Breaking Down the Barriers to Insulin use

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Where do we start?????????

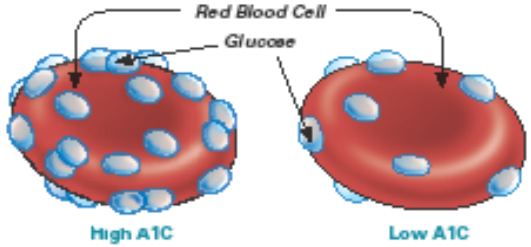
Dear Dr

- **Thank you for seeing Mr Tough guy who is a 48 yrs old builder.**
- ***Type 2 for 8 yrs ,on***
- ***Metformin 850 mg bd***
- ***,Glipizide 10 mg bd ,***
- ***Hba1c is :99mmol/mol(11.2%.)***
- ***Says he take his pills everyday.***
- ***Does not monitor BS says he feels well.***
- ***Has Hypertention ,Hyperlipedemia ,microalbuminuria, early retinopathy was found at last retinal screening.***
- ***Smokes 20 cigs a day.***
- ***Very reluctant to go on Insulin.***
- ***Used to be rugby player. Stopped about 7 yrs ago.***
- ***Says he can beat Diabetes!!!***


DO YOU
FEEL
LUCKY....
PUNK?
WELL....
DO YA?

How to prevent complications?

What is A1C?



Work on your A1C

American Diabetes Association. Implications of the United Kingdom prospective diabetes study. Diabetes Care 2003; 26(Suppl. 1): S28-32

1% Reduction in A1C = **35%** Reduction in risk of complications

Being in control or intensive management* can prevent diabetes-related complications

Eyes
76% reduced risk of developing retinopathy with tight control

Kidneys
34% reduced risk of developing nephropathy with tight control

Nerves
69% reduced risk of developing neuropathy at 5 years with tight control

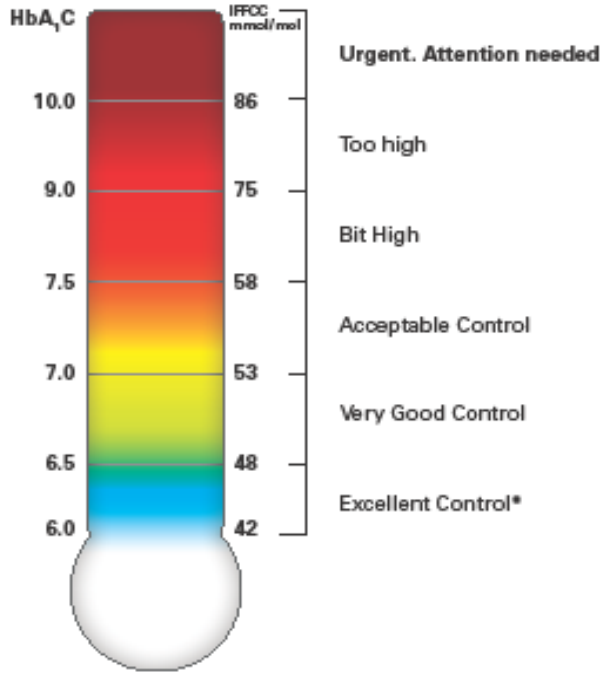
Individualise the target

DCCT % HbA_1C		IFCC mmol/mol		
6 - 6.5%	→	42 - 48	→	Excellent*
6.5 - 7%	→	48 - 53	→	Very Good
7 - 7.5%	→	53 - 58	→	Acceptable
7.5 - 9%	→	58 - 75	→	Bit high
9 - 10%	→	75 - 86	→	Too high
10+%	→	86 and above	→	Urgent. Attention needed

To work out DCCT % HbA_1C in IFCC mmol/mol: -2 – 2 rule
i.e: HbA_1C of 7% = 7 – 2= 5 – 2 = 3 Therefore is 53

Diabetic Control

HbA_1C Thermometer

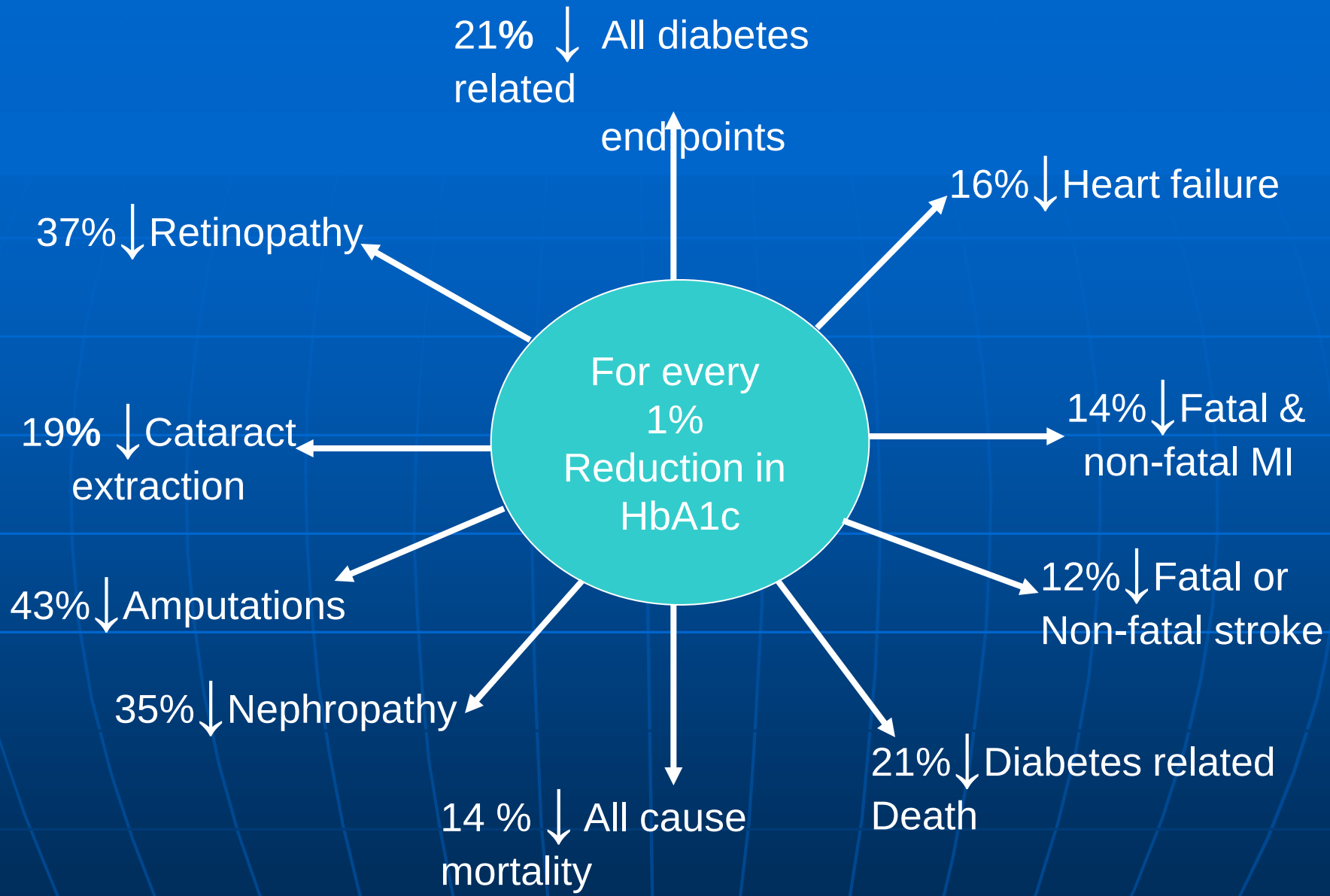


*The targets for everyone is less than 7% though targets should be individualised. **Caution should be taken with targets lower than 7 for those on insulin and sulphonylureas due to risk of hypoglycaemic events.** For pregnant diabetics target 6.0%

HbA1C is the best test of overall diabetic control.

If your result is 8% or more, please contact your nurse or doctor.

Developed by:
Rab Burtun
Diabetes Nurse Specialist



Stratton IM, Adler AI, Andrew H, et al. Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS35): prospective observational study. British Medical Journal 2000; 321: 405-1.1

A great deal of research has established that the HbA1c level is a crucial test for use in the assessment of a diabetic patient's degree of glycemic control. The table shows the reduction in risk of diabetic complications per 1% decrease in HbA1c observed in major studies, emphasizing the robustness of this association across many differing patient groups.

Reduction in Risk of complications for every 1 % decrease in HbA1c

- **Diabetes Control and Complications Trial (DCCT)**

Type 1 diabetes, (n = 1440)
Retinopathy, Nephropathy, Neuropathy
30%-35% decrease

- **Kumamoto Study**

Type 2 diabetes, (n = 110)
Retinopathy, Nephropathy, Neuropathy
30%-38% decrease

United Kingdom Prospective Diabetes Study (UKPDS)

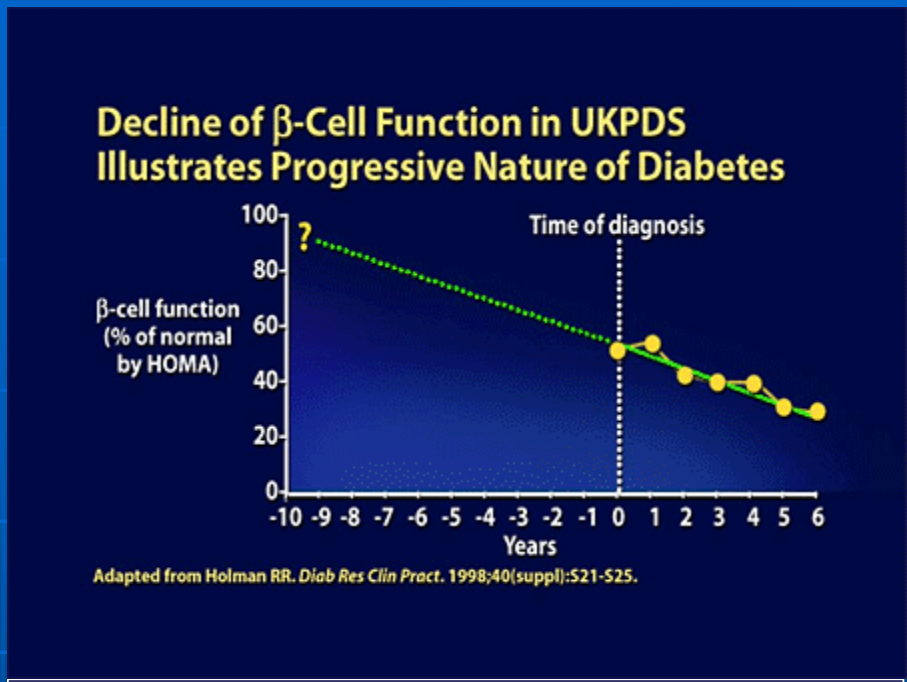
Type 2 diabetes, (n = 4209)
Retinopathy
28% decrease

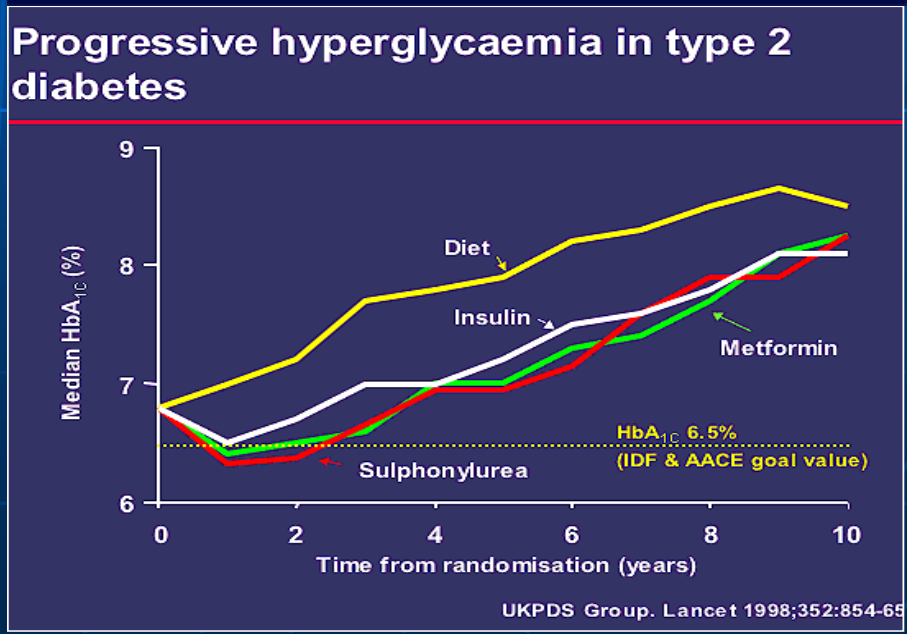
Wisconsin Epidemiologic Study of Diabetic Retinopathy (WESDR)

