Errors in Diagnosis and management of Diabetes

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- Management of DM is a state of art
- Diagnosis should be confidently acknowledged
- Clinical examination should be perfect
- Choice of therapy is tailor-made
- Associated co-morbidities should be effectively treated

Fallout from Diabetes

Toes are sawed off……

kidney fail……

Nerves, heart, brain,

wreck havoc on body,

Daily life becomes……..

grueling struggle……

Diabetes is a marathon, not a sprint,

Pushing too hard for perfection

leads to burnt out

Giving up…….leads to disaster

seek to improve

Your management process yourself

end of the day…….

this is your life to live

Diagnosis of Diabetes
(ADA Diagnostic criteria)

1. A1C ≥6.5%. This test should be performed in a laboratory using a method that is NGSP certified and standardized to the DCCT assay,* **OR**
2. FPG ≥126 mg/dL (7.0 mmol/L). Fasting is defined as no caloric intake for at least 8 hours,* **OR**
3. 2-hour plasma glucose ≥200 mg/dL (11.1 mmol/L) during an OGTT. This test should be performed as described by the World Health Organization, using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water,* **OR**
4. In a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose ≥200 mg/dL (11.1 mmol/L)

DCCT = Diabetes Control and Complications Trial; FPG = fasting plasma glucose; NGSP = National Glycohemoglobin Standardization Program; OGTT = oral glucose tolerance test.

*In the absence of unequivocal hyperglycemia, criteria 1 to 3 should be confirmed by repeat testing.

DUBIOUS VALUES

- **FPG 115 mg/dl, RPG 200 mg/dl, or FPG 130 mg/dl and RPG 180 mg/dl**

  Non-diagnostic

  Repeat on subsequent day
- **HYPERGLYCEMIA DURING AMI, STRESS**

  Revise the diagnosis once the stress is over
- **MILD DIABETES, SEVERE DIABETES**

  Avoid such terms

Fasting Plasma Glucose

- **Advantages**
  - Glucose assay easily automated
  - Widely available, Inexpensive
  - Single sample

- **Disadvantages**
  - Patient must fast for >8 hrs
  - Large biological variability
  - Diurnal variation, sample not stable
  - Some labs use serum instead of plasma

Oral Glucose Tolerance Test (OGTT)

- Sensitive indicator of risk of developing diabetes
- Early marker of impaired glucose homeostasis
- Lacks reproducibility
- Extensive patient preparation
- Time consuming and inconvenient for patient
- Unpalatable
- Expensive
- Influenced by various medications
- Sample not stable, to be done in morning

HbA1c

Advantages

- No fasting
- Sample may be taken any time of the day
- Very little biological variability
- Reflects long term blood glucose concentration
- Assay standardized across instruments
- Concentration predicts micro vascular complications

Disadvantages

- May be affected by decreased life span of RBCs
- Selected hemoglobinopathies may interfere
- May not be available
- Cost

Factors that affect A_1C

DECREASED

- Pregnancy—0.5%
- Vitamin E /C
- Anti retroviral drugs
- Chronic liver disease
- Ethnicity ----Asians
- Hb S,D,G,C,E

INCREASED

Increasing Age----0.4%

High TG/ Bilirubin

Renal failure {carbamted]

Aspirin {acetylation}

Increase Hb F levels

Iron deficiency

Sensitivity and specificity of HbA1c at various cut-off levels in NDM subjects

Cut-off level	Sensitivity	Specificity
5.7	92	63
5.8	92	68
6.0	83	77
6.1	81	81
6.2	76	84
6.3	73	86
6.4	70	87
6.5	65	88
6.6	62	89
6.9	47	91
7.0	42	92

JCEM, Bhansali et al 2010

Errors in Diagnosis

Biological Variation

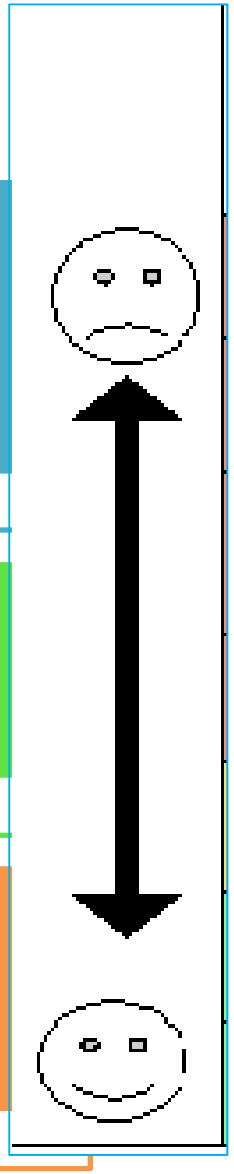
(Intra-individual, inter-individual, day-day variation)

