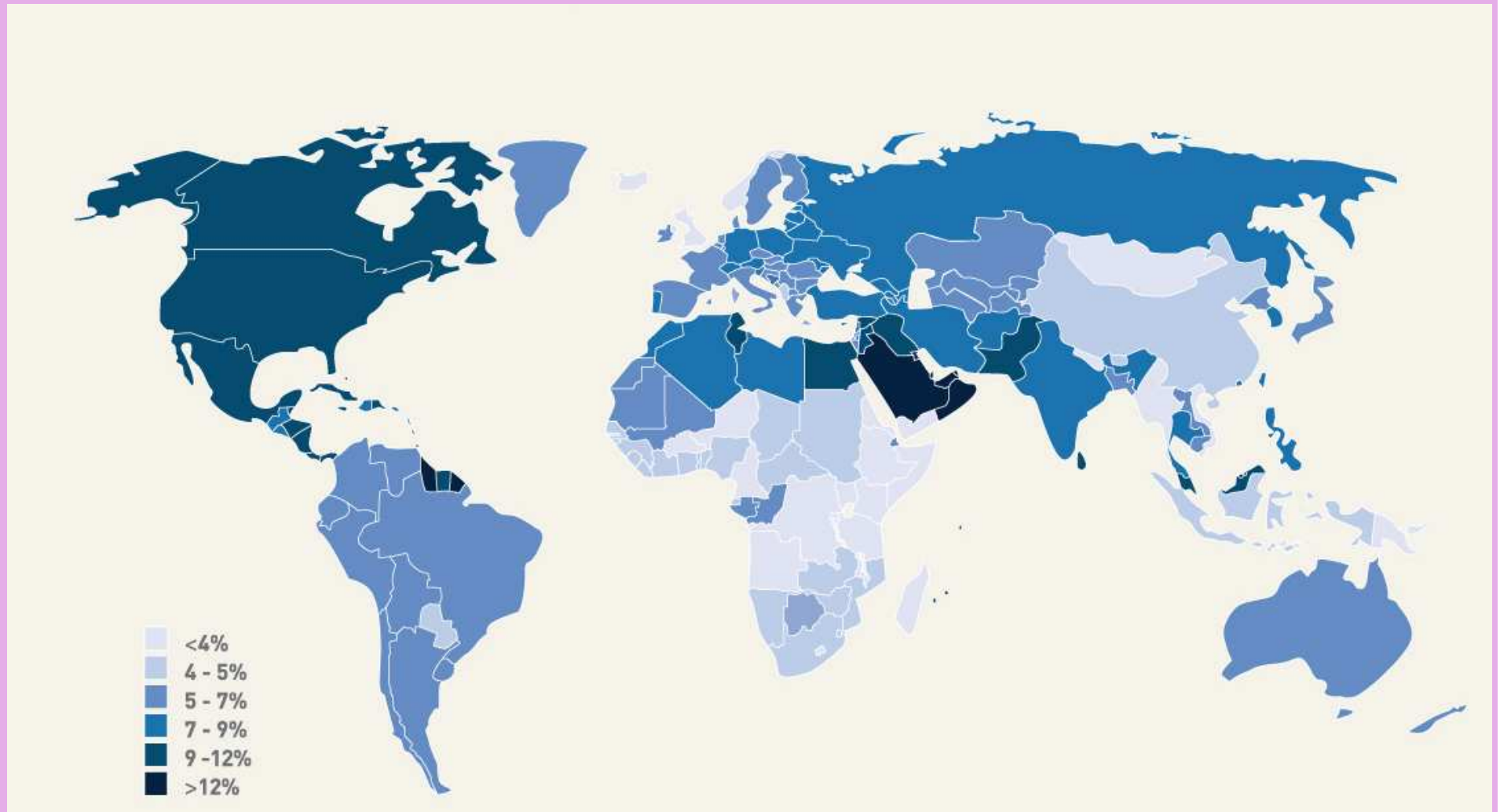


Diabetes Mellitus and Periodontal Disease

Penny Hodge

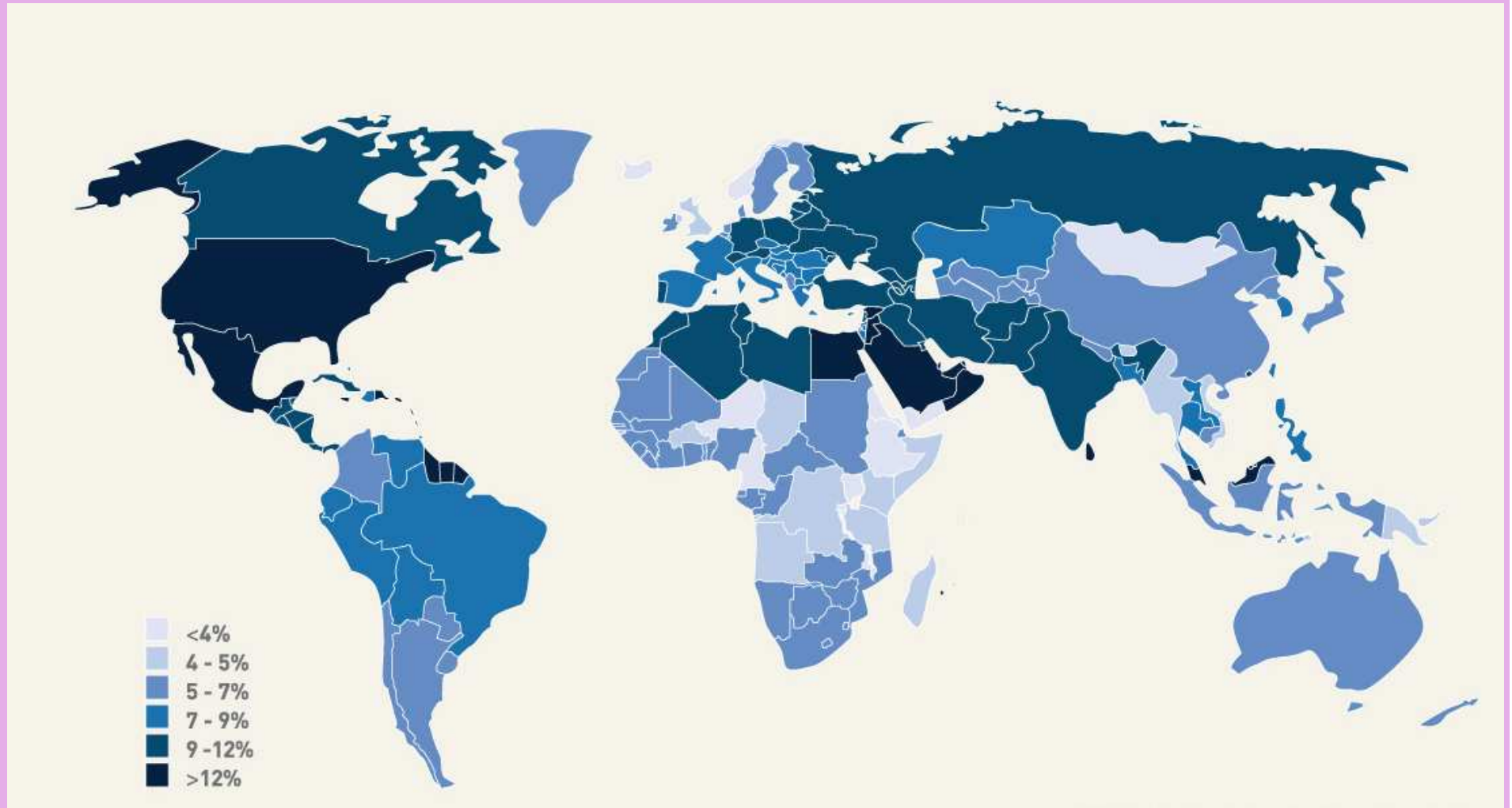


Prevalence (%) estimates of diabetes (20-79 years), 2010



IDF Atlas, 4th ed. © International Diabetes Federation, 2009

Prevalence (%) estimates of diabetes (20-79 years), 2030



IDF Atlas, 4th ed. © International Diabetes Federation, 2009

Periodontal disease

Prevalence

- Consensus is that prevalence of gingivitis and mild/moderate disease is decreasing
Baelum et al 2007, König et al 2010
- Wide variation between countries depending on income
- Prevalence of severe disease is 5-15%

Prevalence - caution

- Many epidemiological surveys used partial mouth recording

Eke et al 2010

- Within high income countries variations depending on socio-economic status

Baelum et al 2007

- Longevity and tooth retention is increasing
- New risk indicators

Periodontitis

Risk Factors

- Cigarette smoking

Tomar and Asma 2000; Bergström 2006

- Type 2 diabetes

Emrich et al 1991; Tsai et al 2003;