Type 2 diabetes
Retinopathy, Nephropathy, Neuropathy, cardiovascular disease
20%-50% decrease

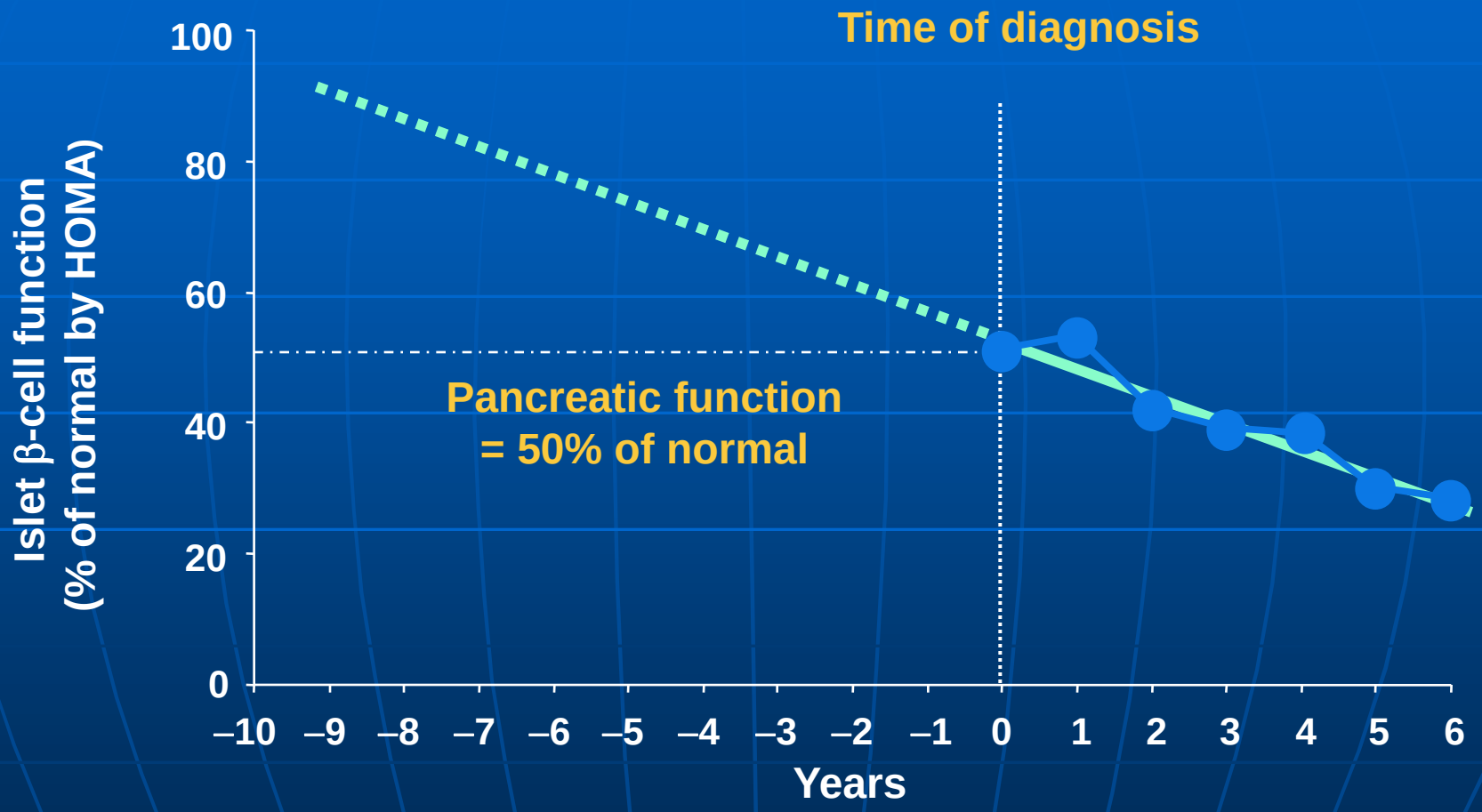
Progressive nature of Diabetes

- ***Before insulin initiation, patients may have spent an average of about 5 years with an A1C >8% and nearly 10 years >7%***
- ***At diagnosis, up to 50% of a patient's β-cell function may have been lost, and may continue to decline by about 4% annually***
- ***Remind patients that diabetes is a progressive disease and that their treatment plans may be adjusted over time. An overall treatment plan to lower A1C consists of diet, exercise, and diabetes medication, which may include insulin.***
- ***50% of Type 2 needs to go on Insulin within 7 yrs (UKPDS)***
- ***Let patients know fear of insulin is not uncommon. Help them understand the facts about insulin therapy***





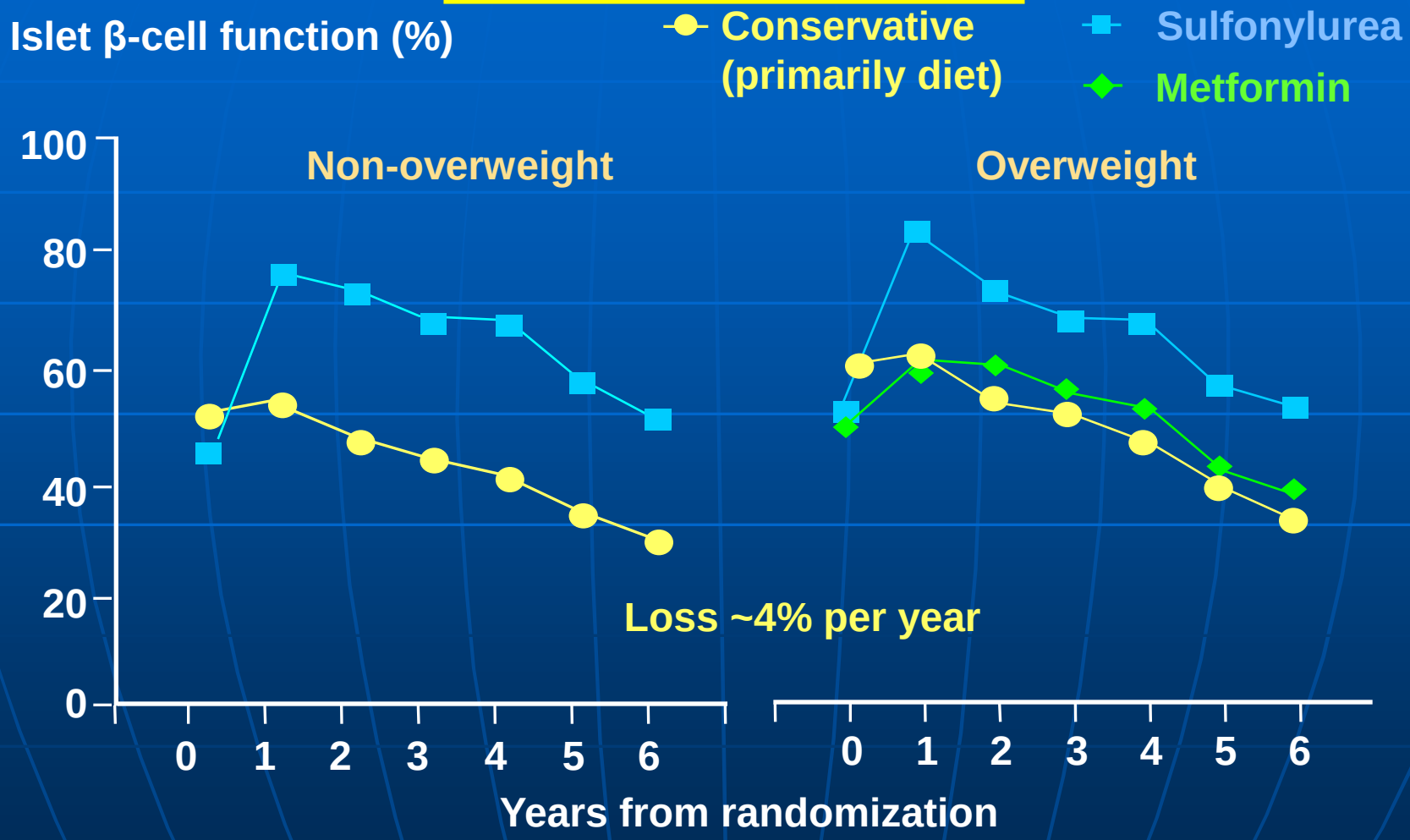
UKPDS: Islet β-cell function and the progressive nature of diabetes



HOMA = homeostasis model assessment

Holman RR. *Diab Res Clin Pract*. 1998;40(suppl):S21-S25;
UKPDS. *Diabetes*. 1995;44:1249-1258

Islet β-cell function (HOMA %B) in the UKPDS

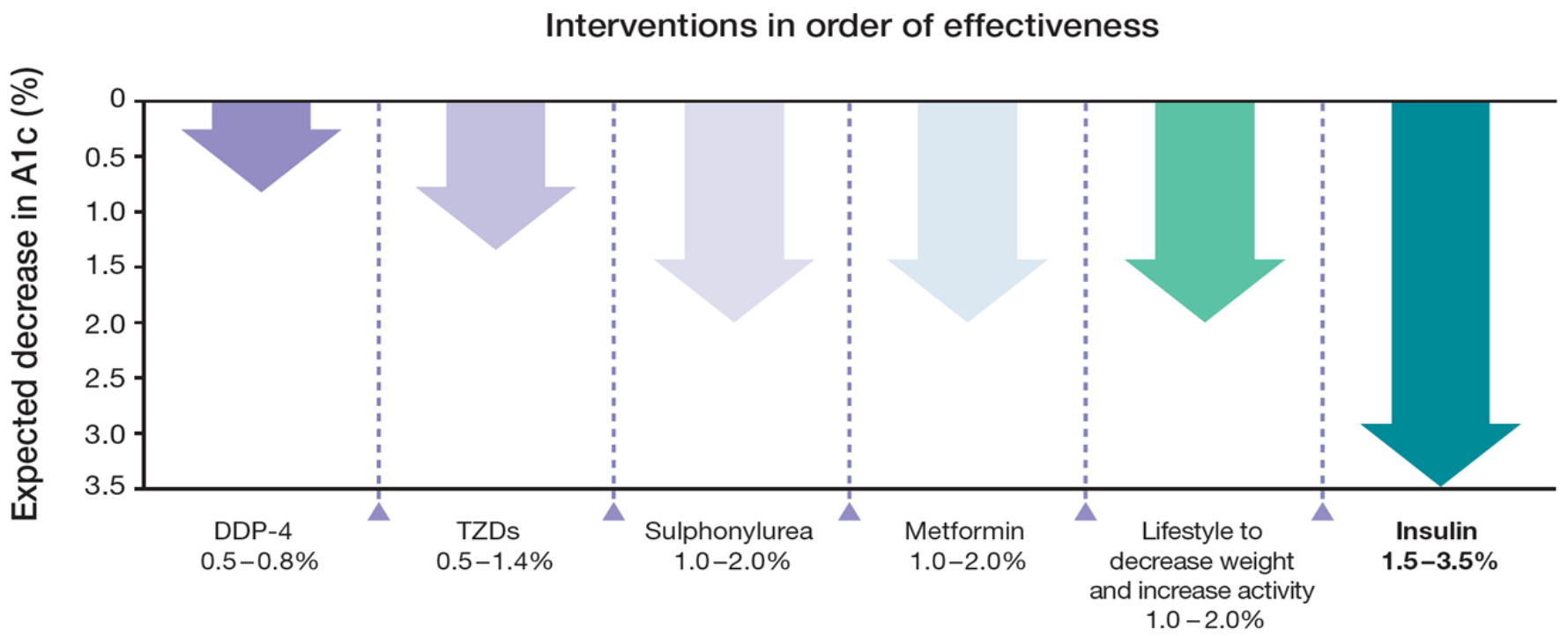


HOMA=homeostasis model assessment; UKPDS=United Kingdom Prospective Diabetes Study

UKPDS Group. *Diabetes*. 1995

Insulin-the most effective intervention[3]

A1c lowering potential of individual therapeutic options[2]



Adapted from Nathan *et al.*, 2009. DDP-4 = Dipeptidyl peptidase-4 inhibitor. TZDs = Thiazolidinedione.

