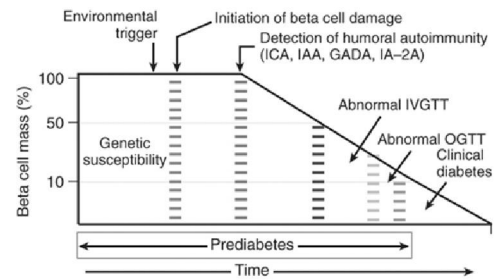


# Diabetes Mellitus Type 1

DG VAN ZYL

## Pathogenesis of Type 1 Diabetes

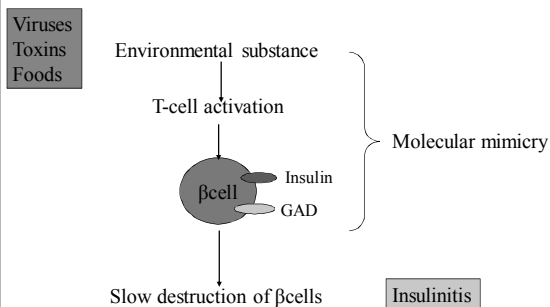


## Pathogenesis

### Genetics of Type 1 Diabetes

- Complex and poorly understood interplay between genetics and environmental factors
- Monozygotic twins 20 – 50% concordance
- Siblings of diabetic patients is 6 – 10% vs. 0.6% for the general population
- Children of diabetic female have a risk of 2.1% and of a male 6.1% to develop diabetes

## Pathogenesis of DM1



## Classification of Diabetes

### Type 1

- Destruction of beta cells
  - Autoimmune (ICA, anti-GAD, anti-Insulin)
  - Idiopathic
- Absolute deficiency of insulin
- Not all patients with late onset of diabetes have type 2 diabetes

### Type 2

- Variable degrees of insulin deficiency and resistance
- No specific test for type 2 diabetes
- Keto-acidosis does not exclude type 2 diabetes

## Insulin Receptor Signaling

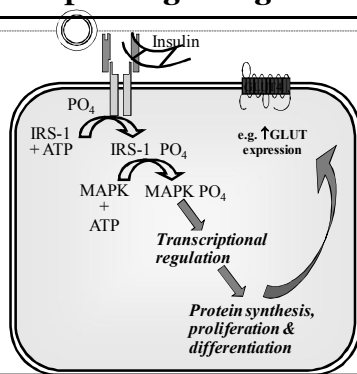
Insulin binding to a subunit  
regulates b subunit activity

↓  
autophosphorylation of b  
sub-unit

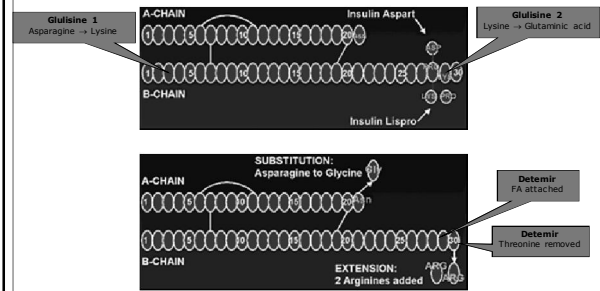
↓  
↑ tyr kinase activity

↓  
phosphorylation of other  
substrates

↓  
phosphorylation of MAP  
kinase



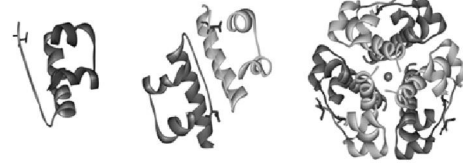
## Synthetic Insulin



## Insulin therapy

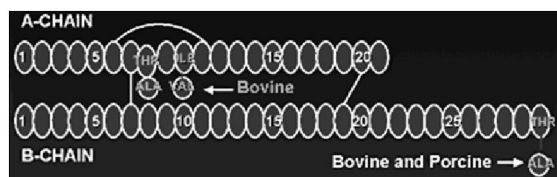
## Self-association of Insulin:

Monomer > Dimer > Hexamer

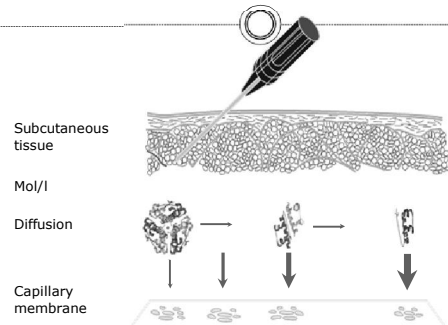


Whittingham JL et al. *Biochemistry* 1998;37:11516-11523.