Khader et al 2006; Taylor 2009; Chávarry et al 2010

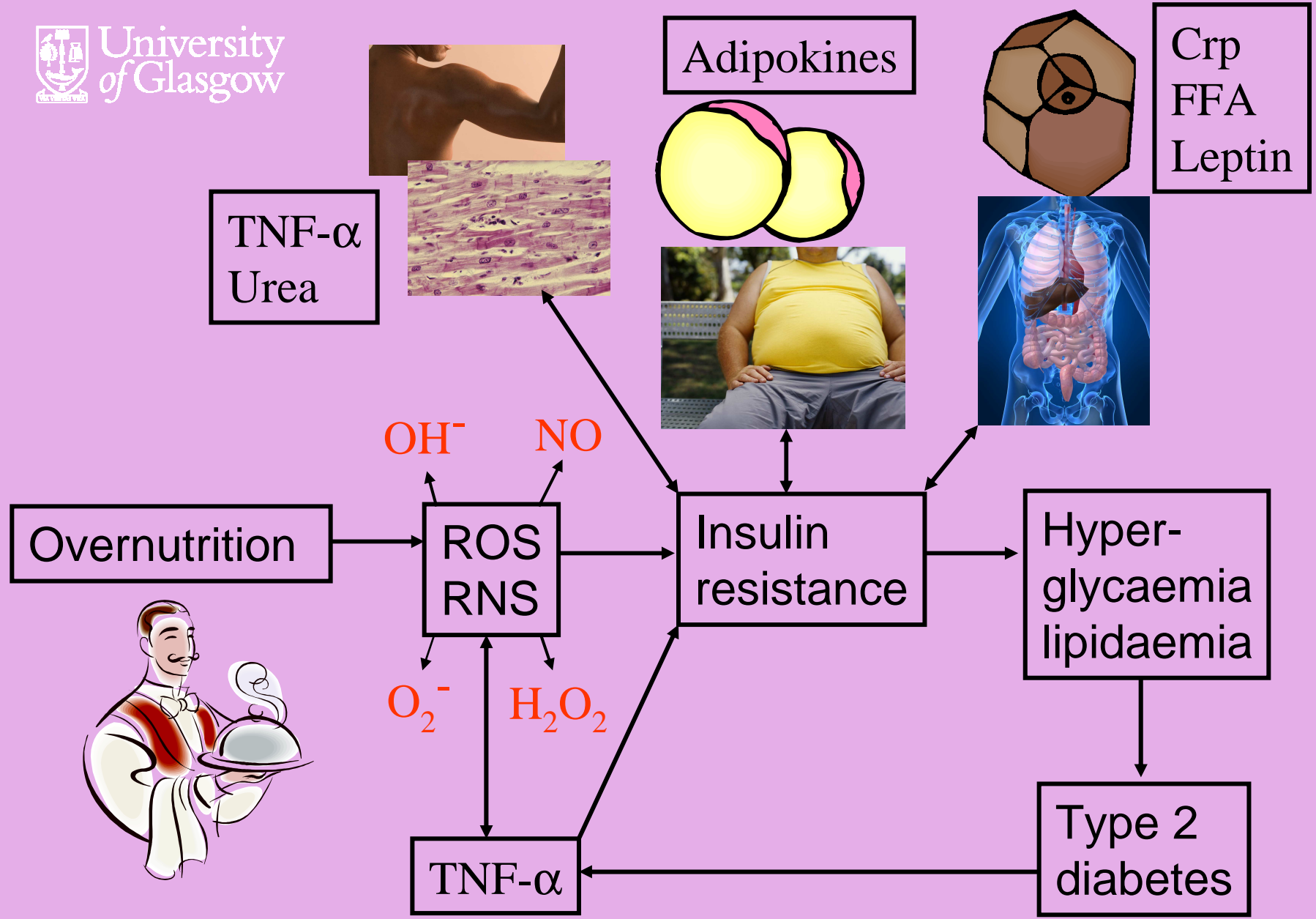
? ? ? IMPORTANT QUESTIONS ? ? ?