Barriers to Insulin Therapy

Patient Factors	Physician Factors
Weight gain	Fear of patients' anger and alienation; losing patients
Social embarrassment	Concern over compliance
Fear of hypoglycemia	Burden of additional training or dealing with crises during transition
Lifestyle changes	Hypoglycemia
Painful injections	Weight gain
Feelings of failure/guilt	
Becoming more ill; disease progression	

Korytkowski M. *Int J Obesity*. 2002;26(Suppl 3):S18-24.

Combination Therapies With Insulin in Type 2 Diabetes

Hannele Yki-Järvinen, MD, FRCP1

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The higher the Hba1c is when Insulin is started the more weight is gained which makes sense .The more the the Glycosuria is the more calories they will keep when Insulin is started .

- If the Hba1c is **12%** when Insulin is started they will put **5 to 10 kg** on
- If Hba1c is **10%** when Insulin is started they will put **3-6 kg** on
- If Hba1c is **7.5%** when insulin is started then they only put on **0.5 to 1 kg on**

10.2337/diacare.24.4.758 ***Diabetes Care April 2001 vol. 24 no. 4 758-767***

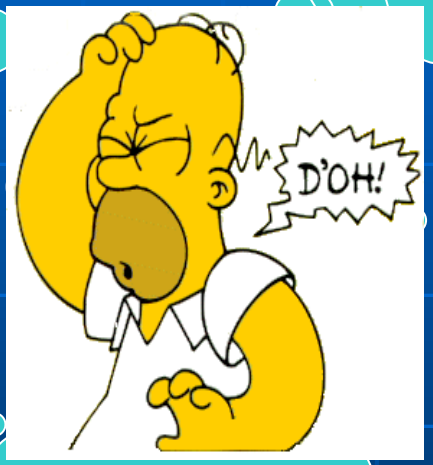
Many factors contributes to fears of insulin!!

Cost? the pen looks nice and expensive! !can I afford that??

Disease getting worst!! Some people have morphine injections when they are about to die!

Hypoglycaemia!!. Seen friend or neighbour call ambulance!! Fitting!! Was scary!!

Pain!!does it go into a vein??Seen it on TV Huge needle and drug addicts have to find a vein!!Too complicated!!



Its forever!! Addiction?? Once you on it you stay on it ?? Cultural beliefs :is it from pigs/Cow

Lifestyle change!!

Travel/work/beer?? Will I still be able to go out and have sweets puddings etc??

Insulin causes complications!!Aunty Nelly was well into her 80s until she went on Insulin she was dead after 3 months on Insulin

Personal failure!!I am a loser !!why I cant beat this ??!!Why have I failed???

Barriers to insulin therapy often come from common fears and misperceptions. Some ways to help address these issues are outlined below.

- **Disease getting worse???**
- *Inform patients that blood glucose may rise over time*
- *Reassure patients that it may not be entirely their fault. The increasing inability of the pancreas to produce enough insulin may be the main reason for disease progression*
- **Hypoglycemia????**
- *Some people are concerned about side effects, such as hypoglycemia.*
- *Acknowledge that hypoglycemia is the most common side effect of insulin*
- *Advise patients taking insulin to regularly check their blood glucose*
- *Teach patients how to recognize and treat hypoglycemia, should an episode occur*
- *Inform patients of the common things that can affect their blood glucose levels, such as medications, changes in food intake, illness, physical activity and stress*
- **It's forever????**
- *Many patients have concerns about chronic use of insulin.*
- *Assure patients that insulin is not physically addictive or habit-forming*
- *Inform patients that you may adjust their insulin doses upwards or downwards over the course of their treatment to assure they are on the proper dose*
- **Why not try it for a month???**

Continued!!

- **Failure??**
- *Reframe the perception of failure and self-blame.*
- *Educate patients that insulin helps to replace what the body isn't adequately making to lower blood glucose*
- *Remind your patients that insulin may be an appropriate choice for them since it is effective at lowering A1C when added to an overall treatment plan*
- *Educate patients about what they can do by making healthy food choices and increasing their physical activity .Address problem of SNACKS or eating in between meals ??????*
- **Lifestyle change**
  Many patients believe that taking insulin will greatly disrupt their lives.
- *Inform patients that insulin may help control blood glucose and lower A1C1*
- *Present insulin as another effective option to add to their daily diabetes management routine*
- *Patients may find that insulin can become a normal part of their routine*
- **Pain**
  If fear of pain is deterring your patient from taking insulin, consider the following:
- *Insulin is injected in the fatty layer just under the skin where there are fewer nerve endings and injections generally cause little discomfort*
- *Tell patients that many people on insulin are surprised by how soon they get used to the injections*
- **Get Partner or Friend ,parent or Children to try needle first!**
- **Provide information about insulin benefits, Would sleep better, have more energy, not feel constantly tired, mood, thirsty, thrush in women!!!, improve erectile dysfunction in men!!!!!**

Safer Journey – Recent Convert

A– ---- here I am fifty six years of age of Maori heritage stemming from the tail of the fish fifty kilometres north of Kaitaia in the cosy settlement of Te Kao.

How do I begin? I've never been one for truly expressing written thanks.

Moemiti (praying) in my faith for whanau, others and myself, however, on this occasion to Rab Burtun Clinical Diabetes Specialist Nurse is first to none. Rab has guided me through a journey I thought was insurmountable.

Being a double figured blood sugar level diabetic(in denial) for quite some time with unsafe readings and reminded by whanau, *our family doctor especially that making the right decision to speak to Rab would save my life. All the diabetes literature wasn't enough for me until the cold hard facts are brought to light by Rab Burtun. My husband and children are a life source that I want to nurture for as long as is possible.* ***Yes, I'm now on insulin*** *with careful monitoring and (as my mum is still with us to reassure me of the care needed) I am not afraid, in fact* ***I feel so much more uplifted with a clearer sense of well being.***

My sleeping patterns have improved, no more drowsiness. Planning for the day is decisive having medicated accordingly. Feeling like a sharper pencil yet not superwoman as I used to think I was before being diagnosed diabetic, I feel 2nd to none in our household. *Maintaining a healthy diet of fruit a vegetables from my husbands garden plays a major part in my constitution. If it isn't with in walking distance I go the supermarket to acquire goodies for the family or the weekly market at the Avondale Market Day.* ***My husband Trevor is my backbone of support, which created a little bit of concern for him with Rab in the picture. Trevor thinks I'm having an affair with Rab****. Alls well, had Rab not been able talk me into my new space, Trevor or our daughters' and Rab would have had a chat to; help me.*

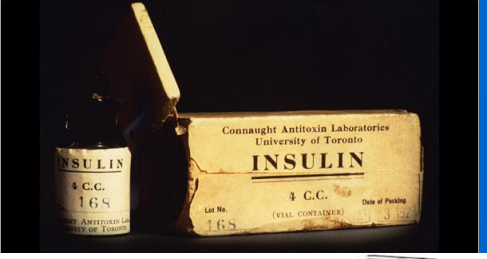
Rab Burtuns' approach is open and honest demonstrating the ins and outs of self administering diabetic medication and the explaination of bodily organs subjected to ill treatment if not taken care of as I thought I was, prior to my diagnosis, compared to now*. Having written all this with all good things in mind, my life expectancy is reassured. Still a workingwoman of deep faith and self mending,* ***had it not been for Rab Burtun his wife and children, the support needed to nurture a Kauri tree of which I liken Rab too; I would wonder how long I could weather the future.***

Thank you Rab.

Piki te Ora/ Good Health

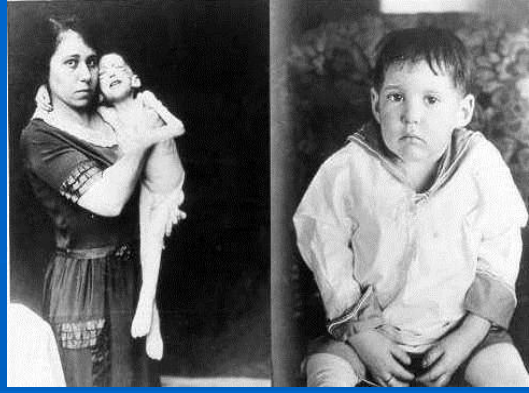
Arohanui

Ana



Miracle of Insulin !!!!!!!!!

Glory enough for all!!!!!!!!



DAUGHTER OF U.S. SECRETARY OF STATE TRIES NEW TORONTO DISCOVERY.
On the left is Mrs. Charles Evans Hughes, who accompanied her daughter to Toronto this week to take a new treatment for diabetes, which has been worked out at the University of Toronto. In the centre is her fifteen-year-old daughter, who is here to take the treatm ent. On the right is Dr. F. G. Banting, 160 Bloor street west, who is the originator of the insulin treatment for diabetes, and who for over a year has been doing research work along with Mr. C. H. Best, of Toronto. The new treatment has already prolonged the lives of many sufferers from the disease.

Elizabeth Hughes, daughter Charles Evans Hughes ,US Sec of states , Age 11 diag T1 just 3 yrs before Insulin discovered. Dr Fred Allen put her on 400 cal per day starvation diet for 3 yrs .Wt loss 75 lbs to 45 lbs .Until Insulin became available

Died with pneumonia in 1981 age 73 yrs .She had 47000 injections over 58 yrs .Successful career in law .

Every few months some miracle drug or other is rolled out with bells and confetti, but only once or twice in a generation does the real thing come along!!!!

<u>These are the blockbuster medications that can virtually raise the dead</u>…., *Insulin was one of them….. Insulin actually put flesh on living skeletons. With insulin, dying children laughed and played again, as parents wept and doctors spoke of biblical resurrections..... mothers all over the globe were writing him heart-wrenching letters: "My dear Dr. Banting: I am very anxious to know more of your discovery," wrote one, going on to describe her daughter's case: "She is pitifully depleted and reduced……"*

