

# Diabetes

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# Diabetes

- **Diabetes - 21st century pandemic**
- **Diabetes is now the single greatest contributor to chronic disease**
- **Obesity will soon become the leading cause of death**



*National Diabetesity Forum*

Obesity can alter the natural history of T2DM by virtue of the role of **visceral** fat with its

Proinflammatory

Prothrombotic

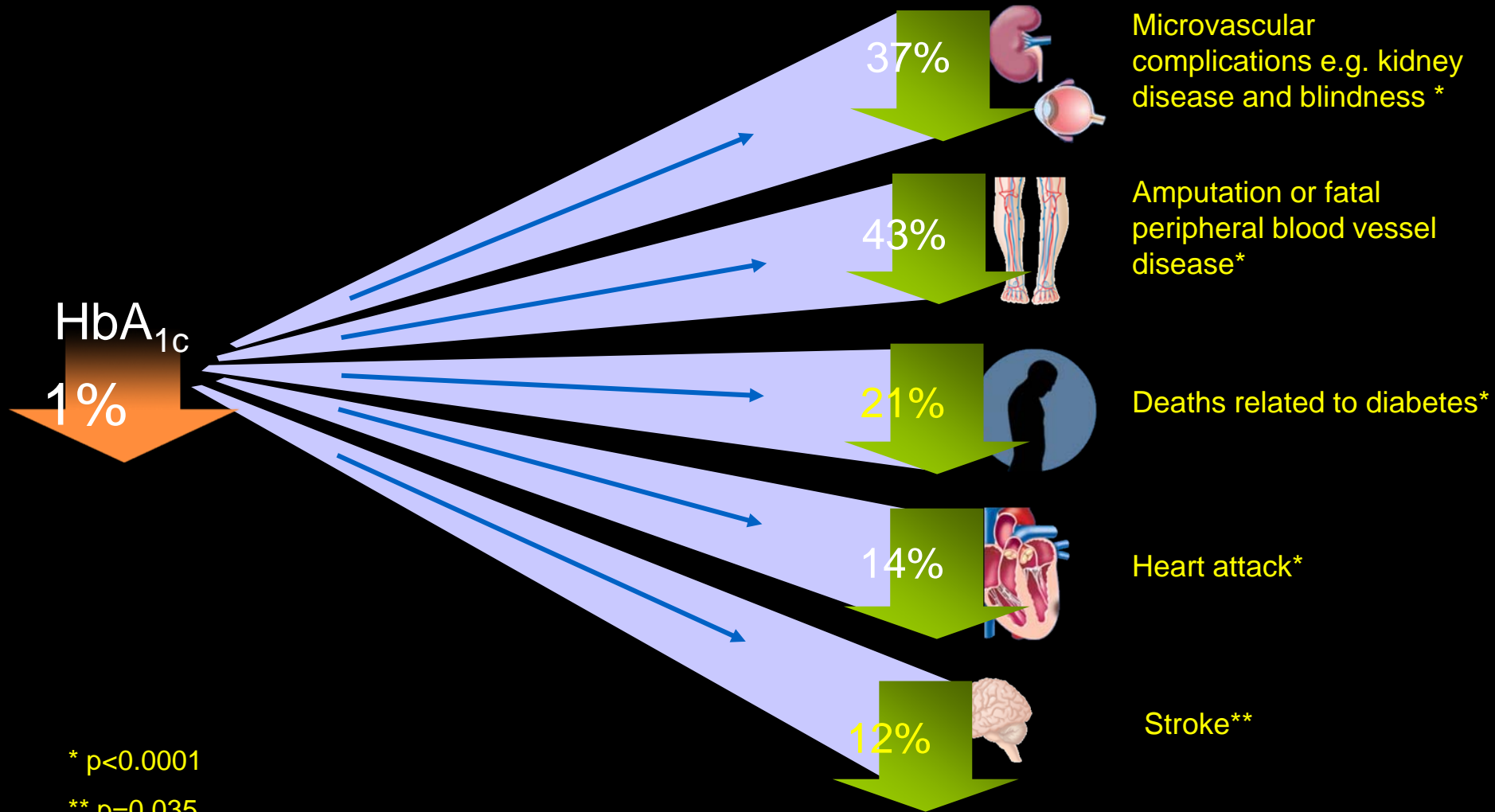
Proinsulin resistant environment.



Weight gain in patients with DM can

- Contributes to patient frustration
- Negatively impact their compliance
- Increases cardiovascular risk

# UKPDS: A 1% decrease in HbA<sub>1c</sub> is associated with a reduction in complications



\* p<0.0001

\*\* p=0.035

# Glycaemic control and body weight

**Weight gain appears unavoidable when patients with Type 2 diabetes are commenced on insulin**

**Body weight increases by 2Kg for each percentage point decrease in HbA1C during the first year<sup>1</sup>**

**Gain in weight mainly represents an increase in fat mass, which enhances insulin resistance and increases the risk of obesity related complications.**

**Calculations of average weight gain are that for every 5 mmol/l reduction in fasting glucose,**

**Or**

**a 2.5% fall in HbA1c,**

**approximate weight gain is 5 kg (Makimattila et al, 1999)**

**Makimattila S, Nikkila K, Yki-Jarvinen H (1999) Causes of weight gain during insulin therapy with and without metformin in patients with type II diabetes mellitus. Diabetologia 42: 406-12**