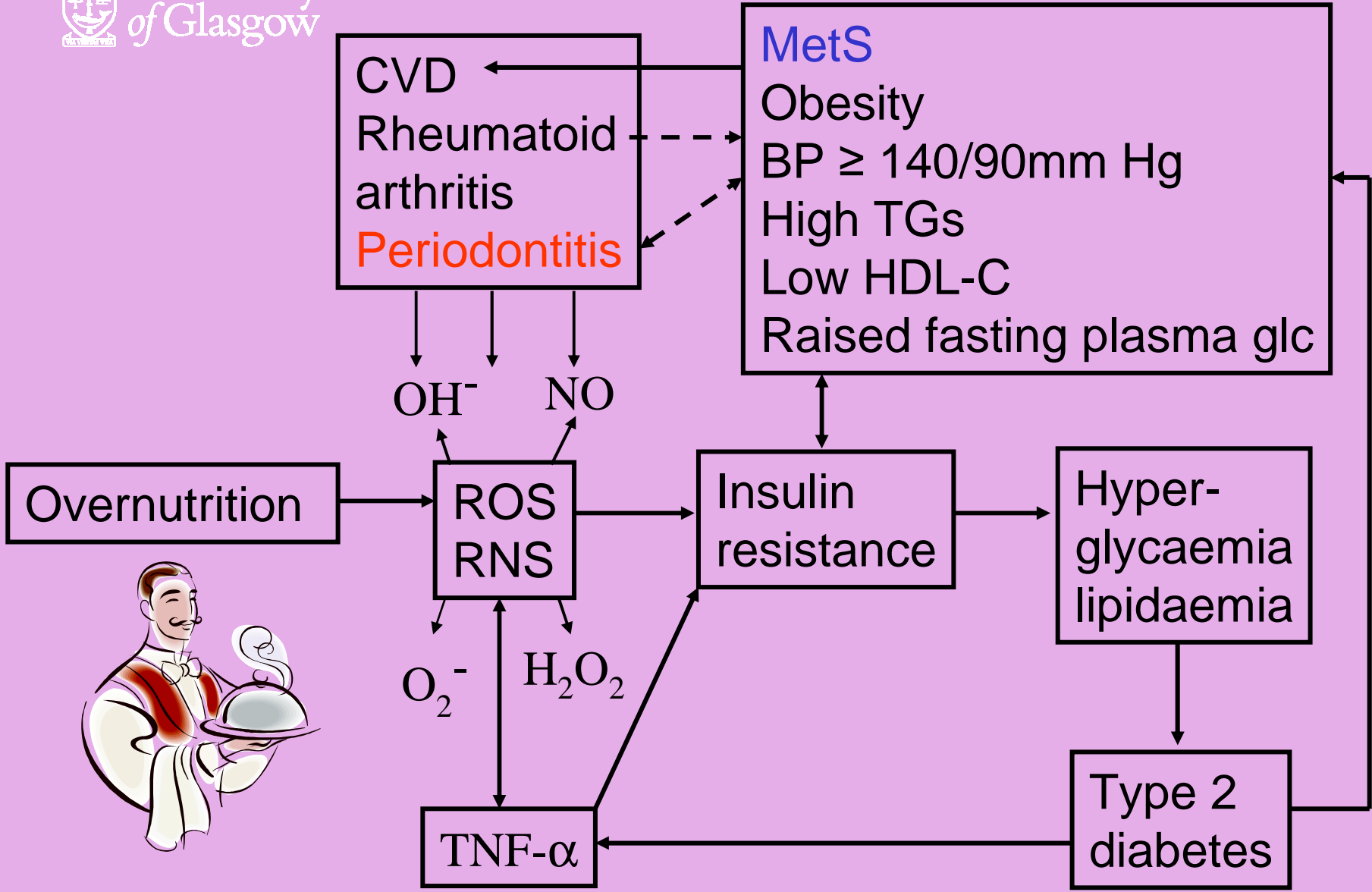
- Is there an association between type 1 diabetes and periodontal disease?

Khader et al 2006; Chávarry et al 2009

- Does diabetes occur before periodontitis or vice versa?
- Can treatment of periodontitis improve glycaemic control in diabetic patients?

Could periodontitis be on the causal
pathway for diabetes?