Normal Insulin Profiles

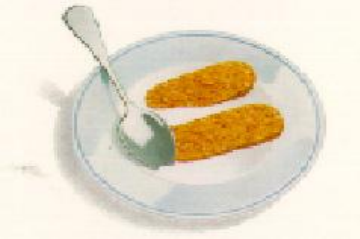
the body needs a constant level of sugar in the blood

the blood sugar rises

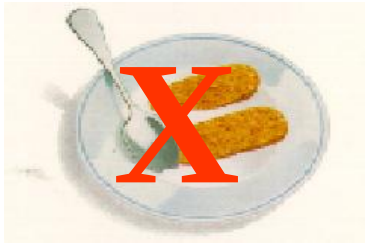
and a background level of insulin

and extra insulin is needed

Normal Insulin Profiles



ABNormal Insulin Profiles



Morning tea

Lunch

Afternoon tea

Dinner

Supper

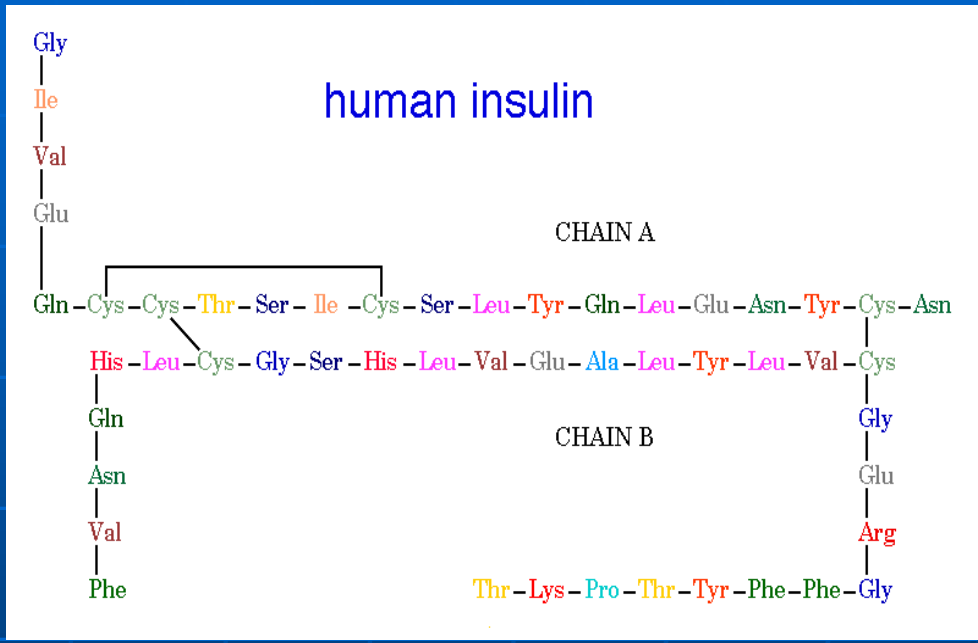
Blood sugar

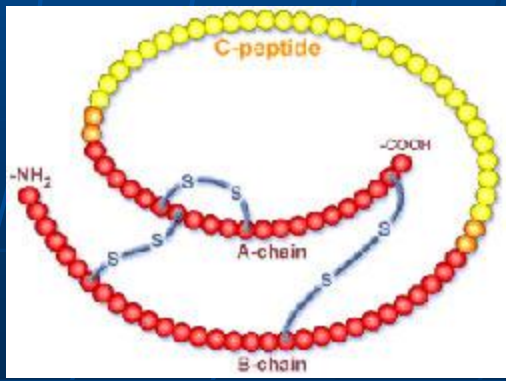
Mealtime insulin

Background insulin

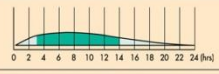
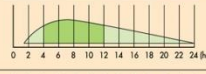
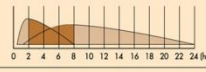
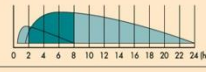
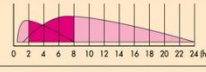
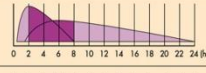
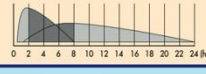
Types of Insulin

- Short acting
- Intermediate acting
- Long acting
- Biphasic
- Analogue Mixtures
- Short Acting Analogues
- Long acting Analogues





NOVO NORDISK - BALANCING INSULIN AND DELIVERY.

Brand	Presentation	Schematic Time-Action Profile*	Insulin Profile*
NovoRapid® *Rapid-acting insulin aspart (rys)*	3mL **Penfill®** 10mL Vial		Onset: 10-20 minutes Peak: 1-3 hours Duration: 3-5 hours
Levemir® *Long-acting insulin detemir (rys)*	**FlexPen®**		Peak: 3-14 hours Duration: Up to 24 hours
Actrapid® *Short-acting human insulin (rys)*	3mL **Penfill®** 10mL Vial		Onset: 30 minutes Peak: 1-3 hours Duration: 8 hours
Protaphane® *Intermediate-acting human insulin (rys)*	3mL **Penfill®** 10mL Vial		Onset: 1.5 hours Peak: 4-12 hours Duration: 24 hours
PenMix® 30 & Mixtard® 30 (10mL) *30% Short-acting & 70% Intermediate-acting human insulin (rys)*	3mL **Penfill®** 10mL Vial		Onset: 30 minutes Peak: 2-8 hours Duration: 24 hours
PenMix® 10 *10% Short-acting & 90% Intermediate-acting human insulin (rys)*	3mL **Penfill®**		Onset: 30 minutes Peak: 2-8 hours Duration: 24 hours
PenMix® 20 *20% Short-acting & 80% Intermediate-acting human insulin (rys)*	3mL **Penfill®**		Onset: 30 minutes Peak: 2-8 hours Duration: 24 hours
PenMix® 40 *40% Short-acting & 60% Intermediate-acting human insulin (rys)*	3mL **Penfill®**		Onset: 30 minutes Peak: 2-8 hours Duration: 24 hours
PenMix® 50 & Mixtard® 50 (10mL) *50% Short-acting & 50% Intermediate-acting human insulin (rys)*	3mL **Penfill®** 10mL Vial		Onset: 30 minutes Peak: 2-8 hours Duration: 24 hours

Please review Data Sheet before prescribing. Full Data Sheet is available from the Novo Nordisk Customer Care Centre 0800 733 737. *In clinical practice, the duration of insulin action may be shorter or longer than the durations specified. Variations between and within patients may occur depending upon injection site and technique, insulin dosage, as well as diet and exercise. ® Registered trademark of Novo Nordisk A/S. Novo Nordisk Pharmaceuticals Ltd, PO Box 51268 Pakuranga, Auckland. www.novonordisk.co.nz

Novo Nordisk Customer Care Centre
0800 733 737
www.novonordisk.co.nz

novo nordisk®

Lilly Insulin Range†

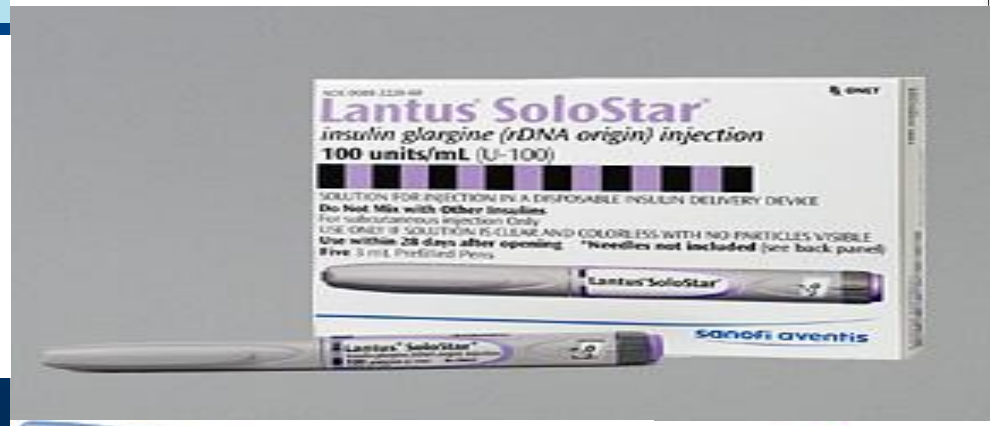
FULL RANGE NOW FUNDED*

Brand Name†,‡	Type of Insulin (generic name) / Product Description	Presentation	Schematic Action Profile*
Humalog®	insulin lispro Rbe RAPID-ACTING	10mL vials and 3mL cartridges	Onset: 0–15 mins Peak: 1 hour Duration: 3.5–4.5 hours
Humulin® R	insulin neutral (Soluble) SHORT-ACTING	10mL vials and 3mL cartridges	Onset: 30 mins Peak: 2–4 hours Duration: 6–8 hours
Humulin® NPH	isophane (NPH) INTERMEDIATE ACTING	10mL vials and 3mL cartridges	Onset: 1 hour Peak: 4–10 hours Duration: 16–18 hours
Humalog® Mix25®	25% insulin lispro, 75% insulin lispro protamine suspension Rbe PREMIXED INSULIN LISPRO	3mL cartridges	Onset: 0–15 mins Peak: 1 hour Duration: 16–18 hours
Humalog® Mix50®	50% insulin lispro, 50% insulin lispro protamine suspension Rbe PREMIXED INSULIN LISPRO	3mL cartridges	Onset: 0–15 mins Peak: 2 hour Duration: 16–18 hours
Humulin® 30/70	30% insulin neutral, 70% isophane (NPH) PREMIXED INSULIN	10mL vials and 3mL cartridges	Onset: More rapid than NPH alone Peak: 2–12 hours Duration: 16–18 hours

HUMAPEN LUXURA CAN ONLY BE USED WITH LILLY 3mL INSULIN CARTRIDGES. BEFORE PRESCRIBING PLEASE REVIEW THE PRODUCT DATA SHEET.

HumaPen® LUXURA

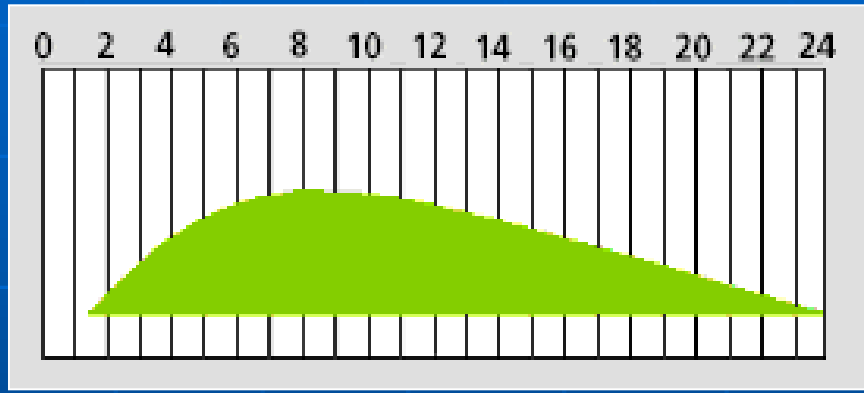
Lilly



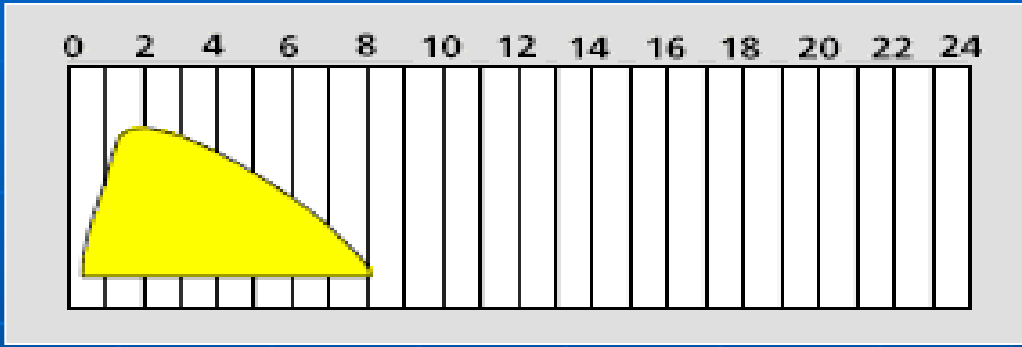
sanofi aventis
Because health matters

Time Action Profiles

- Insulin/glucose levels in the blood
- Stylized format showing
  - Onset
  - Peak
  - Duration
- Intended as a guide ONLY



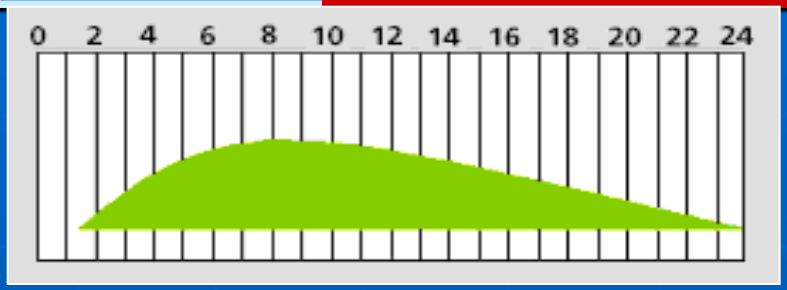
Short Acting Insulin Actrapid or Humilin R