**Causes of weight gain in Type 2 Diabetes?**

# Causes of weight gain

- **Reduced glycosuria**
- **Anabolic action of insulin**
- **Fluid retention**
- **Hypoglycaemia and increased calorie consumption**
- **Excess insulin administration**
- **Combination of obesity and muscle impairment: 'sarcopenic obesity'.**

# ***Diabetes Team***

- **Endocrinologist**
- **Diabetes Nurse specialist**
- **Dietitian**
- **Physiotherapist**
- **occupational therapists**
- **Social worker**
- **Psychologists**
- **Bariatric surgeon**

# Evaluation:

## Detailed History

- Perception
- Motivation
- Hunger pattern
- Body image
- Glycaemic excursion

# Evaluation:

- **Psychological state**
- **Anthropometry**
- **Problems with ADL** (activities of daily living)
- **Mobility**
- **Sleep study**
- **Endocrine abnormality**

# Diabetes-Management?



## Potential benefits of 10kg weight loss in individuals of 100kg

- 20–25% fall in total mortality
- 30% fall in diabetes-related deaths
- 40–50% fall in obesity-related cancer deaths
- 50% fall in fasting blood glucose
- 10mmHg fall in BP(diast and syst)
- 30% fall in Tgs, 15% fall in LDL-C; 10% fall in total chol; 8% increase HDL-C

# Hunger pattern

- Grazer
- Volume eater
- Sweet eater

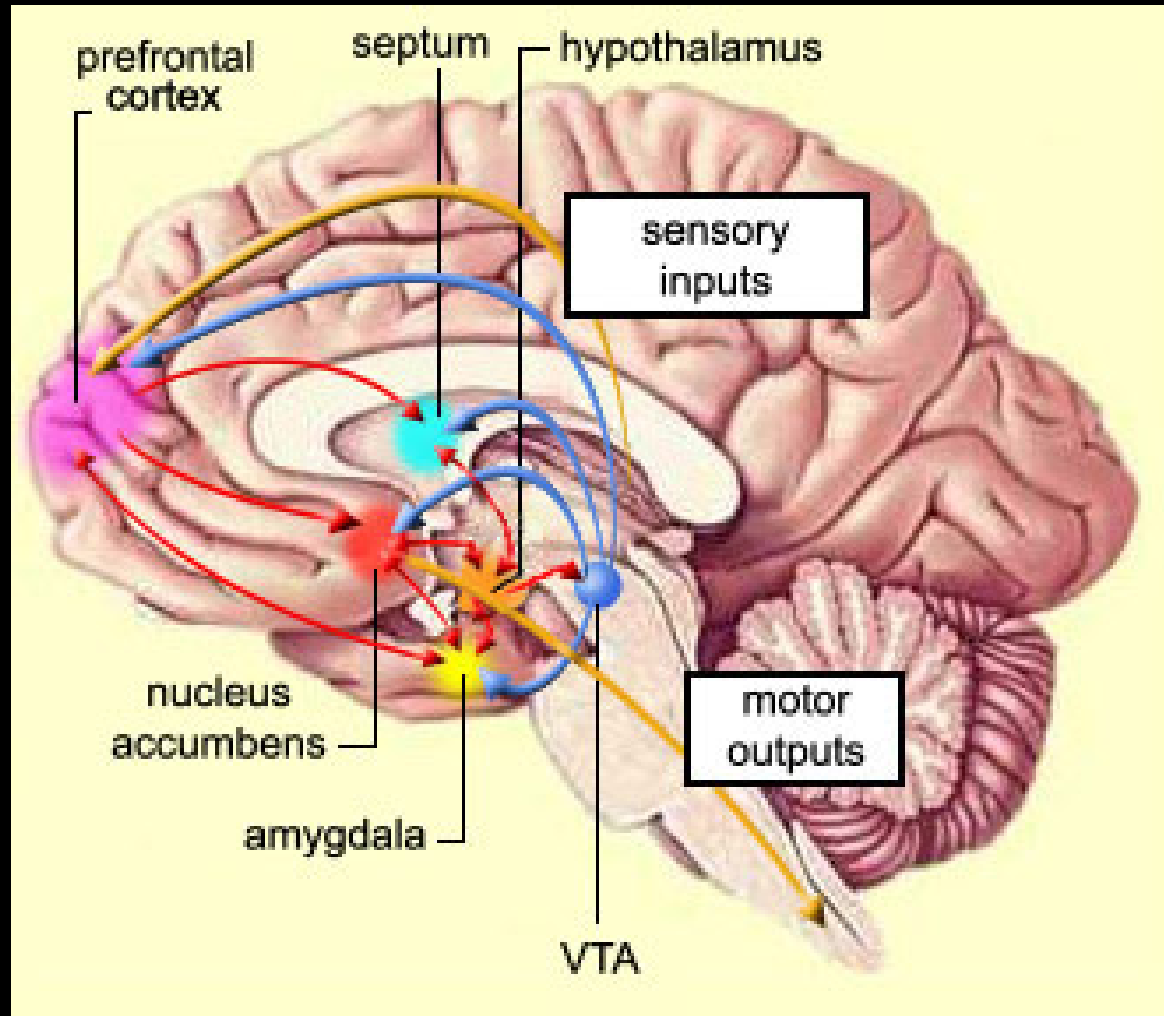
?reactive hypoglycaemia

**Maximum wt before diagnosis of diabetes is an important predictor of weight gain in patients taking insulin and that assessment of this should be part of routine care (Larger et al, 2001).**