Pre-analytical variation

pertain to the specimen before it is measured

Analytical variation

Differences resulting from the measurement



Implications

- Affects treatment choices and risk management
- Can have psychological and financial implications
- Undermines quality of care and research

Biological variation

Glucose

- Intra-individual variation in a healthy person 5.7–8.3%
- Inter-individual variation of up to 12.5%

HbA_1C

- Intra-individual variation of A1C in healthy people is minimal, with CV <1%
- Variability between individuals is greater

Other important factors

- **Diurnal variation:** NHANES III (Based on FPG, prevalence of DM in afternoon half than that in morning

- **Time to analysis: PG** decrease in the test tube by 5–7% per hour due to glycolysis

- **Nature of specimen: PG** in whole blood are 11% lower than that in plasma

  Capillary PG can be 20–25% higher (mean of 30 mg/dL) than venous PG during an OGTT

Pre-Analytical factors (Glucose)
Acute increase in plasma glucose concentration

- Acute illness
- Major Surgery

- Corticosteroids
- Sympathomimetics
- Isoniazid
- Olanzapine
- Diazoxide
- Niacin

Pre-Analytical factors (Glucose)
Acute decrease in PG concentration

Physiological factors	Acute illness	Drugs	Spurious hypoglycemia
Pregnancy Prolonged fasting or starvation Intense exercise	Sepsis Acute Renal insufficiency Adrenal insufficiency	OHAs Antibiotics (Cipro/ gatifloxacin) Quinine and chloroquinine Salicylates Alcohol	Prolonged storage of blood sample Leukocytosis and leukemias

Analytical variation (Glucose)

Within lab imprecision	The analytical variability (CV<2.5%) is considerably less than the biological variability, which is up to 8.3%.
Different calibrator	Biases ranging from -6 to +7mg/dL(-6 to +7%) at a PG of 100 mg/dL.
Inter-lab differences	6.9% above or below the mean (1/3rd of time PG results on a single sample measured in 2 labs could differ by 14%)

Defining medication errors

“ Any preventable event that may cause or lead to inappropriate medication use or patient harm”

Such events may be related to:

- Professional practice
- Health care products
- Procedures and systems
- Product labeling
- Packaging, nomenclature

- Dispensing
- Distribution
- Administration
- Education
- Monitoring

Classifying medication errors

1. Circumstances exist for potential errors to occur
2. An error occurred but did not reach the patient
3. Error reached the patient but did not cause harm
4. Patient monitoring required to determine lack of harm
5. Error caused temporary harm and some intervention
6. Temporary harm with initial or prolonged hospitalization
7. Error resulted in permanent patient harm
8. Error required intervention to sustain the patient's life
9. Error contributed to the patient's death

Some reasons errors occur

- Verbal orders
- Poor communications within healthcare team
- Poor handwriting
- Improper drug selection
- Missing medication
- Incorrect scheduling
- Poly-pharmacy
- Drug interactions
- Availability of floor stock (no second check)
- Look alike / sound alike drugs
- Hectic work environment
- Lack of computer decision support

Uh oh, did "I" do that ?

TREATMENT

- X,60M

Rx

Tab Glibenclamide 5 mg TID
Tab Metformin 500 mg BD
OR
Tab Glibenclamide 5 mg BD
Tab Glimepiride 2 mg OD

COMMENTS

- **WRITE PROPER AND COMPLETE DIAGNOSIS**

  T2DM, obese/non obese, microvascular & macrovascular complications and hypertension

- **CALORIES SHOULD BE PRESCRIBED**

  22 kcal/kg of IBW and add 25%, 50% or 75% according to activity

- **LSM SHOULD BE STRESSED**

Prescription, usually silent

Ideal body weight, existing weight

Duration of diabetes

Type of diabetes

Associated illnesses, complications

Previous A_1C values

Drugs history

Omissions

Time of medication

Targets

Follow up duration

Monitoring intervals

Self care

Lack of education

- A key component of reducing errors in prescription in diabetes is patient ‘’education’’
- May reduce ‘’slips & lapses’’ in prescription about
    - Disease
    - Medications
    - Benefits/side effects
    - Complications of diabetes