- Soluble
- Clear
- Onset 30 minutes
- Peak 1 - 3 hours
- Duration up to 8 hours

Prandial Insulin

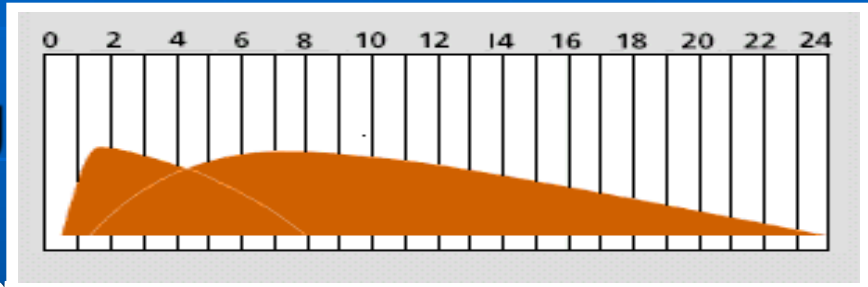
Intermediate Acting Insulin Protaphane or Humulin NPH



- Crystals in suspension (need re-suspending)
- Cloudy
- NPH (Humilin N)or Protophane (**NPH** = **N**eutral **P**rotamine **Hagedorn**)
- Onset 1 $^{1}/_{2}$ hours
- Peak 4 - 10 hours
- Duration 16 to 18 hours

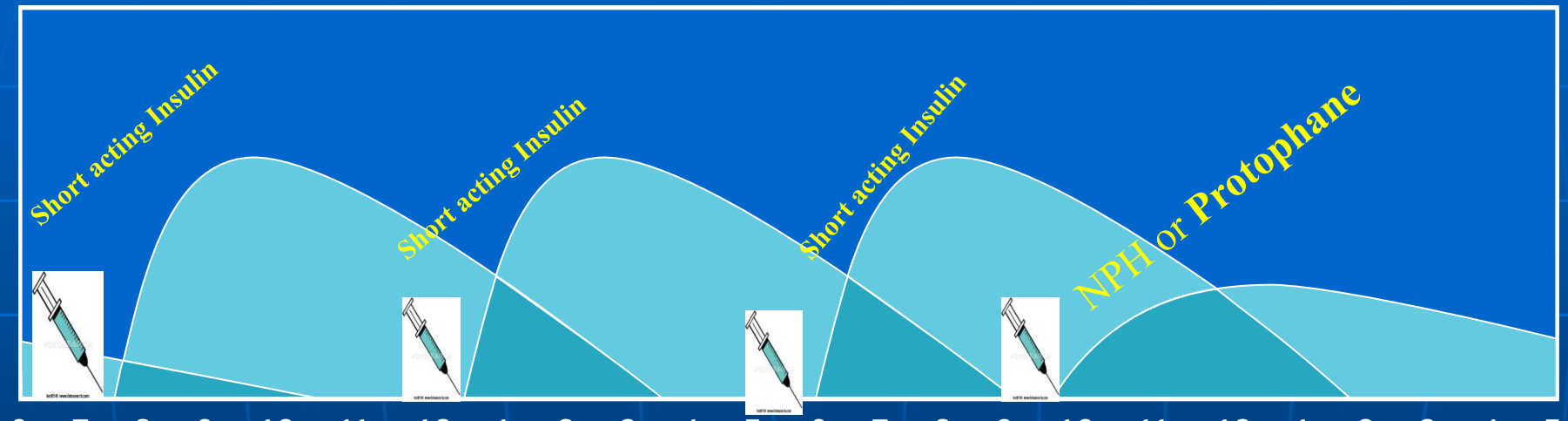
Premixed Insulins/ Biphasic Insulins

Humilin 30/70(lilly) or Penmix 30/70(Novo Nordisk)



- Pre-mixed combinations of short and intermediate acting insulins (biphasic)
- Cloudy (needs re-suspending)
- 5 different combinations (30, 40, 50)
  - e.g. 30/70 Mixture = 30% fast acting
    + 70% intermediate acting
  - **Onset 30 minutes**
- Peak 2 - 8 hours
- Duration up to 24 hours

4 Injections Per Day
3 Short + 1 Intermediate Acting
(Basal Bolus)
using Actrapid and Protaphane or Humulin R and NPH



Breakfast

Lunch

Evening Meal

Sleep

Need for Analog Insulins

Current insulin time action profiles not ideal

- Disadvantages of existing insulins:

Short acting

- • must be injected up to 30 mins before meal
- • duration of action up to 8 hours/overlap

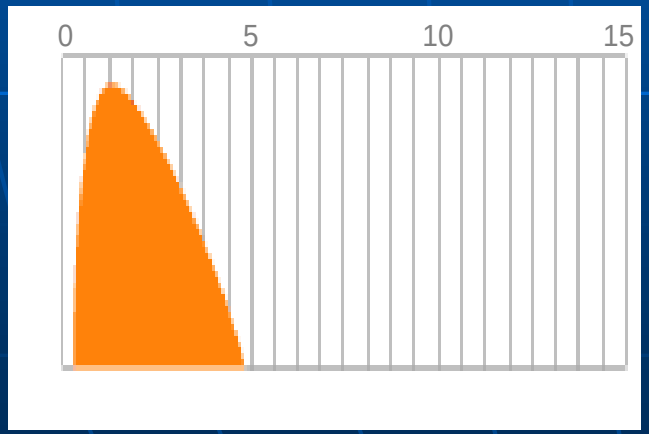
Intermediate acting

- • insulin peaks too early in night
- • increases risk of nocturnal hypoglycaemia
- • after peak, action wanes too rapidly

Rapid-acting insulins Novorapid (Insulin Aspart) NovoNordisk
Humalog(Lispro)Lilly,
Apidra (*insulin glulisine*) Aventis

- Clinical benefits
  - improved metabolic control compared with human soluble insulin
  - fewer hypoglycaemic episodes
  - no post-prandial hypoglycaemia

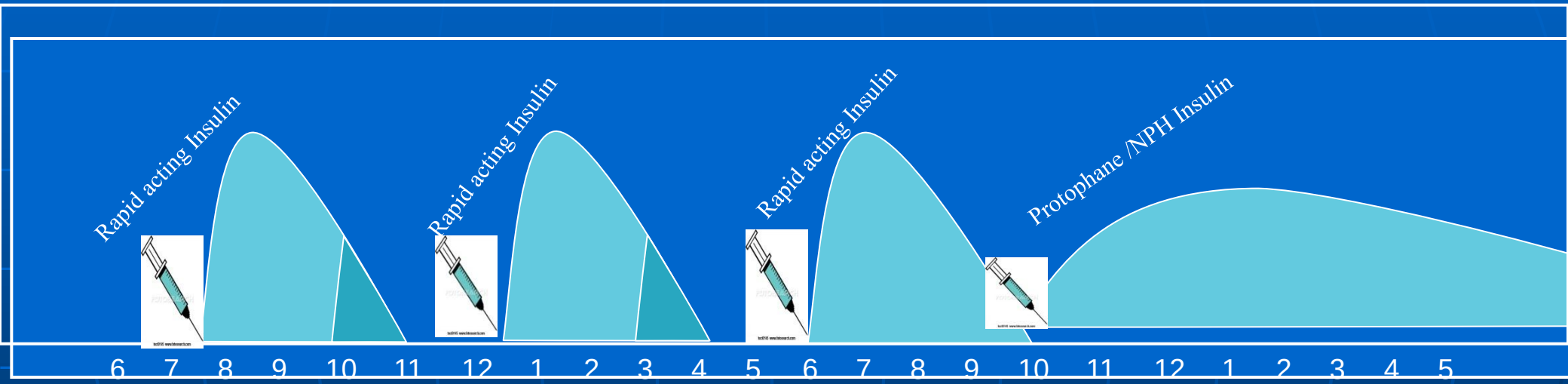
Prandial Insulins



- rapid onset of action
- short duration of action
- better quality of life and improved convenience