# Investigations

- Full blood count
- Urea & Electrolytes
- Liver Function Test
- HbA1C
- 9AM Free Testosterone only if symptoms of erectile dysfunction
- 24 Hour urinary cortisol if cushingoid
- Sleep study if Epworth score more than 12

# Brain Reward System



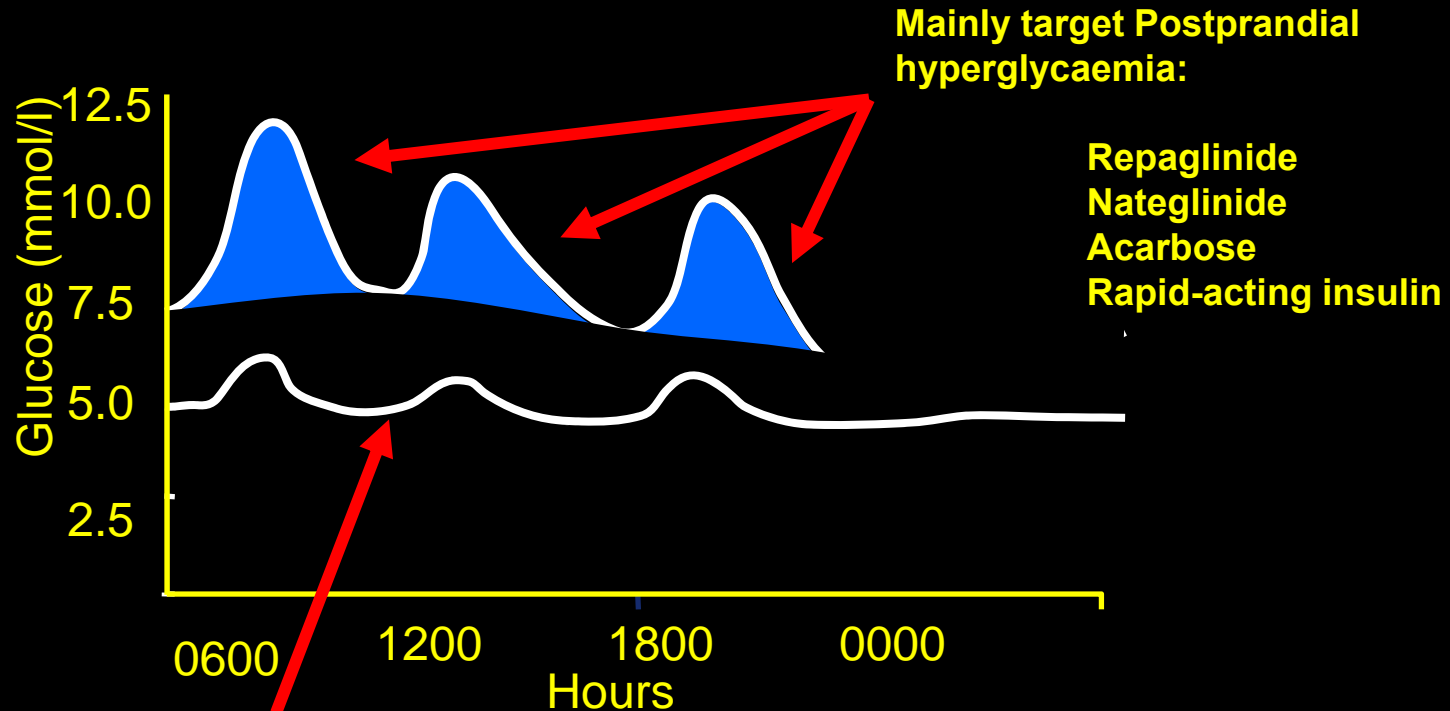
# Reducing weight gain with treatment

**Metformin appears to have an insulin-sparing effect and reduces weight gain with insulin treatment.**

**Patients with T2DM should remain on metformin when they convert to treatment with insulin.**

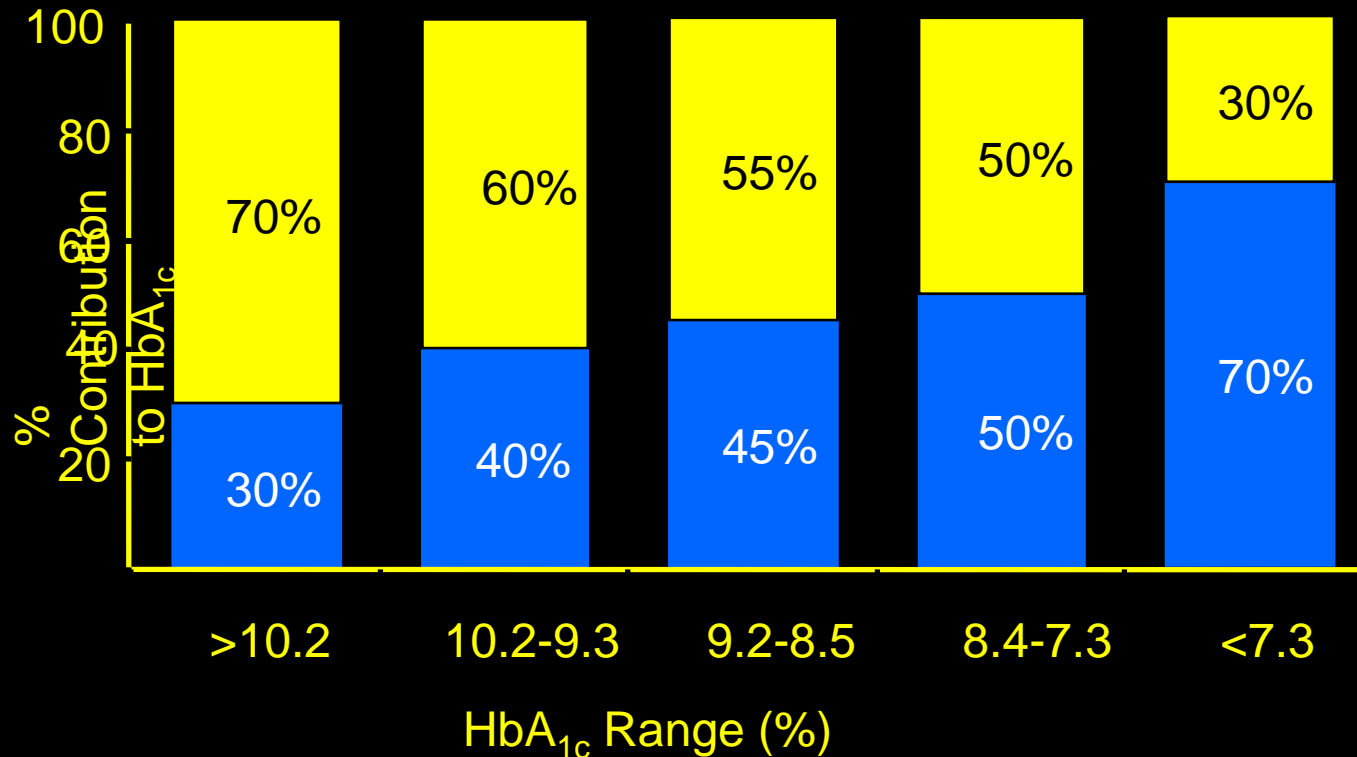
**This should be routine practice unless there is a history of metformin intolerance or evidence of renal impairment.**

# Contribution of Postprandial Glucose (PPG) to 24 hour hyperglycaemic profile



- Postprandial Hyperglycemia
- Basal Hyperglycemia

# As patients get closer to HbA<sub>1c</sub> target, the need to manage PPG increases



- Fasting Plasma Glucose (FPG)
- Post Prandial Glucose (PPG)

**Hyperinsulinaemia should be avoided to prevent weight gain and to optimise glycaemic control**

**GAME regimen: insulin aspart and glimepride**

**HbA1c decreased from 9.4 to 7.0 and net change in weight 4-5 Kg less than predicted**

**( de Boer,2006).**

**H. de Boer, R. Keizers, M. Jansen,2 L. Verschoor, J. Ruineman-Koerts (2006). Glycaemic control without weight gain in insulin requiring type 2 diabetes: 1-year results of the GAME regimen.Diabetes, Obesity and Metabolism.Vol8(5);517-523.**

## **Basal Insulins: Glargine vs Determir?**

**A 52-week randomized study comparing insulin detemir and insulin glargine ...