CLINICAL EXAMINATION

1) **HEIGHT AND WEIGHT: NOT MEASURED**

- BMI, calorie calculations, choice of therapy (obese/non obese)

2) **WAIST LINE: NOT MEASURED**

- Non obese but centrally obese
- Correlates with insulin resistance

3) **PERIPHERAL PULSES ARE NOT PALPATED**

-Carotid bruit: surrogate marker of CAD

-Posterior tibial: PVD

-Renal bruit: renal artery stenosis

-Caution for use of ACEI

CLINICAL EXAMINATION

- **FOOT EXAMINATION**
- Usually ignored
- Callosities, nails, pulses, arch
- Major cause of mortality

- **FUNDUS-NOT EXAMINED**
- Most common cause of painless blindness
- To be seen with dilated pupil

WHAT IS OUR TARGET?

- BLOOD GLUCOSE
- HbA1C

COMPREHENSIVE CONTROL OF DM

	GOOD	ACCEPTABLE
• FPG	<100 mg/dl	<130 mg/dl
• PPG	<140 mg/dl	<180 mg/dl
• HbA_{1C}	<6.5%	<7%
• TG	<150 mg/dl	<200 mg/dl
• LDL	<70 mg/dl	<100 mg/dl
• URINARY ALBUMIN	<30mg/24hr	30-300mg/24h