Onset Action : 10-20 min Peak : 1 – 3 hrs Duration : 3 – 5 hrs

4 Injections Per Day
3 rapid acting + 1 intermediate Acting
(Basal Bolus)
Rapid Acting and Protopahne /NPH



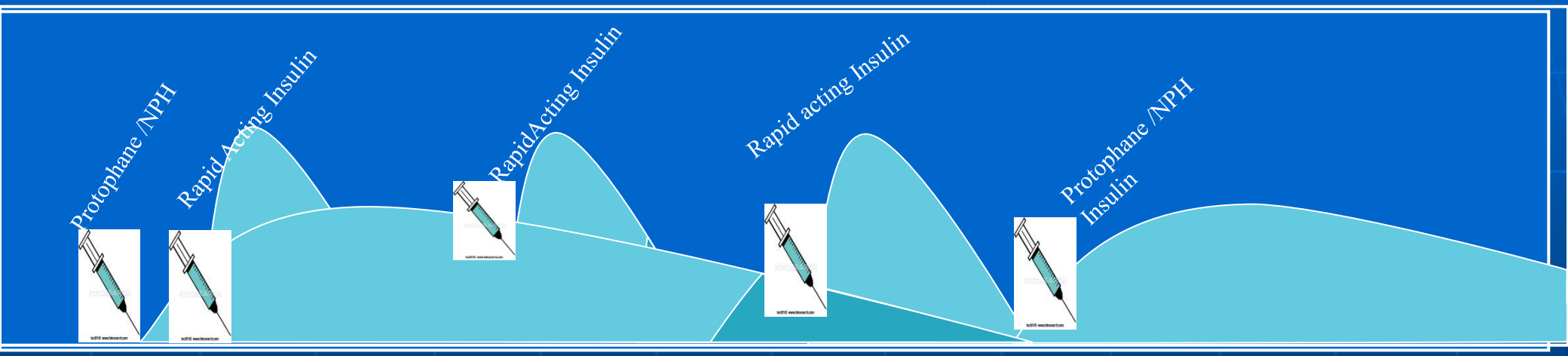
Breakfast

Lunch

Evening Meal

Sleep

4 Injections Per Day
3 rapid acting + 1 long Acting
(Basal Bolus)
Rapid Acting and Protophane or NPH BD



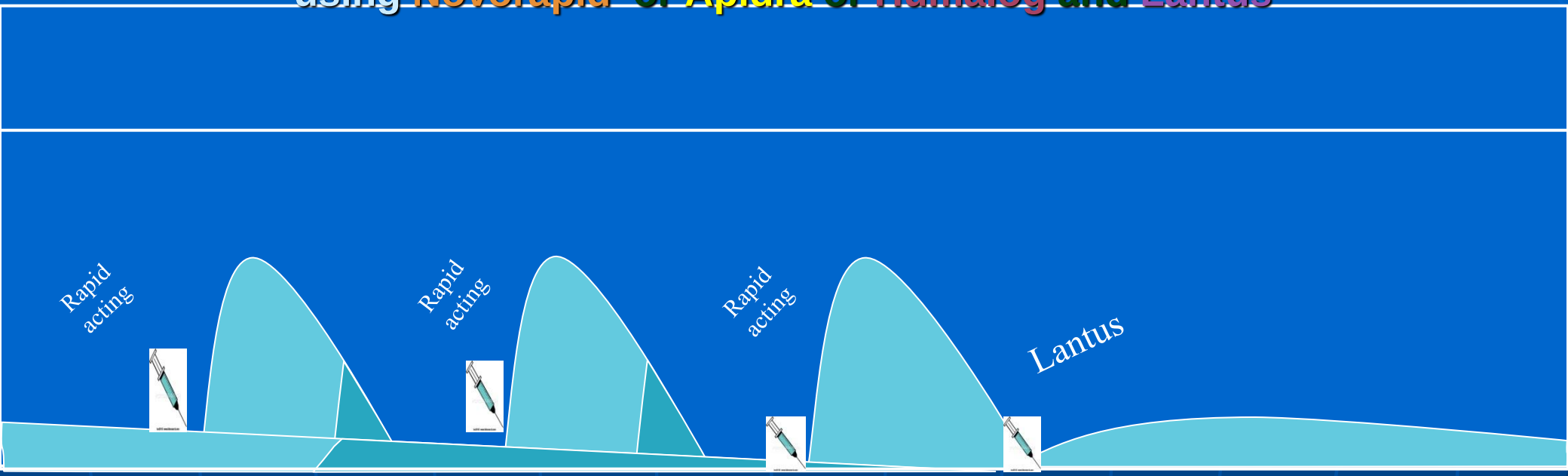
Breakfast

Lunch

Evening Meal

Sleep

4 Injections Per Day
3 rapid acting + 1 long Acting
(Basal Bolus)
using Novorapid or Apidra or Humalog and Lantus



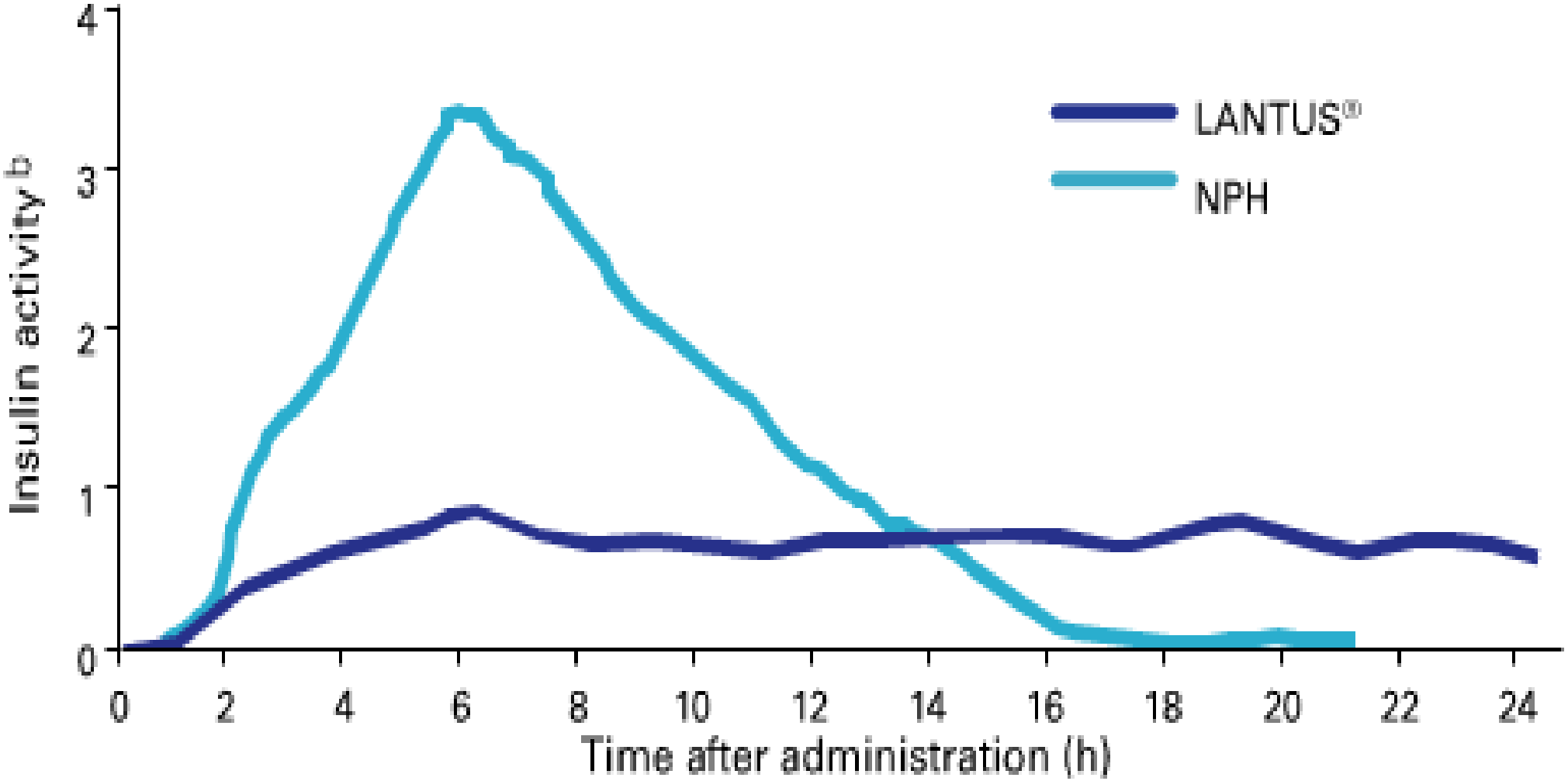
Breakfast

Lunch

Evening Meal

Sleep

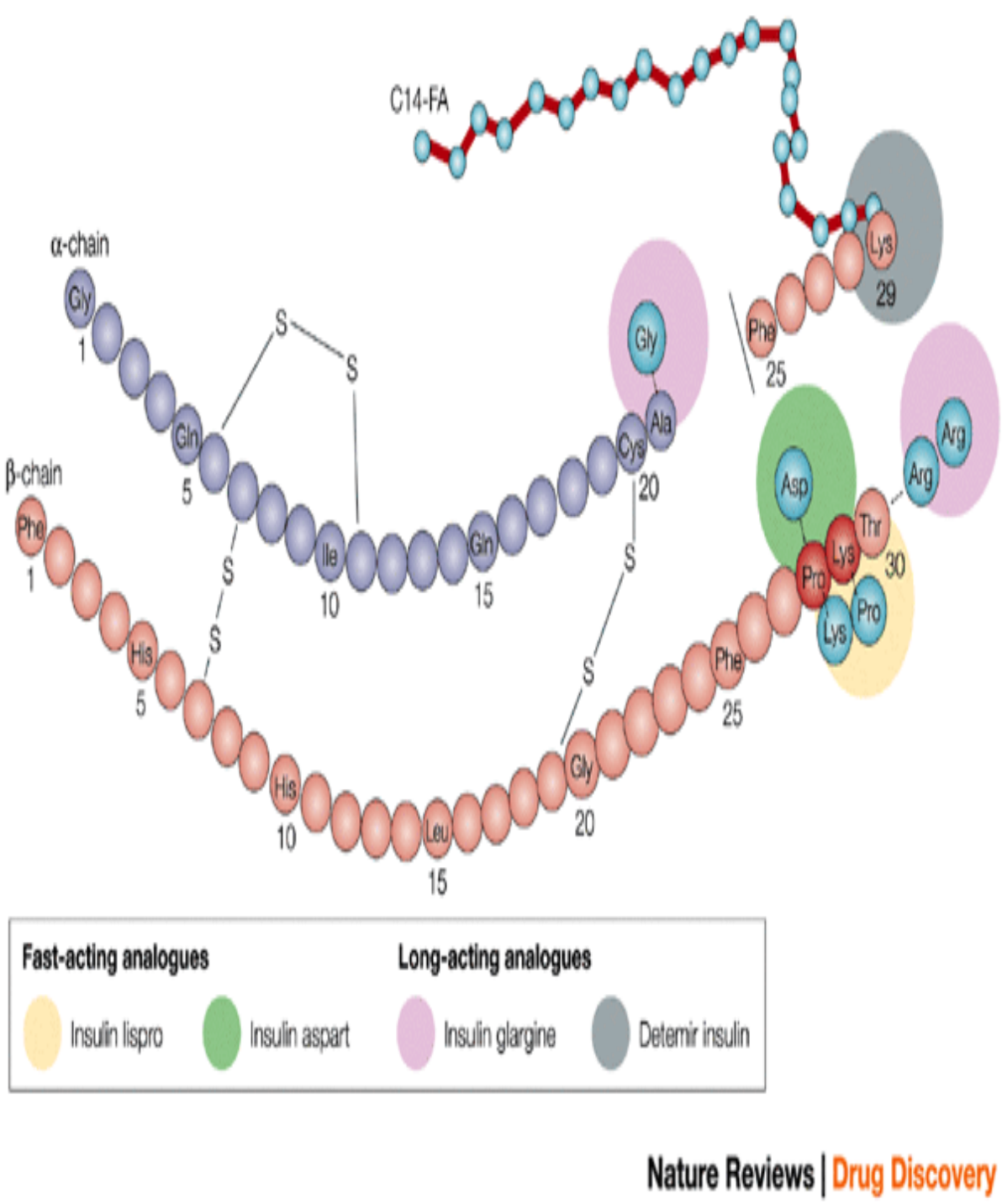
Profile of LANTUS® vs NPH in Patients with Type 1 Diabetes [a] [3, 19]

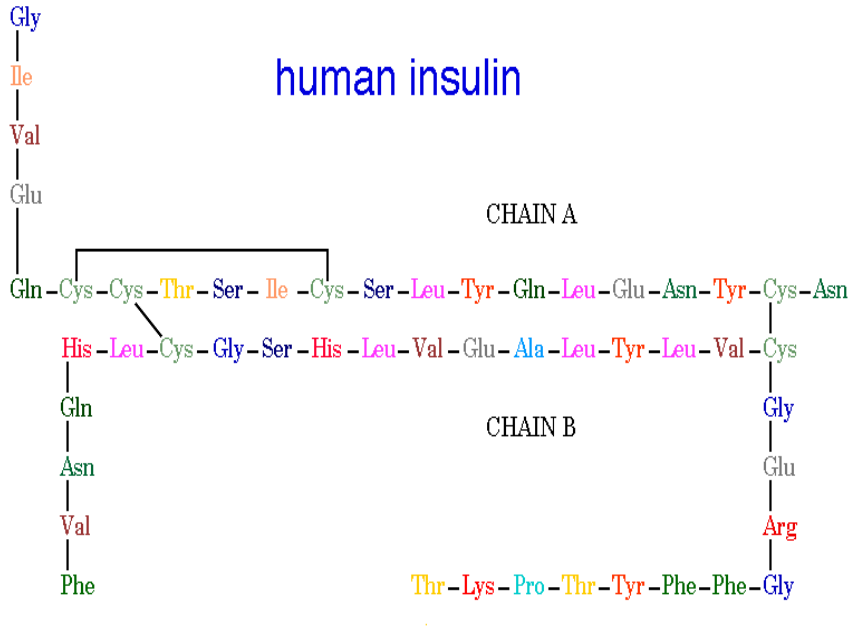


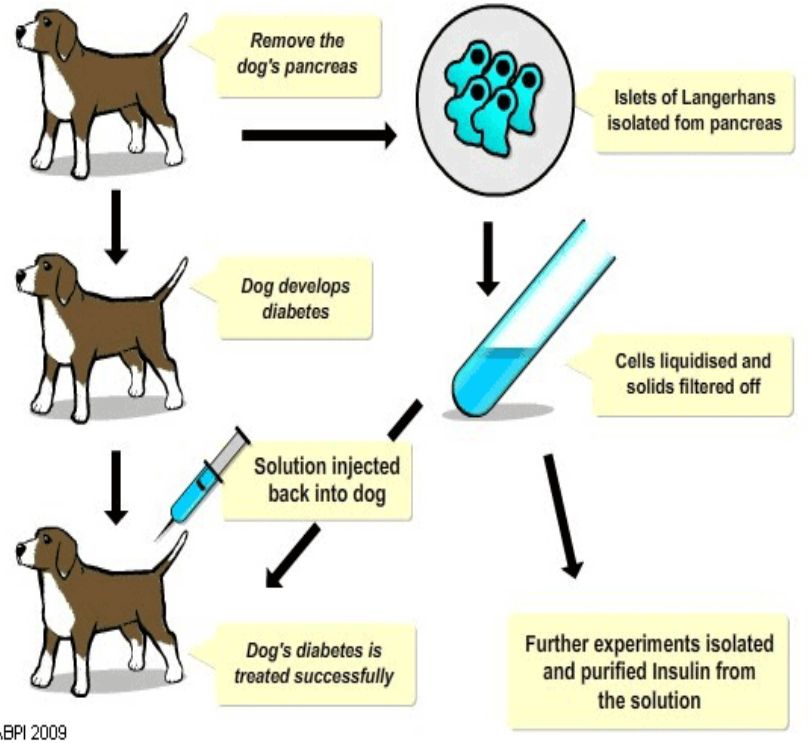
Long Acting Analogues

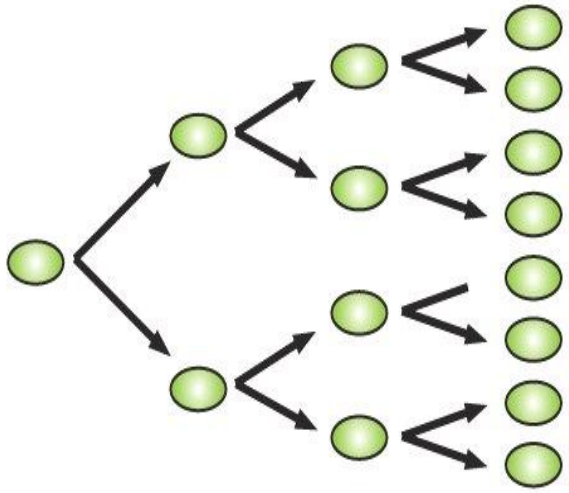
- Lantus

- Delayed and prolonged absorption from injection site
- Flatter profile (peak removed): Less hypos
- Longer duration of action