**

**Weight gain was lower with insulin detemir than with insulin glargine (3.0 kg vs 3.9 kg,  $P = .01$ ), regardless of similar A1C levels.**

**Patients completing the study on once-daily insulin detemir showed a weight gain of 2.3 kg, whereas those treated with twice-daily detemir gained 3.7 kg. Similar effect was noticed in the insulin glargine group.**

**ADVANCE trial:** Weight gain was negligible even in the intense-therapy group when patients were followed by diabetes educators throughout the study.<sup>[1]</sup>

The use of newer basal analogue insulin instead of NPH-based therapy may also minimize weight .

## **Mix 50 Advantages**

**The TDS regime uses appropriate dose of prandial insulin (to improve glycaemic control) in conjunction with a reduction in the total daily dose of insulin ( facilitating wt loss) while maintaining adequate basal insulin therapy (given TDS) over a 24 hour period**

**Absorption is better when the dose is split and prevents stacking**

**Simple dosage regime and single delivery device**

## **Mix 50 case studies**

**NJ Asian 54 years with T2DM diagnosed 1990**

**On Lantus 84 units OD with evening meal  
Humalog 22-22-50**

**Metformin 850 mg tds**

**HbA1C 9.5% and weight 81Kg**

**HBG 5-15mmol/l with hypos occasionally in the morning**

# Titration

$$\frac{\text{Total insulin dose} - 10\%}{3}$$

$$= \text{Dose of Mix 50}$$

**After three months on Humalog Mix 50**

**Dose 54-52-54 units**

**HbA1C 8 %**

**Weight 78 Kg**

**No hypos**

# Initiating Insulin: Basic Recommendations

No set formula.....

- If FPG is elevated, start with long-acting (basal) insulin;
- If PPG is elevated, rapid-acting (prandial or bolus) can be used.