## Insulin Structure



## Insulin Aggregation and S.C. Absorption



Adapted from Brange, *Diabetes Care* 1990;13:923-954.

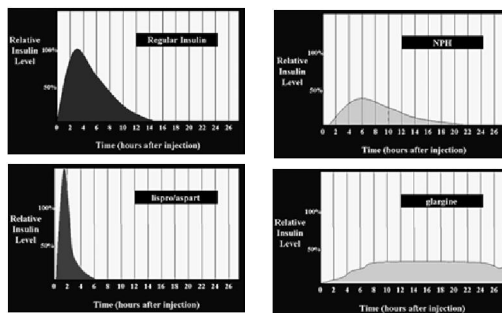
## Insulins

Treatment	Onset of Action (h)	Peak (h)	Duration (h)
<b>Conventional Human Insulin</b>			
NPH	2-4	4-6	12-16
Lente	2-4	4-12	12-18
Ultralente	6-10	10-16	18-20
Regular	30-60 min	2-4	6-8
<b>Analog</b>			
Glargine (Lantus)	2	flat	~24
Detemir (Levemir)	2	flat	~14-16
Lispro (Humalog)	5-15 min	60 min	4-5
Aspart (Novolog)	5-15 min	60 min	4-5
Gulisine (Apidra)	5-15 min	60 min	4-5

## Treatment Strategies

- Most patients require an insulin dosage of 0.5 – 1.0 U/kg daily
- Athletes and patients near their ideal body weight generally require less insulin than obese patients and those leading a sedentary lifestyle
- Be aware of the honeymoon period
- Constantly reassess and adjust the insulin dose until the patient stabilizes

## Insulin Pharmacokinetics



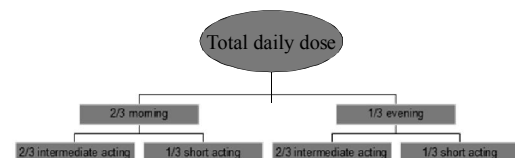
## Insulin Regimens

- Traditional once or twice daily injections
  - ⊙ No longer recommended
  - ⊙ Still appropriate in many cases
    - # Initial therapy
    - # Patients with poor understanding of the disease
- Flexible diabetes therapy
  - ⊙ Basal
  - ⊙ Meal time
    - # require a intelligent and motivated patient
    - # 4 injections needed daily

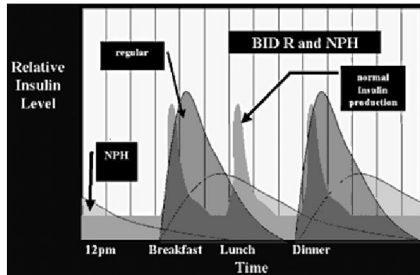
## Bio-availability of Insulin

- Factors that affect bio-availability and absorption rate of insulin
  - ⊙ Site of injection
  - ⊙ Depth of injection
  - ⊙ Insulin concentration
  - ⊙ Insulin dose
  - ⊙ Insulin mixing
  - ⊙ Heat application or massage
  - ⊙ Exercise