C14-FA
α-chain
β-chain
Gly
Ile
Val
Glu
Gln
Phe
His
Leu
Cys
Ala
Asp
Pro
Lys
Thr
Arg
S
1
5
10
15
20
25
29
30
Fast-acting analogues
Insulin lispro
Insulin aspart
Long-acting analogues
Insulin glargine
Determir insulin
Nature Reviews | Drug Discovery


human insulin
CHAIN A
CHAIN B
Gly
Ile
Val
Glu
Gln – Cys – Cys – Thr – Ser – Ile – Cys – Ser – Leu – Tyr – Gln – Leu – Glu – Asn – Tyr – Cys – Asn
His – Leu – Cys – Gly – Ser – His – Leu – Val – Glu – Ala – Leu – Tyr – Leu – Val – Cys
Gln
Asn
Val
Phe
Gly
Glu
Arg
Thr – Lys – Pro – Thr – Tyr – Phe – Phe – Gly


Remove the dog's pancreas
Islets of Langerhans isolated fom pancreas
Dog develops diabetes
Cells liquidised and solids filtered off
Solution injected back into dog
Dog's diabetes is treated successfully
Further experiments isolated and purified Insulin from the solution
© ABPI 2009

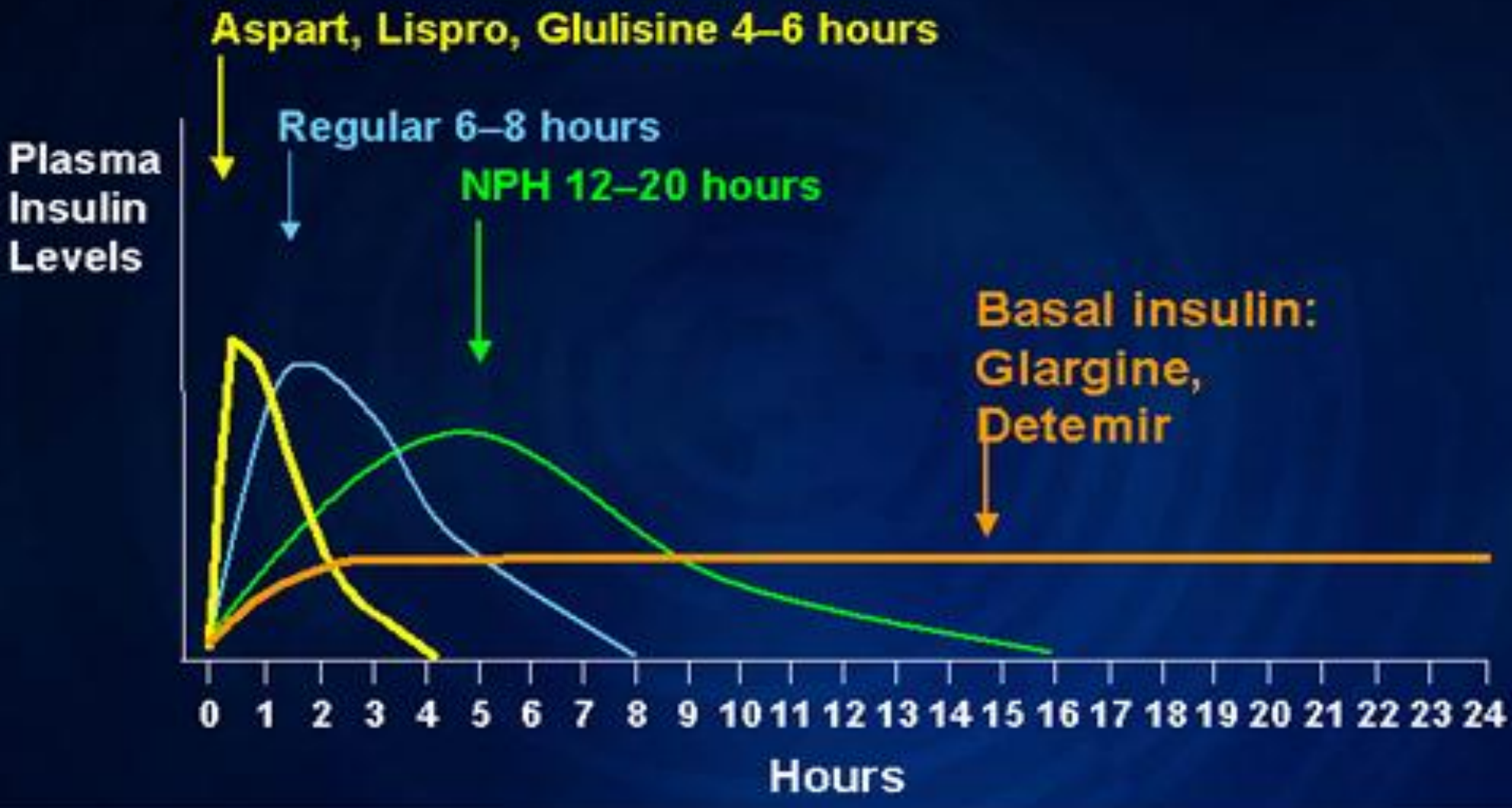


8 Grow trillions of new insulin-producing bacteria.

Figure 4-3 (4) Biology Today, 3/e (© 2004 Garland Science)


PLAY!
gene enzyme cuts out gene
Enzyme cuts bacterial DNA and inserts insulin gene

Action Profiles of Injectable Insulins



Type 2 Diabetes Insulin Options

- Basal
  - NPH / Protophane at bedtime and/or a.m.
  - Glargine(Lantus) once daily at any time of the day .(Now Funded for all Type 2)
  - Detemir once or twice daily (*not funded in NZ*)
- Premixed
  - Premixed once or twice a day
- Pre Mixed Analogues :*Humalog Mix 25 ,Humalog Mix 50/50(Injected before breakfast and before dinner)GOOD FOR POST PRANDIALS*

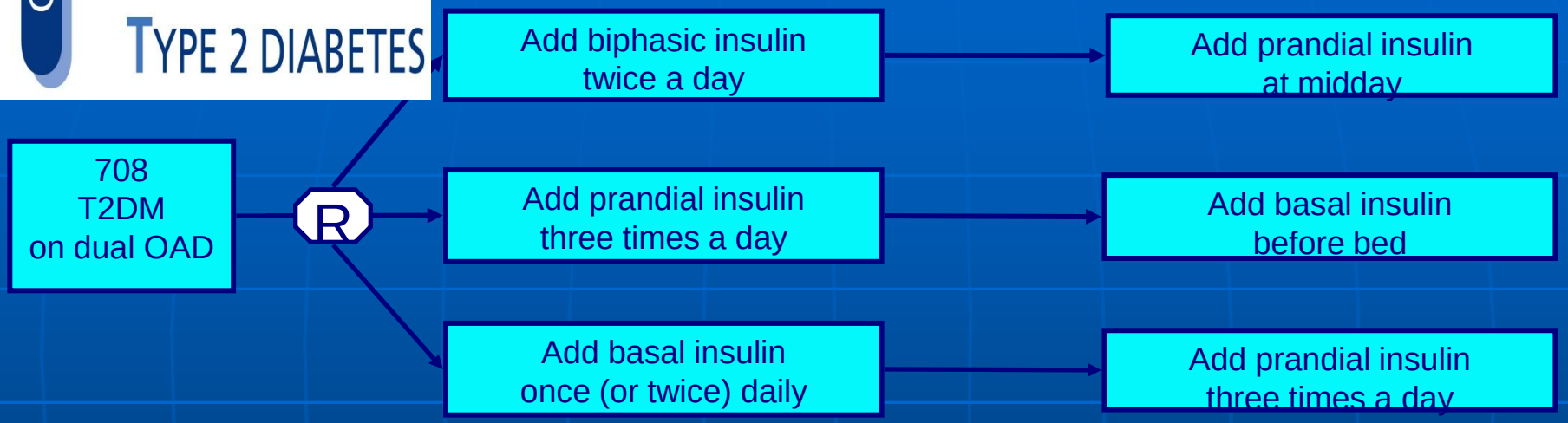
Novomix 30/70 : *Not Funded in New Zealand*

  - Meal-time insulin or Basal + one or Basal Plus 2
  - Multiple daily injections (meal-time + basal)

Insulin Timeline

- 1922 Banting and Best use bovine insulin extract on human
- 1923 Eli Lilly and Company (Lilly) produces commercial quantities of bovine insulin
- 1923 Hagedorn founds the Nordisk Insulinlaboratorium in Denmark forerunner of Novo
- 1926 Nordisk receives Danish charter to produce insulin as a non-profit
- 1936 Hagedorn discovers that adding protamine to insulin prolongs the effect of insulin
- 1946 Nordisk formulates Isophane porcine insulin a.k.a. Neutral Protamine Hagedorn or NPH insulin
- 1946 Nordisk crystallizes a protamine and insulin mixture
- 1950 Nordisk markets NPH insulin
- 1953 Novo formulates Lente porcine and bovine insulins by adding zinc for longer-lasting insulin
- 1978 Genentech produces synthetic 'human' insulin in Escheria coli bacteria using recombinant DNA technology
- 1981 Novo Nordisk chemically and enzymatically converts porcine insulin to 'human' insulin
- 1982 Genentech synthetic 'human' insulin approved, largely thanks to its partnership with Eli Lilly and Company, who shepherded the product trough the U.S. Food and Drug Administration (FDA) approval process
- 1983 Lilly produces synthetic, recombinant 'human' insulin, branded Humulin
- 1985 Axel Ullrich sequences the human insulin receptor
- 1988 Novo Nordisk produces synthetic, recombinant 'human' insulin
- 1996 Lilly Humalog "lispro" insulin analogue approved by the U.S. 2003 Aventis Lantus "glargine" insulin analogue approved in USA 8
- 2004 Sanofi-Aventis Apidra insulin "glulisine" analogue approved for clinical use in the USA.
- 2006 Novo Nordisk's Levemir "insulin detemir" analogue approved in USA

TREATING TO TARGET IN TYPE 2 DIABETES



* *Intensify to a combination insulin regimen in year one if unacceptable hyperglycaemia*

Three-arm trial in 708 patients with type 2 diabetes from 58 UK and Irish centres
Evaluating addition of three different analogue insulin regimens to dual oral antidiabetic therapy
Open-label randomisation to:

- Twice a day biphasic insulin (NovoMix 30)
- Three times a day prandial insulin (NovoRapid)
- Once a day basal insulin (Levemir) before bed, with a morning injection added if necessary

N Engl J Med 2007; 357: 1716-30

Outcomes at One Year

Primary

- To compare HbA_{1c} levels achieved by the three regimens

Secondary outcomes include:

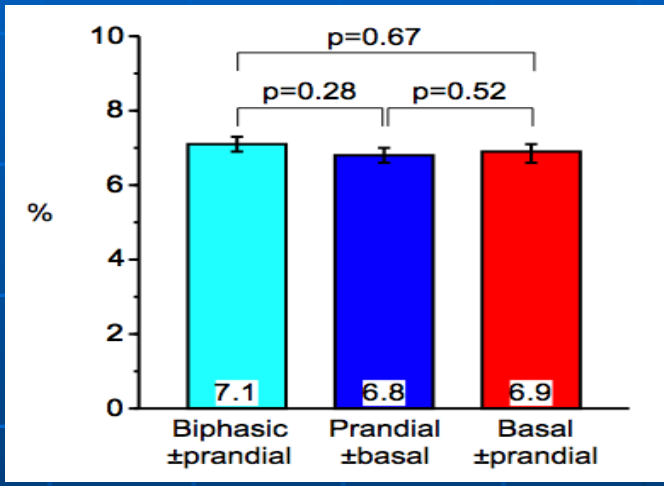
- Proportion with HbA_{1c} ≤6.5%
- Proportion with unacceptable hyperglycemia
  i.e. HbA_{1c} >10% or two successive values >8.5%
  at or after 24 weeks
- Hypoglycaemia rates
- Impact on body weight
- Quality of Life (EQ-5D)
- Eight-point self-measured capillary glucose profiles
- Proportion requiring a morning basal insulin injection

Results Comparisons

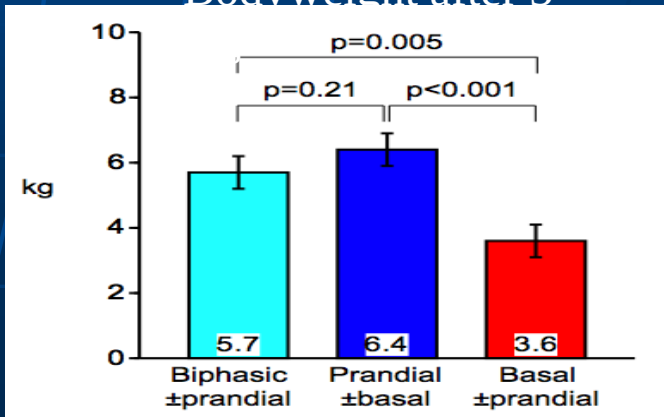
- **Results – Harms:**
- • Basal Insulin: *gained less weight than those in the biphasic or prandial insulin groups*
- Weight gain in Kg
- *Basal* *+1.9 kg*
- *Bi –Phasic* *+ 4.7 kg and*
- *Prandial* *+ 5.7 kg, P<0.001).*
- • *The weight gain was significantly higher in the prandial group than the biphasic group (P=0.005).*
- • Basal group: *significantly less likely to experience more severe hypoglycaemia than those in the biphasic or prandial groups (median: 0, 3.9 and 8.0 events per patient per year).*

- **Results – benefits:**
- • The reduction in HbA1c from baseline: -
-1.3% in the biphasic group,
-1.4% in the prandial group
- 0.8% in the basal group.

Hba1c after 3 yrs



Bodyweight after 3



Basal Insulin Summary

- One injection a day, with two capillary glucose tests for dose titration
- One third of patients require a morning insulin injection in addition
- More patients require a second insulin formulation than with Biphasic or Prandial insulin
- Basal slightly less HbA_{1c} lowering than with Biphasic or Prandial insulin
- Basal Insulin causes less weight gain and less hypoglycaemia than with Biphasic or Prandial insulin
- No change in QoL as assessed by EQ-5D

N Engl J Med 2007; 357: 1716-30

What about their oral Medications ??

- Hang on!!!!!!

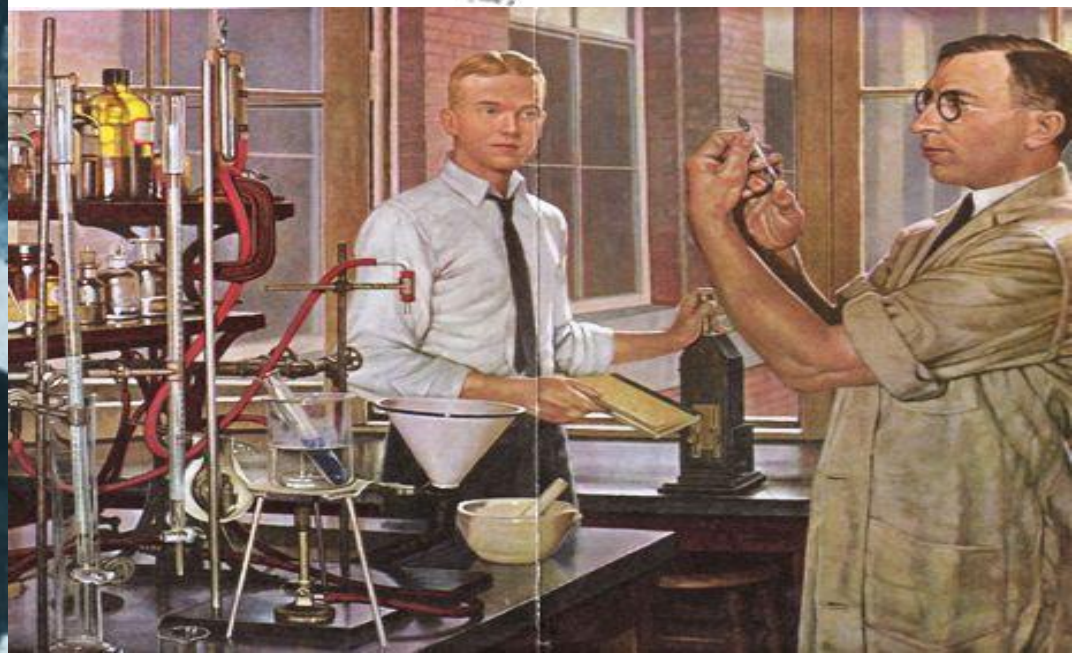
- Don’t throw away the Metformin????????

Metformin and Insulin: the benefits *Arch Intern Med. 2009;169(6):616-625*

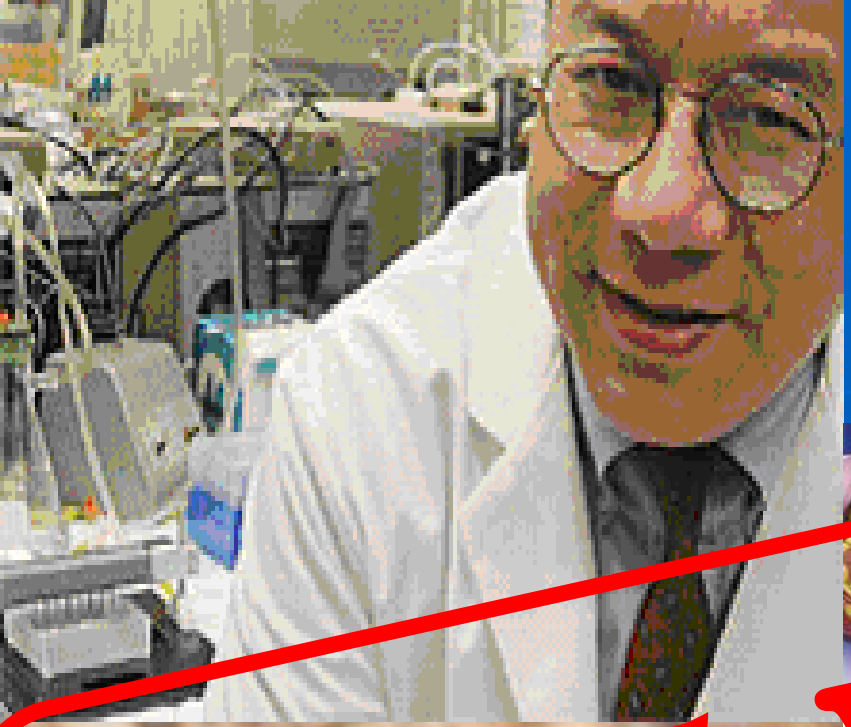
- 390 patients RCT with Metformin 850 tds or placebo added to insulin with mean 4.3 year follow-up
- Metformin patients on average:
  - Hba1c 0.4% better, Weight3.07kg lighter
- Needed ~20 units less insulin
- Lower macrovascular event rate (NNT 16)
- Metformin reduces risks cancers

Glory enough for all !!!!!!

Soon after its discovery, insulin captivated media attention (Banting Digital Library)

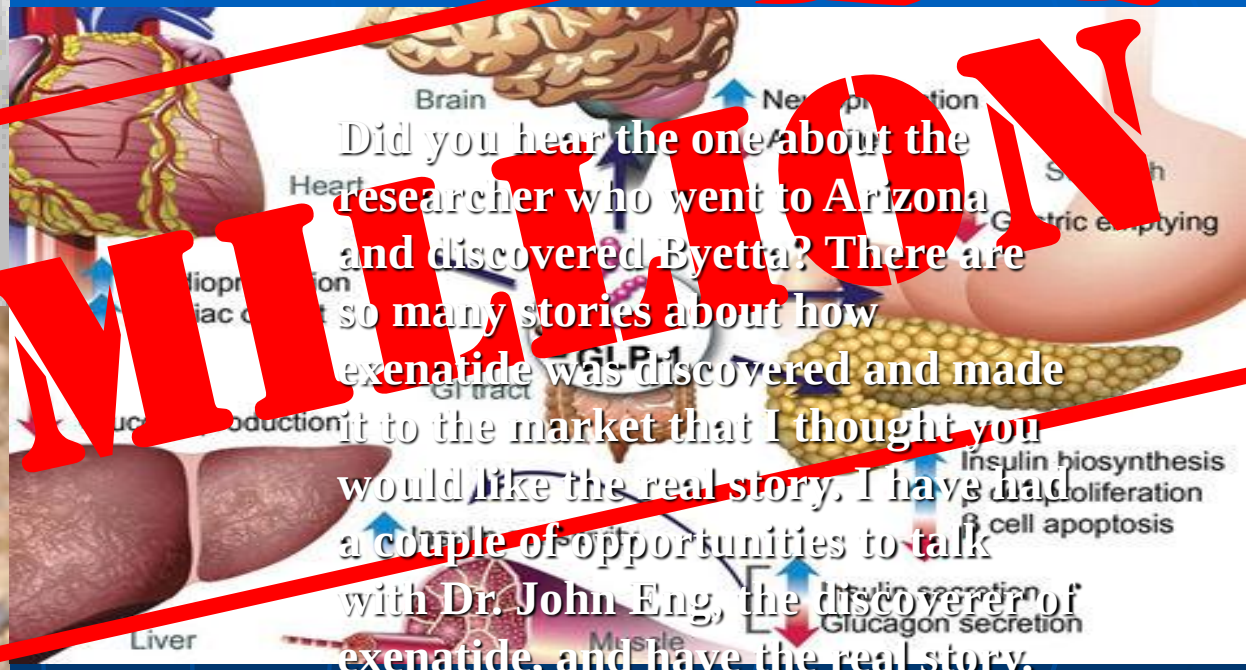


FOOD(*Money*) FOR THOUGHT!!!!!!!!



Thought for food!!!!!!!!

Dr. John Eng's Research Found That The Saliva Of The Gila Monster Contains A Hormone That Treats Diabetes Better Than Any Other Medicine



$325 MILLION

Did you hear the one about the researcher who went to Arizona and discovered Byetta? There are so many stories about how exenatide was discovered and made it to the market that I thought you would like the real story. I have had a couple of opportunities to talk with Dr. John Eng, the discoverer of exenatide, and have the real story.

SEVEN DECADES OF DIABETES SUCCESS RECOGNISED

Waitakere Hospital diabetes nurse Rab Burtun always thought 78-year-old **(now 83yrs)** Winsome Johnston deserved a medal – so he set about ensuring his inspirational patient receive just that.

On 12 September Mrs Johnston will be the first New Zealander to be awarded the Diabetes UK Macleod Medal for living successfully with insulin-dependent Type 1 diabetes for more than 70 years **(77 yrs)** She will also receive Diabetes New Zealand's Sir Charles Burns Memorial Award.

"I tell my patients about Win's story every day. She's living proof that it's possible to live long and well with diabetes. She's an inspiration to everybody – me included," Rab says.

A Type 1 diabetic himself, Rab was diagnosed 30 years ago and wrote to Diabetes UK last month to share Winsome's story because of the motivation and encouragement it offers others.

"She hasn't got a single complication of diabetes, she's had three successful pregnancies – one with twins - and now has eight grandchildren and two great-grandchildren.

"Pregnancy itself is an achievement for people with diabetes because their blood sugar …….


THANK YOU!!!!

References

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