# GLP and insulin

**Currently use of Insulin and GLP-1 analogues or not licensed to be used**

# **Gliptins and Insulin**

**Currently only Sitagliptin is licenced to be used with insulin**

**MAGE**

**(Mean Amplitude of Glycaemic Excursion)**

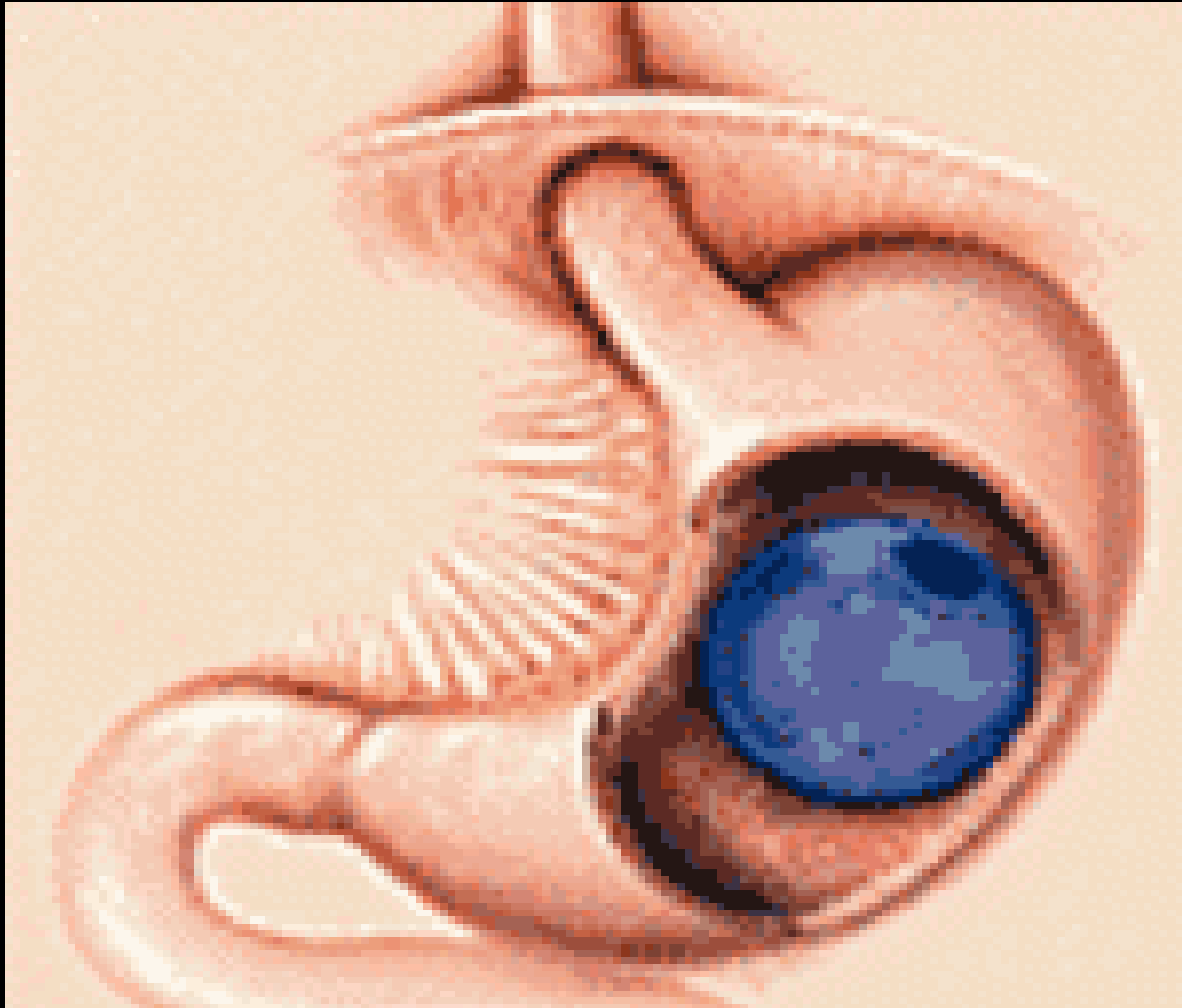
- **NEAT: Non exercise activity thermogenesis**
- **Eating until full and quickly increased the risk for overweight in men and women.**
- **Important principle is to avoid over-insulinisation, which may result in patients feeling hungry between meals.**
- **Dieting cause weight gain**