Damage:
Blood vessels
Eyes
Kidneys
Periodontium

Overnutrition



OH⁻ NO
ROS
RNS
O₂⁻ H₂O₂

RAGEs

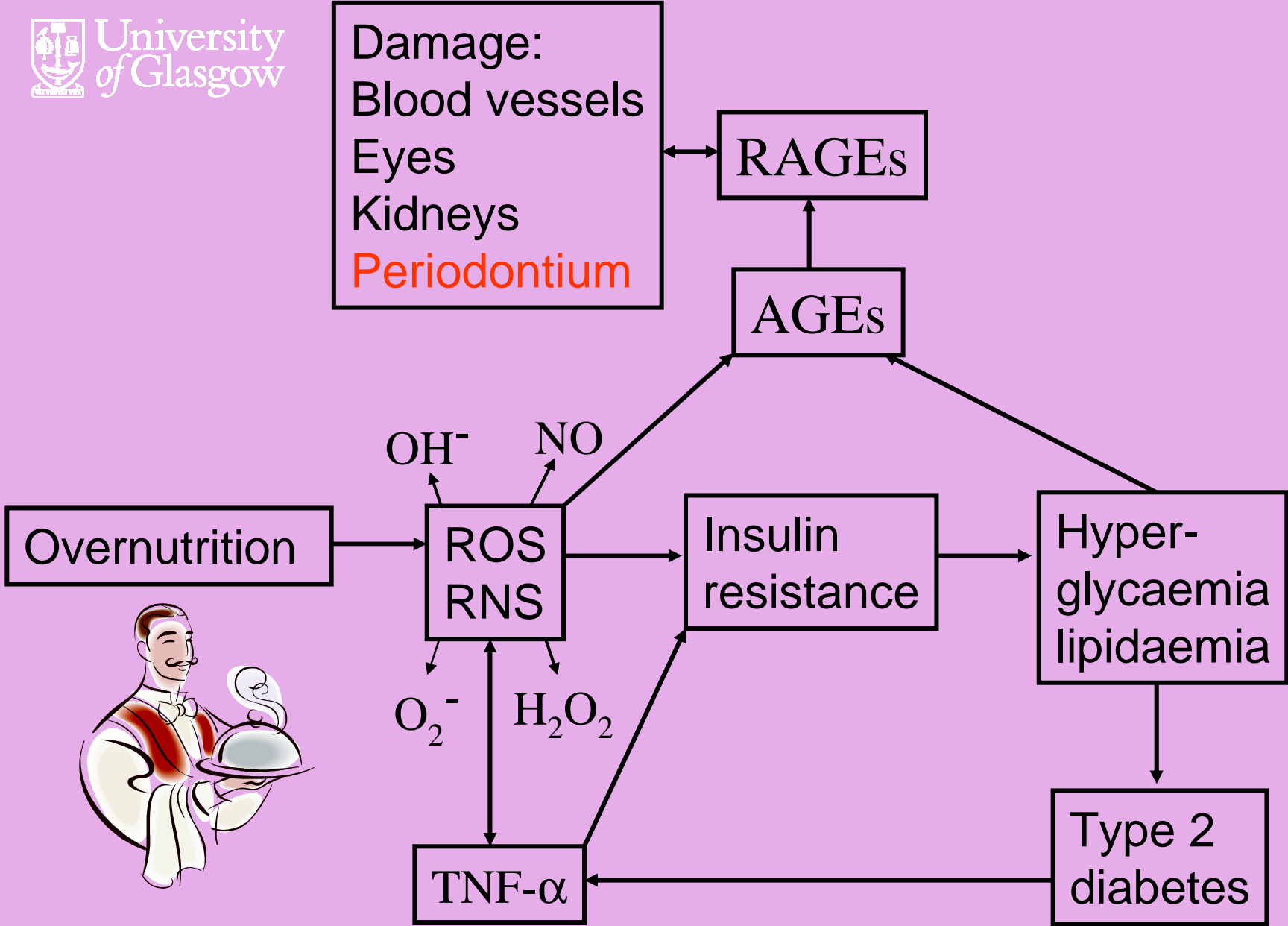
AGEs

Insulin resistance

Hyper-glycaemia
lipidaemia

TNF- α

Type 2 diabetes



Periodontitis

- It appears that peripheral blood neutrophils may be hyperactive in CP and AgP patients

Matthews et al 2007

- Total antioxidant capacity is decreased in the periodontal tissues in periodontitis

Chapple et al 2007

- There is increasing evidence of the effect of AGE and RAGE in pathogenesis and progression of periodontitis

Takeda et al 2006, Katz et al 2005

Markers of oxidative stress in diabetes and periodontitis

- iNOS a marker of nitric oxide is increased in periodontitis and in diabetic patients with periodontitis

Lappin et al 2000; Pan et al 2010

- Plasma lipid peroxidation is correlated with levels of periodontitis in diabetes

Colin et al 2000; Sonoko et al 2006

Following treatment of periodontitis in diabetic patients

- Decrease in plasma hsCRP between baseline and one month has been found to correlate with reduction in HbA1c levels at six months *Katagiri et al 2009*

- Reduced serum ROS, IL-1 β , IL-6, TNF α compared with baseline

Iwamoto et al 2001, Al-Mubarak et al 2002, O'Connell et al 2008

Clinical studies

Cross-sectional studies

Deep periodontal pockets and alveolar bone loss have been associated with impaired glucose tolerance in Japanese adults

Saito et al 2004, 2006

In another Japanese study a relationship was found between severity of periodontal disease measured using CPI and HbA1c levels

Hayashida et al 2009

Clinical studies

NHANES I

Does baseline periodontal status predict incidence of diabetes during 20 years of follow up?

9,296 initially diabetes free participants

Increased levels of periodontitis at baseline predicted a 2x increase in incident diabetes

BUT

Absence of HbA1c or FPG levels at baseline

Demmer et al 2008

Study of Health in Pomerania (SHIP)

Is periodontal disease related to HbA1c progression in diabetes-free subjects?