ADA 2007

INDICATIONS FOR TIGHT GLYCEMIC CONTROL

- GDM
- POST RENAL TX
- AMI AND STROKE
- All Young Diabetics

STRESSFUL SITUATIONS AND DIABETES

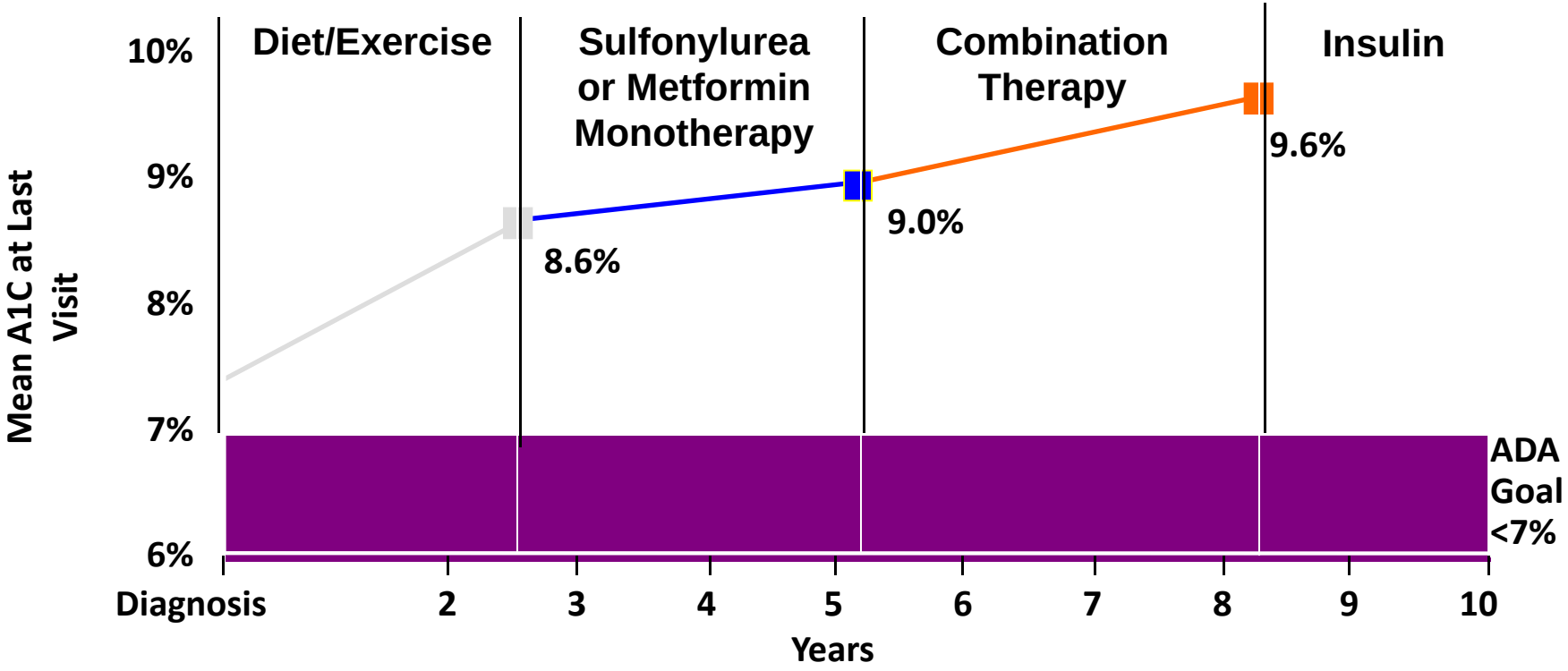
- **AMI, SEPSIS- OHA'S ARE CONTINUED**

- Always switch to insulin
  (DIGAMI, Van Den Bergh et al)
  - Consistent and predictable
  - Pleiotropic effect
  - Anti-inflammatory
  - Vasodilatory and ↑NO synthetase activity

MONITORING OF DM

PARAMETERS	FREQUENCY
FPG PPG(2hr)	INTENSIVE CONTROL:4-7 POINT PROFILE CONVENTIONAL CONTROL: INITIALLY WEEKLY, ONCE STABLE FORTNIGHTLY
HbA1C	ONCE IN 3 MONTHS
LIPIDS	ONCE IN 3 MONTHS
MICROALBUMI-NURIA	ONCE A YEAR
FUNDUS	ONCE A YEAR
FOOT EXAMINATION	ONCE A YEAR

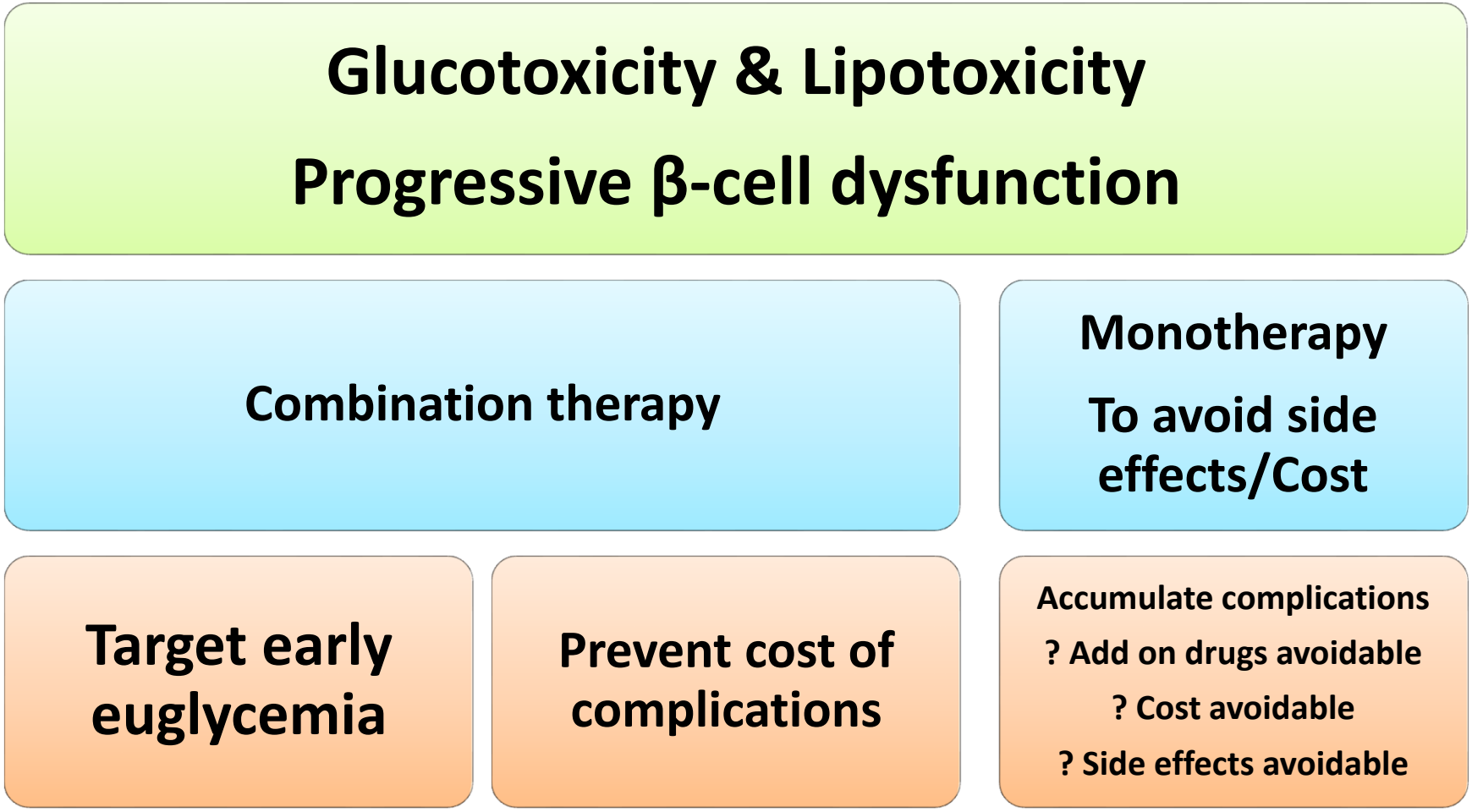
Standard Approaches to Therapy Result in Prolonged Exposure to Elevated Glucose