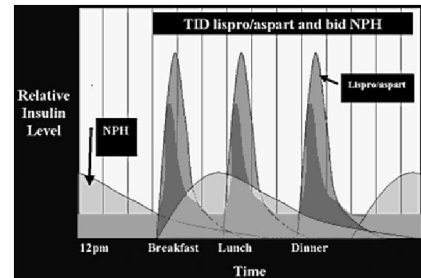
## Twice Daily Regimen



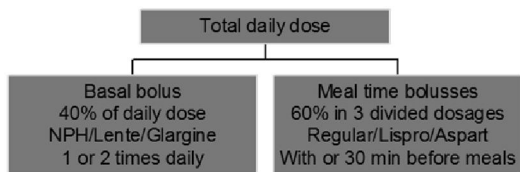
### Twice Daily Regimen



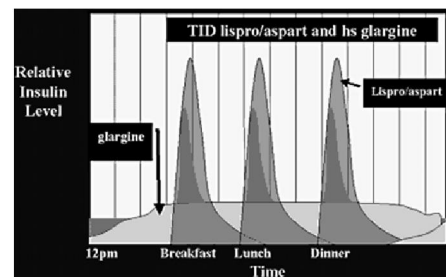
### Lispro/Aspart and NPH



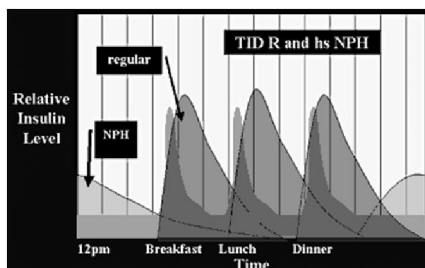
### Flexible Diabetes Therapy



### Lispro/Aspart and Glargine



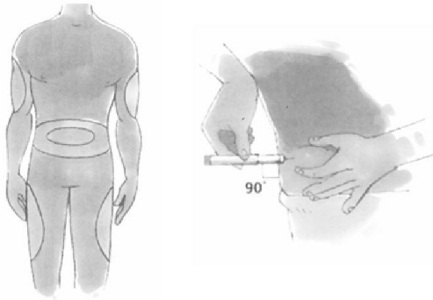
### Regular Insulin and NPH



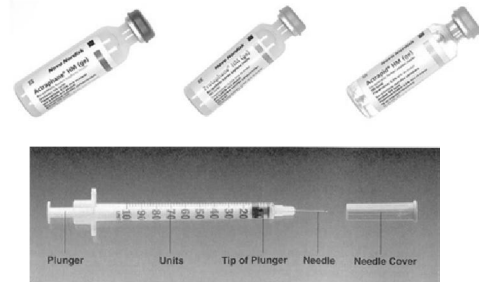
### Carbohydrate Counting

- Patients must be taught to count the grams of CH they anticipate eating, the dose of insulin is adjusted according to this
- On average 1U lispro/Aspart for every 15g CH
- This needs to be individualized and patients should experiment a little to become acquainted with their disease

## Injection Sites and Technique



## Vials and Syringes



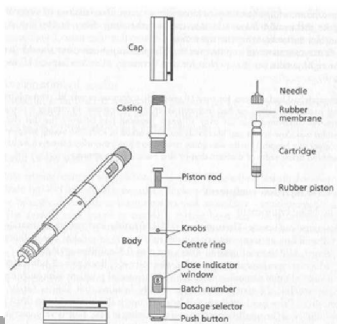
## Lipohypertrophy



## Insulin Pumps



## Novopen



## Insulin Pumps



## Barriers of Initiation of Insulin



## Home Glucose Monitoring

## Starting Insulin: Practical Points

- Set the stage early
- Be matter-of-fact
- **Insulin is not a punishment**

## What is Structured Testing?

It all begins with testing for a reason...

Structured Testing		
Type of SMBG	Purpose	Action
Routine Testing		
Type 1	Insulin Management	Insulin Dosing
Type 2	Glycemic Control/ Insulin Management	Behavior Change/ Insulin Dosing
Focused Testing		
Pattern Testing	Problem Identification/ Education and Engagement	Behavior Change/ Therapy Adjustment
Paired Testing	Education and Engagement	Behavior Change/ Monitor Therapy
Titration Testing	Therapy Management	Therapy Adjustment

Regimens vary depending on:

- Type of diabetes
- Current treatment & goals
- General state of health
- Current glycemic control problems

## Starting Insulin: Practical Points

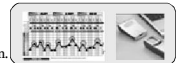
- Get over needle fear
  - **Get the needle through the skin**
  - Start with abdomen injection
- Use pens
- Use demonstration solutions

## Glucose Focused Testing Examples

Actionable information for informed decision-making

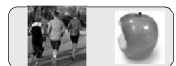
### Pattern Testing ...

Multi-point BG profiles for a specific duration to use pattern analysis to identify problem areas for remediation.



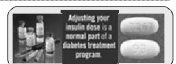
### Paired Testing ...

Testing to explore cause and effect BG variance related to life events or activities, such as diet, lifestyle, and current medication. Supports patient self-learning and engagement.



### Titration Testing ...

BG testing to support activities to determine dose titration.

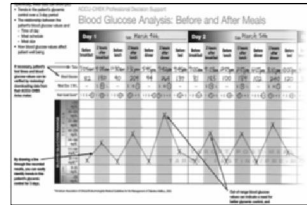


## Three Day – Day profile

**Paper-Based** – No software or computer required

**Simple Concept** – Patient tests 7 times per day over 3 day period; Record results on easily-understood form

**Comprehensive** – Allows recording of BG, meal size, “feel-good” score and more



**Enhances Patient / HCP Interaction**