- 2,793 adults aged 20-79 years
- Baseline HbA1c and at 5 years
- Split into four groups with increasing % sites ≥ 5 mm CAL at baseline
- Adjustments for age, sex, region, smoking, waist:hip ratio, education, SBP, TGs and exercise

Demmer et al 2010

Study of Health in Pomerania (SHIP)

Results

- Difference in the change in lowest % CAL and highest % CAL in HbA1c over five years was 0.08% (p=0.025)
- The increase in change in HbA1c was greater in those with highest %CAL who also had high levels of hsCRP \geq 1mg/l compared with those with <1mg/l (p=0.01)

Demmer et al 2010

Study of Health in Pomerania (SHIP)

Results

Longitudinal data

When those who were healthy at baseline and follow-up were compared with the group with the highest % CAL at baseline and whose periodontal health deteriorated during the five years of the study, the change in mean HbA1c was much greater in the latter group (0.143% cf 0.005% $p=0.003$)

Demmer et al 2010

Study of Health in Pomerania (SHIP)

Interpretation

- Multiple comparisons in the x-sectional analysis
- Interaction between change in CAL and hsCRP is interesting
- Longitudinal data indicate that deteriorating periodontal health may have a detrimental effect on HbA1c but there may be other common confounding factors

Demmer et al 2010

Periodontal Disease and Incident Diabetes: a seven year study

- 5,848 Japanese civil servants took part
- Periodontal status defined by CPITN at baseline
 - 3 - represented moderate disease
 - 4 - severe disease
- Annual health check included:
 - Height and weight; BP
 - smoking status
 - plasma glucose; HDL-C; TGs

Ide et al 2011

Periodontal Disease and Incident Diabetes: a seven year study

Results

- 3883 male and 1965 female subjects
- 287 incident cases of diabetes were diagnosed
Follow-up 6.5 years; 82% had FPG 6 times
- 9.9% males and 5.4% females had severe periodontitis (SP)
- After adjusting for age, sex, smoking, high BMI no association between moderate or SP
HR = 1.04 (0.77-1.3), HR = 1.43 (0.99-2.07), p=0.056)

Periodontal Disease and Incident Diabetes: a seven year study

Interpretation

- Authors concluded that having periodontitis at baseline was not an independent risk factor for incident diabetes in this population
- CPITN is an imprecise tool for assessing severity and extent of periodontitis

Baelum & Papapanou 1996

- No inter or intra reliability scores were recorded for the examiners

What are the possible links between diabetes and periodontitis?

- Age
- Obesity
- Genes
- Smoking
- Stress
- Socio-economic status
- Infection
- Rheumatoid arthritis
- Cardiovascular disease