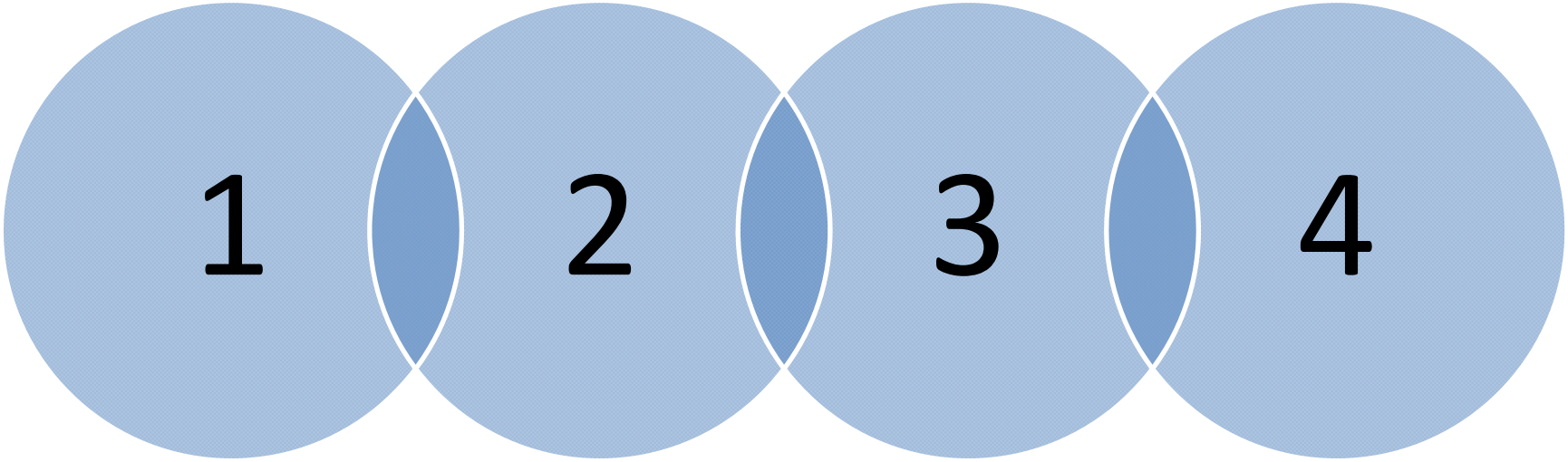


At insulin initiation, the average patient had:

- 5 years with A1C >8%
- 10 years with A1C >7%

Brown JB, et al. *Diabetes Care*. 2004;27:1535-1540.