**Surgery**

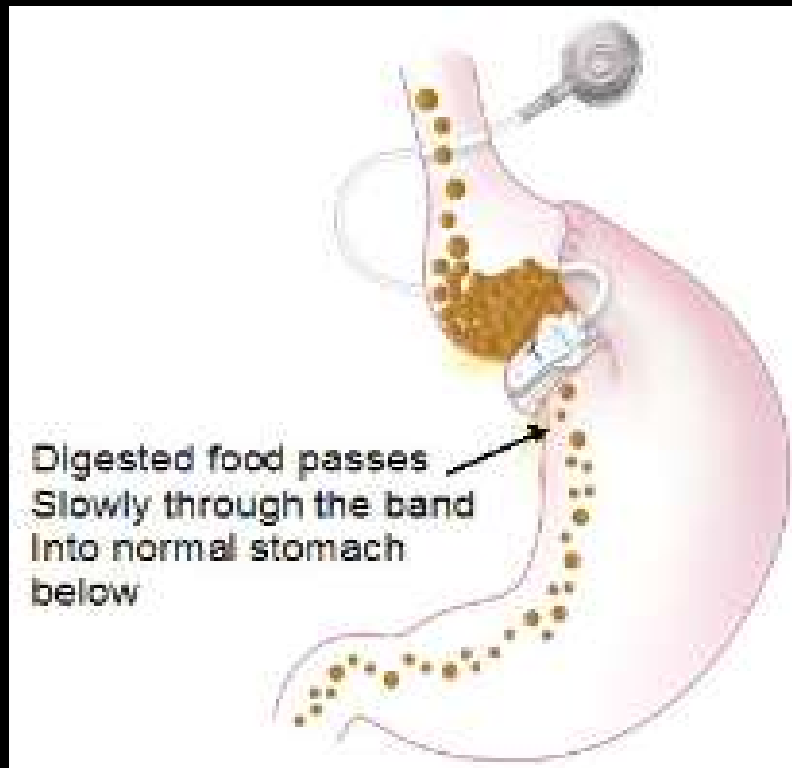
**Effective Early Intervention  
for**

**Diabetes?**

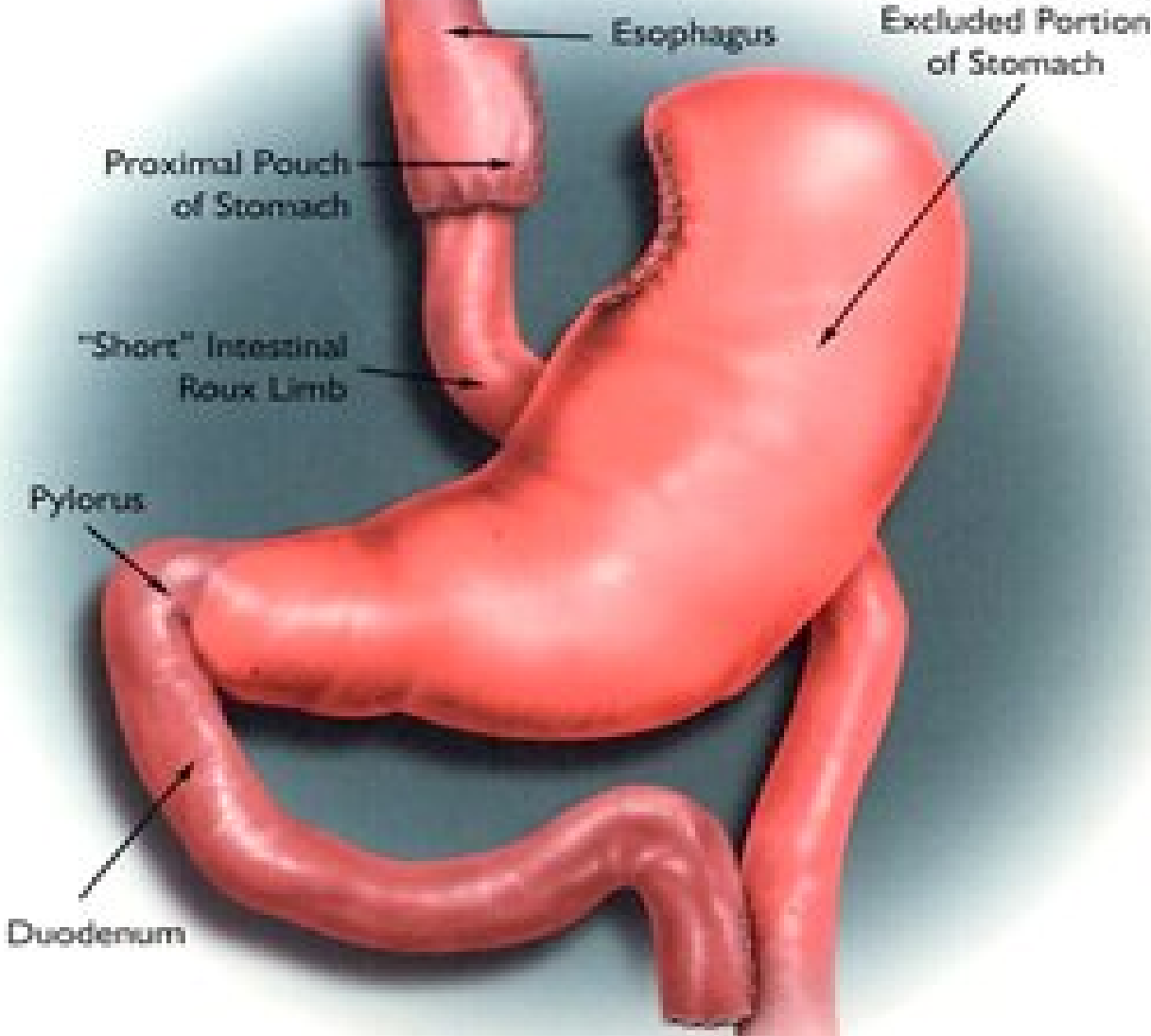
# Gastric balloon



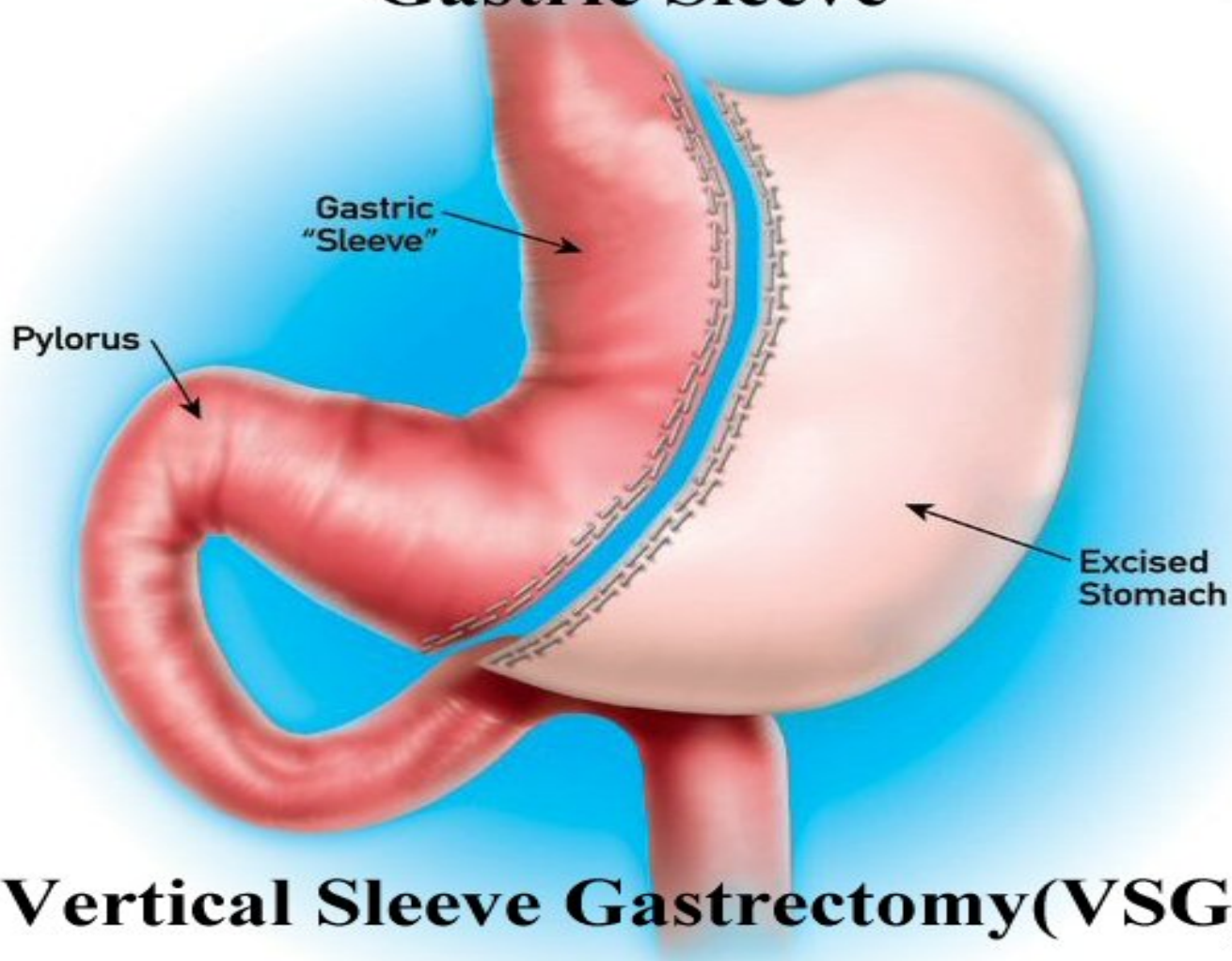
# Gastric Banding



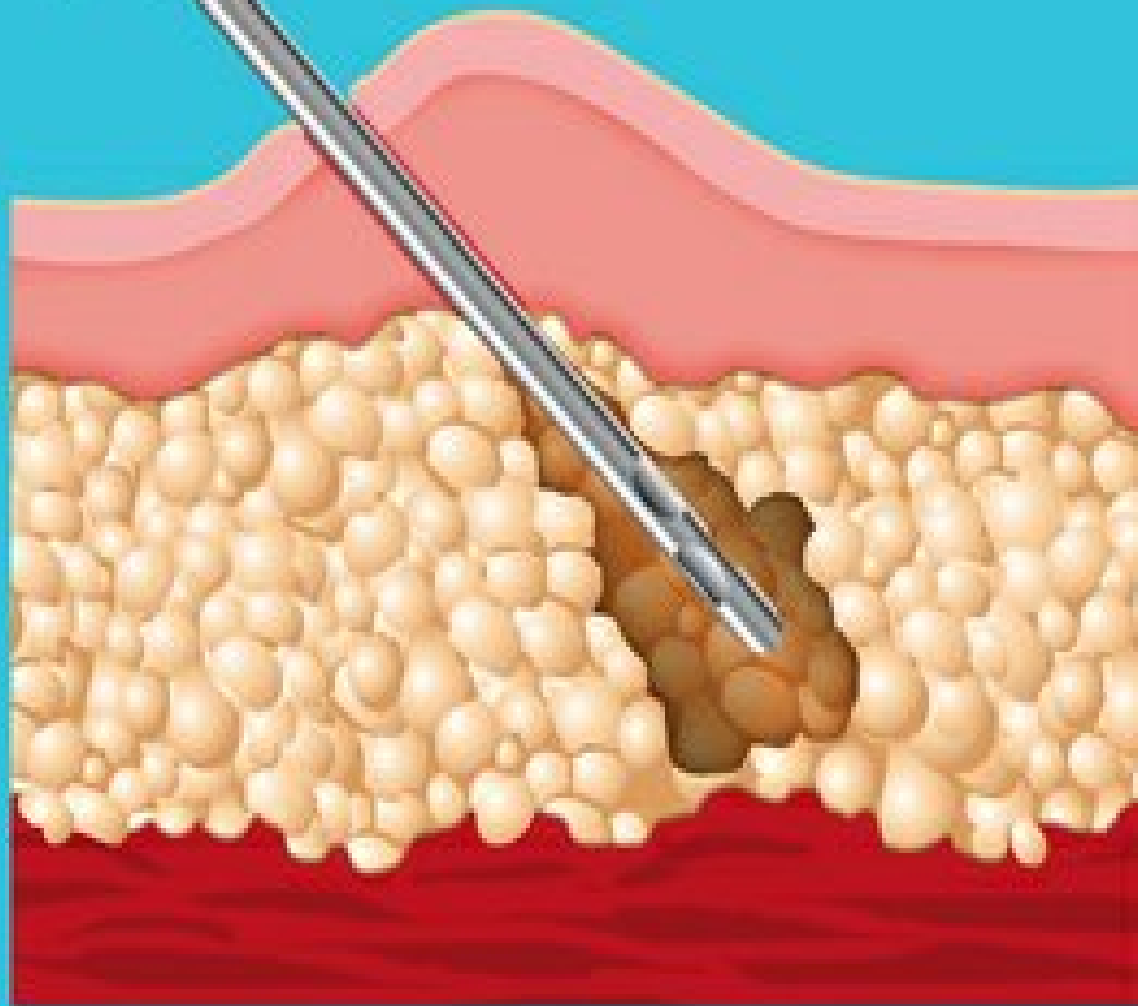
# Gastric Bypass



# Gastric Sleeve



# LipoSuction--Suction of Fat Below Skin



**SR**

**Age 31 years**

**Admitted with recurrent hypoglycaemia and reduced mobility**

**H/o weight gain, increasing facial hair, irregular periods and erratic blood glucose**

**Medications: Rosiglitazone , Metformin, norethisterone.**

**Child hood.....**

**Menstrual.....**

**Family.....**

**Social history.....**

**Personal history.....**

**H/o weight loss management &  
medical history**

**Motivation to lose weight ?**

**Eating habits and hunger pattern?**

**Examination:**      **Weight 237 Kg (37.3 stones)**

**Gross oedema lower limbs extending to anterior abdominal wall**

**Facial hirsutism    +++**

**BP 150/98**

**No clinical evidence of heart failure**

## Investigations:

FBC- N            Urea-12.3    Creatinine- 213