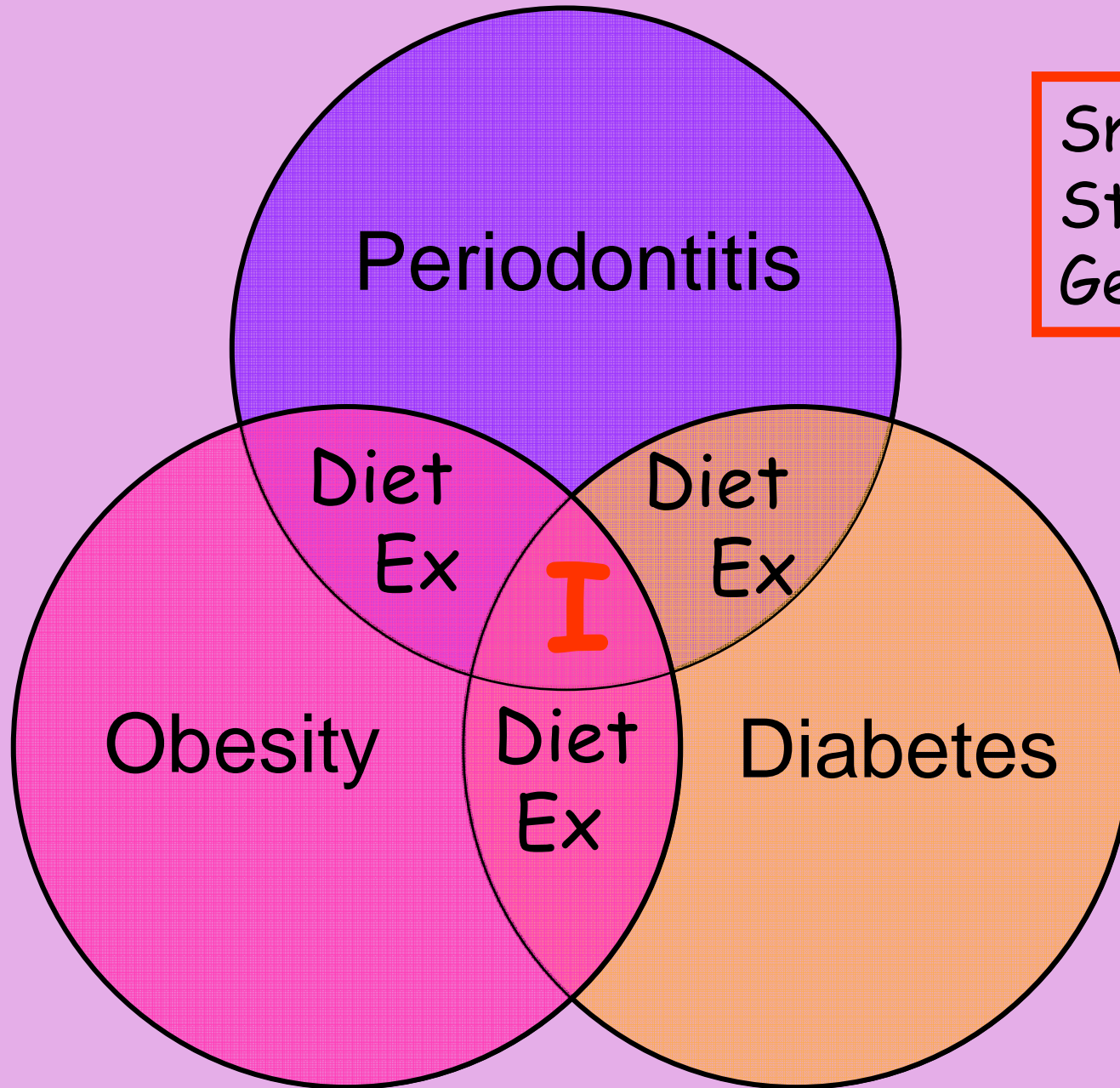
Obesity and periodontitis

First study in animal model which associated obesity with periodontitis

Perlstein and Bissada 1977

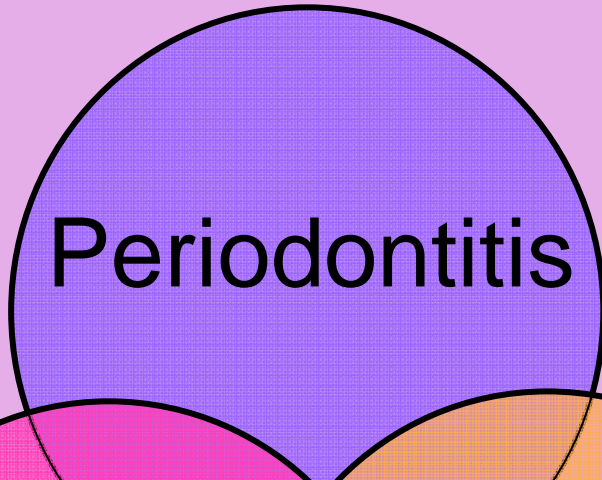
Since late 1990s have been several studies which have associated obesity with periodontitis

Genco et al 2005; Pishon et al 2007; Saxlin et al 2011



Smoking
Stress
Genes

CRP
IL-1
TNF α
IL-6



Periodontitis

Obesity

Diabetes

I

Adipokines
e.g.
chemokines
leptin

HbA1c
AGEs

Does treatment of periodontitis improve glycaemic control?

Four systematic reviews and meta-analyses:

Janket et al 2005 - JDR

Darre et al 2008 – Diabetes and Metabolism

Teeuw et al 2010 – Diabetes Care

Simpson et al 2010 – Cochrane Collaboration

Janket et al 2005 meta-analysis - JDR

- Data sources:

 - Medline

 - Evidence-based Medicine Reviews

 - Cochrane Register of Controlled Trials

- Restricted to English language 1980 - 2005
- Minimum duration two months
- 10 studies = 456 patients included
- The weighted average decrease in HbA1c was:
 - 0.4% (95% CI: -1.5 to 0.7) all studies
 - 0.7% (95% CI: -2.2 to 0.9) type 2 diabetes
 - 0.7% (95% CI: -2.3 to 0.9) +antibiotics

Darré et al 2008 - Diabetes & Metabolism

- Data sources:

Medline; Embase; LILACS; Cochrane Library; Pascal; IADR abstracts and Current Contents
hand searching of bibliographies