Glucotoxicity & Lipotoxicity
Progressive β-cell dysfunction
Combination therapy
Monotherapy
To avoid side effects/Cost
Target early euglycemia
Prevent cost of complications
Accumulate complications
? Add on drugs avoidable
? Cost avoidable
? Side effects avoidable



HbA1c deteriorated to >9% before therapy intensification

The second agent was not added until an average of 30 months after the first HbA1c level of > 8% was recorded

This is highly relevant because the time spent in a hyperglycemic state is a key determinant of the risk for developing diabetic complications

Browns JB, Slow response to loss of glycemic control in type 2 diabetes mellitus, Am J Manag Care 2003

LIFE STYLE MODIFICATION

- Advised after evaluation for

  -DOE (NYHA III, IV), PVD & obvious foot disease

  -Proliferative diabetic retinopathy
- 4 km in 40 min/7 days a week
- Should be at a stretch

TIME OF ADMINISTRATION

- Acarbose-just before a major meal
- Glitazones-any time (before meals)
- Metformin-with or immediate after meal
- Regular insulin-30 min prior to meal
- Short acting insulin analogues- 5 min before meal
- Long acting insulin analogues- fixed time

- **BEST RESPONDERS TO SUs**
  - Duration of DM<5yr
  - BMI< 25 kg/m^2
  - FPG 150-200 mg/dl
  - Insulin requirement < 25 units/day

- **CONSIDERATIONS FOR SU THERAPY**

- Avoid long acting SUs in elderly and with renal insufficiency
- Avoid with organ failure (liver, cardiac, renal)

SU: DOSES, FREQUENCY AND TIME OF ADMINISTRATION

DRUG	**OPTIMAL DOSES**	**FREQUENCY**	**TIME**
GLIBENCLAMIDE	10 mg	BD	30 min prior to meal
GLIPIZIDE	20 mg	BD	30 min prior to meal
GLICLAZIDE	160 mg	BD	30 min prior to meal
GLIMEPIRIDE	4 mg	OD/BD	30 min prior to meal

COMBINATIONS OF SUs

- Should be avoided
- Hyperinsulinemia $\rightarrow$weight gain $\rightarrow$ insulin resistance
- β cell exhaustion

BIGUANIDES

- **Metformin**
- With/after meal
- Sustained release can be given once a day

GLITAZONES IN OBESE T2DM

- Obese T2DM better responds than non-obese T2DM
- Improved insulin sensitivity despite weight gain
  - Adipocyte differentiation
  - Fat steal phenomenon
  - Redistribution of body fat

ACARBOSE AND METFORMIN

- **ACARBOSE COMBINED WITH METFORMIN**
- Both increases GLP-1
- Worsening of GI intolerance
- **ACARBOSE INDUCED HYPOGLYCEMIA: Rx WITH TABLE SUGAR**
- Should be treated with glucose

DPP IV Inhibitors

- A new class of drug

  -Glucose dependent insulin secretion

  -Decreases glucagon

  -β cell neogenesis
- Should be used as add on to metformin
- Delayed use should be avoided.

Treatment	Comments
• 45 M, T2DM Obese, Duration of DM 8 yr Rx • Tab Gliclazide 80 mg BD • Tab Metformin SR 1 gm BD • Tab Pioglitazone 30 mg OD	• Addition of 2 sensitizers of different class is reasonable • First try full doses of metformin and later add glitazones/or half of the doses of both to begin with • Sign of evoluting β-cell exhaustion

Early Insulin Therapy : Advantages

- β cell preservation
- Smooth and stable glycemic control
- Weight gain and hypoglycemic events are lesser
- Restoration of β cell-glucose axis

Insulin

- Do not mix 2 different insulins, use pre mix
- Do not share syringes
- Use, strength U -40
- Use needles /syringe –once{needle tip-bents, hooks breaks}
- Fill syringe, with air/inject in vial
- Look for air bubbles, decrease dose