Billirubin-224                    rest of LFT-N

Prolactin-1917                    LH/FSH < 0.1

Testosterone-2.4 ,    Oestradiol-252    IGF-1- 4.9

TFT-N

Mid night cortisol-495

1.5 mg Post Dexa supp test -167

**Direct Coombs test + mild compensated  
Haemolytic anaemia**

**Rh factor + 67**

**Hepatitis screen –Negative**

**Haptoglobin- Normal and Copper –  
elevated (40)**

**Echo - NAD**

**Abdomen USS- NAD**

# Management

**All drugs stopped**

**Frusemide 40 mg BD**

**VLCD with supplementmnts**

**Clinic review: Weight 136 Kg ( Admission wt-237Kg)**

**weight loss- 100Kg**

**Frusemide stopped , no oedema**

**Mobilising independently**

**GTT- normal ,**

**Renal and Liver function- Normal**

**Menstrual periods restored to normal with normal prolactin concentration**

**Cause for weight loss??????**

MA 62 years

T2DM 8 years

Weight 102 Kg BMI 56 Kg/m<sup>2</sup>

HbA1C 10.3 %

On Metformin, Lantus 64 units BD

Increasingly tired

And

Day time sleepiness

OSA ruled out

? Hypogonad

Testosterone 6.6 nmol/l

Testosterone replacement

After 4 months reduced Lantus to 32 units BD due to hypoglycaemia

Weight 90KG

HbA1C 8.1%

No day time sleepiness !!!!!!!

# Summary

- **Whilst trying to optimise glycaemic control, increase in body weight should be avoided .**
- **Any attempt to minimize weight gain associated with insulin therapy should further extend the benefits of better glycaemic control.**
- **As patients get closer to HbA<sub>1c</sub> target ( $\leq 8.0\%$ ) PPG becomes the most significant contributing factor and appropriate changes to insulin regime and dose should be made**

**•When a combination of OHAs fails to achieve glycaemic control, one may consider GLP-1 agonist. For this mode of treatment to be effective there should be adequate beta cell reserve.**

**•Basal bolus regime should not be considered a gold standard for optimal glycaemic control in patients with Type 2 diabetes.**

- **Not every option is appropriate for every individual.**
- **Holistic approach is the key in a **DIABESITY** Clinic**
  - **Glycaemic control**
  - **Body weight and hunger pattern**
  - **Psychological issues**
  - **Underlying endocrine abnormalities**

