	**With intravenous access:** • Administer 5 to 25 g of 50% dextrose immediately • Notify the patient's physician **Without intravenous access:** • Apply glucose gel inside the mouth in a semiobtund patient or treat with 1 mg of glucagon intramuscu- larly or subcutaneously • Repeat the blood glucose test in 15 minutes • Establish intravenous access and notify the patient's physician

Conclusion

- Prevention and control of periodontal disease must be considered as an integral part of diabetes control.
- Well controlled diabetics have a similar incidence of periodontitis as do non diabetics.
- Diabetic patients must be educated about the maintenance of good oral hygiene, which can improve their periodontal health as well as glycemic control.