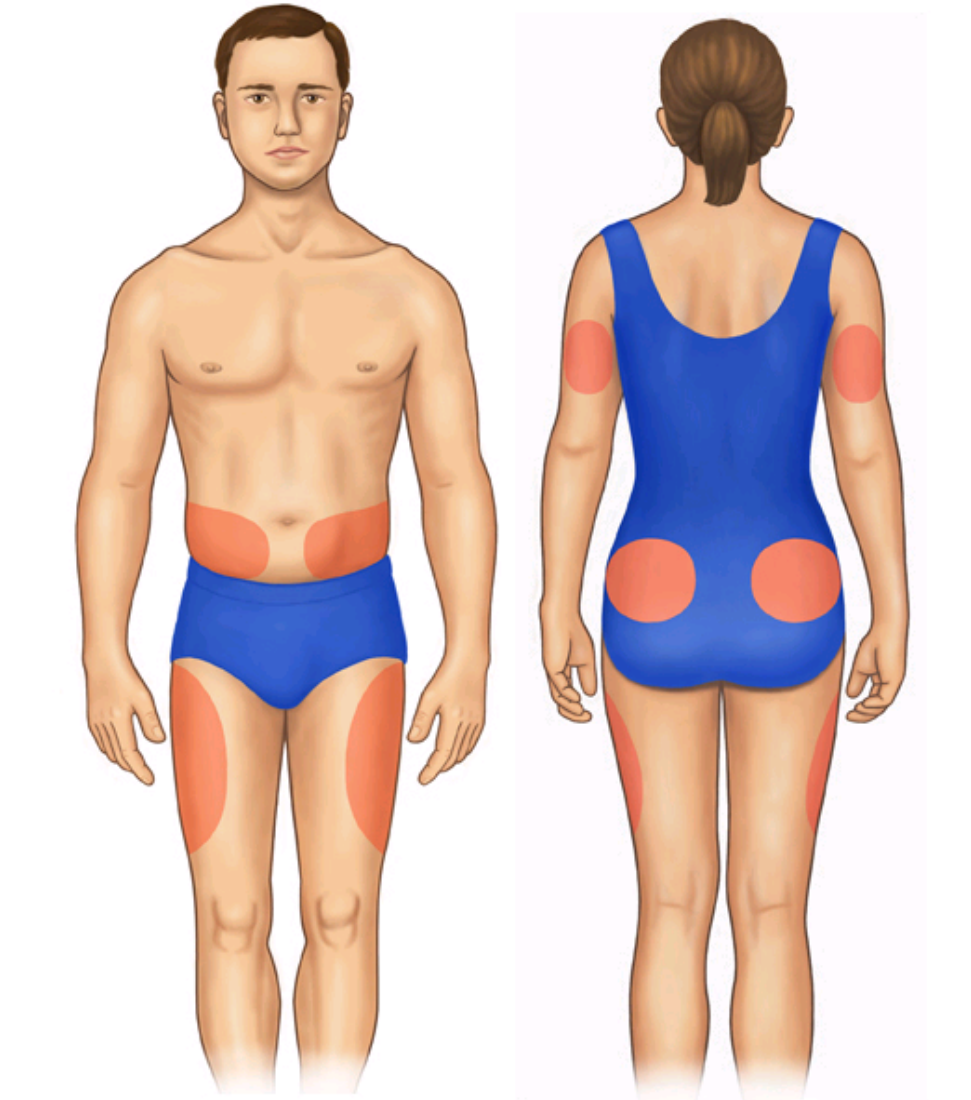
Insulin

- SU with regular insulin, given pre- meals along acting insulin in old age/renal failure
- Detemir /glargine – clear insulins
- Nil orally –administration of insulin
- Sliding scale—episodes of hypos high

INSULIN ANALOGUES

- To be used in selective subsets of patients
- Short acting analogues
  - School going children
  - Busy executives
  - RT feed
- Long acting analogues
  - Elderly, ICU setting, brittle diabetes

Diabetic injection sites



The shaded areas may be used for insulin injections. Injection sites should be rotated. Insulin is absorbed more rapidly when injected into the abdomen, as compared to the arms or legs.

LIPIDS AND T2DM

- **TARGETS ARE NOT DEFINED**
- LDL< 70-100 mg/dl, TG <150 mg/dl, HDL >45 mg/dl
- **HIKE IN DOSES OF STATINS IS NOT OPTIMAL?**
- 10 mg Statin - ↓ LDL by 26%, further ↑ in 10 mg decreases LDL by 6% only
- IF BASELINE LDL > 165 mg/dl: Start Statin & Ezetemibe/ Statin 20-40mg
- **TIME OF ADMINISTRATION**
- Preferably at bed time
- **HDL IS NOT TARGETTED?**
- Niacin is a good option

HYPERTENSION AND T2DM

- **BP IS NOT MONITORED?**
- BP in sitting position and look for postural drop
- Measure at each visit
- **TARGET IS NOT DEFINED?**
- BP 130/80 mmHg (JNC VII)
- BP 125/75 mmHg –Diabetic nephropathy

NON SPECIFIC SELECTION OF ANTI-HYPERTENSIVES

- Control of BP in T2DM: polytherapy
- Normotensive microalbuminurics: ACEI
- Hypertensive microalbuminurics: ACEI
- Mild renal insufficiency: ARB'S
- Macroproteinurics: ACEI + ARB'S
- Start with 2 drugs if initial BP is >160/100 mmHg
- IF BP "UNCONTROLLED"
  - Intermediate acting CCB's
  - Hydrochlorthiazide
  - α BLOCKERS
- Associated CAD: β blockers