- No language restriction 1976 - 2007
- 9 CCT = 485 patients included in meta-analysis
- Standardised mean difference of 0.46 in HbA1c; used global SD to transform SMD into HbA1c: 0.79% (95% CI: 0.19 to 1.40)
- If removed one non-randomised study the SMD became 0.27 (95% CI: -0.01 to 0.60)

Teeuw et al 2010 - Diabetes Care

- Data sources:

Medline

Cochrane Central Register; hand searching

- Language restriction English 1960-2009
- Only CCT (2) & RCT of at least 3 months duration
- 5 studies = 371 patients included in meta-analysis
all in type 2 diabetic patients
- Weighted mean difference in HbA1c :
0.4% (95% CI: -0.04 to -0.77; p=0.03)
- *Significant heterogeneity between studies*

Simpson et al 2010 - Cochrane Database

- Data sources:

Medline; Cochrane Register; Embase; Cinahl; Zetoc
ISI Web of Knowledge; LILACS; hand searching

- Language restriction English 1950-2010

- RCTs only; minimum 3 months duration

- 7 studies systematic review

- 3 studies = 244 patients included in meta-analysis

- Mean difference in HbA1c:

0.4% (95% CI: -0.78% to -0.01%; p=0.04) all

0.8% (95% CI: -1.73% to 0.13%) no antibiotics

0.36% (95% CI: -0.83% to 0.11%) +antibiotics

Relevance to care of diabetic patients

UKPDS

Each 1% reduction in HbA1c was associated with a reduced relative risk of:

21% for any diabetes endpoint

21% for diabetes related mortality

14% for MI

35% for microvascular complications

Stratton 2000

Recommendations for future studies

- Control group - withhold treatment?
 - usual care
- Adequate sample size - use data from existing trials
- Clear definitions of diabetes and periodontitis
Periodontal **I**nflamed **S**urface **A**rea
Nesse et al 2008, 2009
- Adequate and transparent reporting of methodology

Recommendations for future studies

- Should include data relating to confounding factors
- Studies should investigate the effect in type 1 and type 2 patients
- Update the findings of Cochrane Review
- Outcome measures to include:
 - HbA1c
 - periodontal
 - quality of life
 - impact on diabetes complications

Diabetes and Periodontal Therapy Trial

- Phase III randomised controlled clinical trial
- Aim: to determine if non-surgical therapy is efficacious compared with delayed therapy in reducing HbA1c, 6 months post randomisation in subjects with T2 DM & untreated moderate to advanced chronic periodontitis
- Estimated enrolment – 600
- Estimated completion date June 2013
- Study chair – Dr Steven Engebretson, Stony Brook University, New York

“Management of periodontal disease is moving from the repair model to a wellness model of patient care”

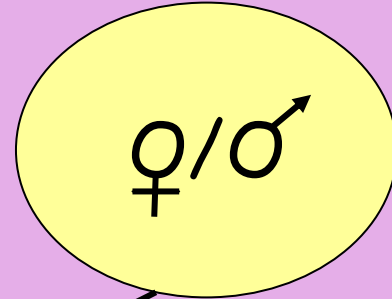
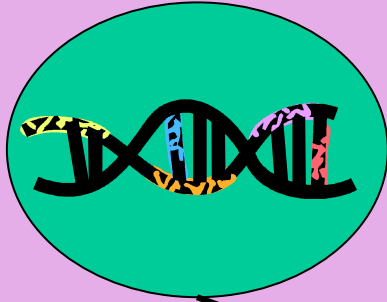
Page et al 2002



Global Burden

	2010	2030
Diabetes		
Global prevalence	6.6	7.8
Comparative prevalence	6.4	7.7
Number of people (millions)	285	438
Impaired Glucose Tolerance		
Global prevalence	7.9	8.4
Comparative prevalence	7.8	8.4
Number of people (millions)	344	472

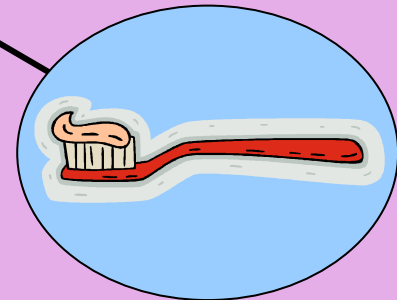
FIXED



Systemic Disease



Stress



MODIFIABLE

Nutrition

Potential mechanisms underpinning the nutritional modulation of periodontal inflammation

Chapple J Am Dent Assoc 2009; 140;178-184

Micronutritional approaches to periodontal therapy

Van der Velden et al J Clin Periodontol 2011; 38 (Suppl. 11): 142-158

Thank *your* for *your* attention