Self Monitoring of Blood Glucose (SMBG)

T2DM

- On OHA's : Equivocal
- On insulin

- 4 times per week
- FPG and PPG – 2 values each
- Additional measurements if required, at bed time and before meals

Other superfluous errors

- Clinical trials may be biased
- Diabetic experts and drug industry ties
- Medications frequently influenced by pharma
- Affordability factors and compliance
- Role of chemist and drug distributors
- Alternative drugs claiming to be curing diabetes
- Media hype

US cracks down on ayurvedic, homeopathic diabetes remedies

Friday, July 26, 2013

Washington: The US Food and Drug administration is cracking down on the sale of alternative remedies, including ayurvedic and homeopathic products and dietary supplements, for the treatment of diabetes.

The agency has issued letters warning 15 companies including some that procure alternative diabetes remedies from India, that the sale of their illegally marketed diabetes products violates federal law.

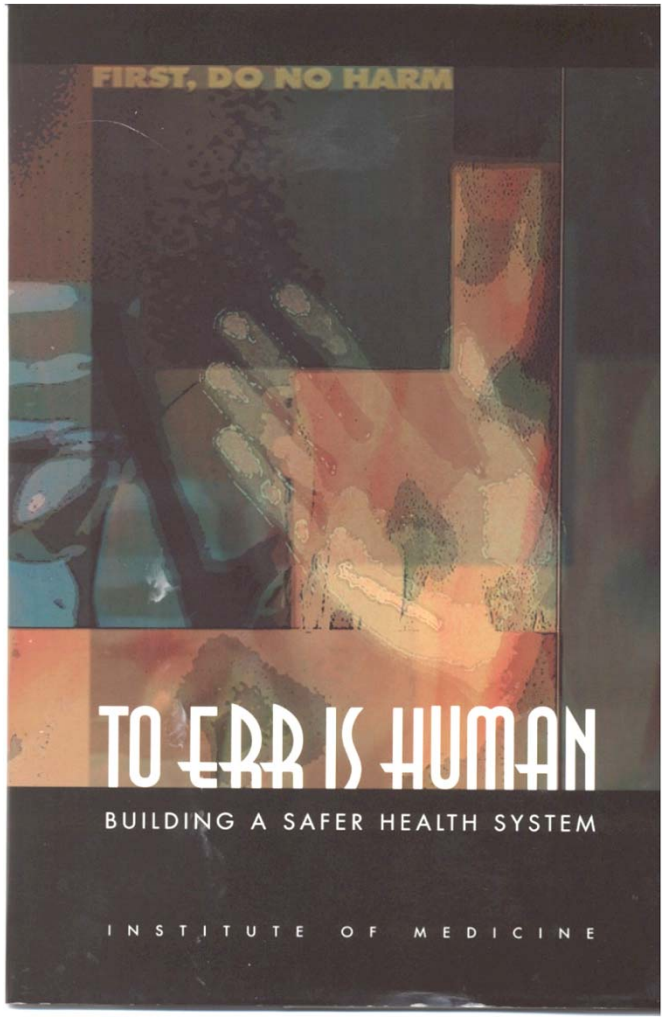
Foreign and domestic companies whose products claiming to mitigate, treat, cure or prevent diabetes and related complications, were sold online and in retail stores have been asked to tell FDA within 15 days how they will correct the violations.

The FDA has also advised consumers not to use these or similar products because they may contain harmful ingredients or may be otherwise unsafe, or may improperly be marketed as over-the-counter products when they should be marketed as prescription products.

Many of the illegally sold products include claims such as “prevents and treats diabetes,” and “can replace medicine in the treatment of diabetes,” FDA said.

Key messages

- Insulin and other anti-diabetic agents are a significant cause of hospital admissions
- Medication errors involving insulin are responsible for a disproportionate number of serious adverse events
- Several common errors are known to occur in the prescribing of anti-diabetic medications
- Education and training may prevent some errors


FIRST, DO NO HARM
TO ERR IS HUMAN
BUILDING A SAFER HEALTH SYSTEM
INSTITUTE OF MEDICINE


THANK YOU