

# Taming the Curve

New Approaches in Dealing  
with Feline Diabetes

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(protamine zinc recombinant human insulin)

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## Agenda

- Feline diabetes overview
- Case study - “Cassie”
- Current treatment options
- New treatment - **ProZinc™**
- How BI can help



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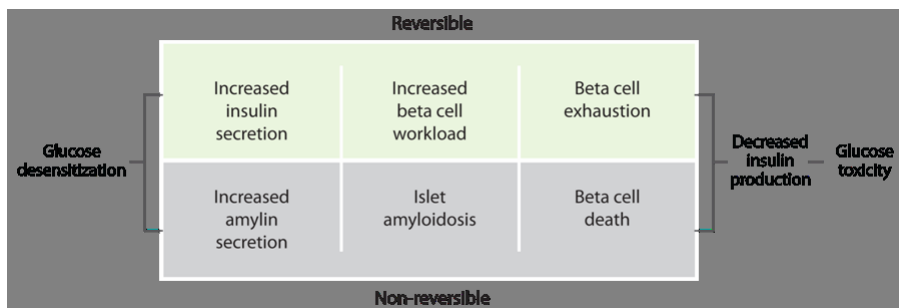
# Feline Diabetes Overview

## Why do cats get diabetes?

- Obesity
  - Important factor in diabetes mellitus
  - Leads to insulin resistance
- Diet
  - Dry cat food and the carbohydrate dilemma
- Concurrent disease - insulin resistance
- Inactivity - obesity
- Genotype - abnormal pancreas<sup>1,2</sup>



# Insulin Resistance



## NIDDM vs. IDDM

Non-insulin dependent diabetes mellitus (NIDDM)	Glucose desensitization	May go into remission
	Beta cell exhaustion	
	Glucose toxicity	
Insulin dependent diabetes mellitus (IDDM)	Amyloid build up in beta cells	WILL NOT go into remission
	Beta cell dysfunction and death <sup>1,2</sup>	

## Disorders Causing Insulin Resistance

### Severe and persistent

Cushing's disease

Glucocorticoids

Acromegaly

Adrenal tumors

### Mild and fluctuating

Obesity

Pancreatitis

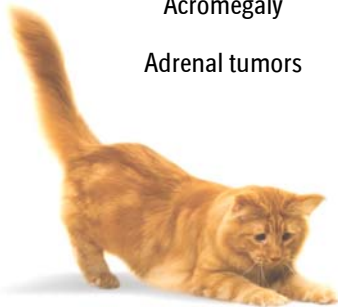
Gingivitis

IBD

Infection

Renal insufficiency

Thyroid disease<sup>2</sup>



## Chronic Pancreatitis

- A common complicating factor
  - May affect over 50% of diabetic cats<sup>4</sup>
- May be an important factor in remission
- Gradations of severity
- Waxing and waning disease
  - Cats have good weeks and bad weeks
- Impact of inflammatory mediators
  - IL-5 and TNF alpha
  - Role in insulin resistance



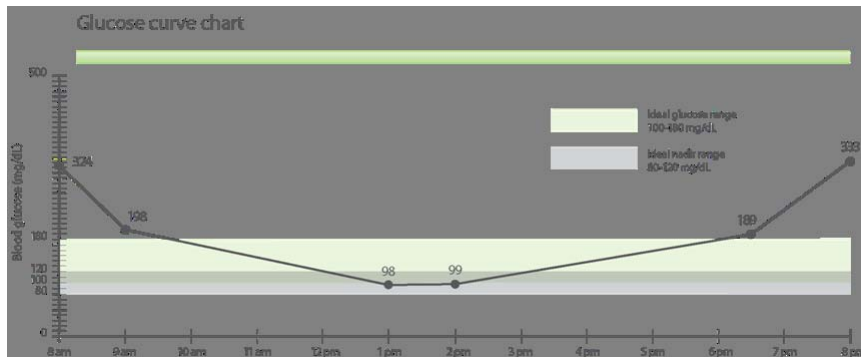
## Case Study

### “Cassie”



- 14 yo DSH FS
- Overweight
- Diabetes mellitus diagnosed in 2007
- Managed with PZI VET<sup>®</sup> (protamine zinc insulin)
  - 2 IU BID
  - Purina Veterinary Diets<sup>®</sup> DM Diabetic Management<sup>®</sup>
- Regulated quickly
  - Clinical signs resolved
  - Blood glucose curve

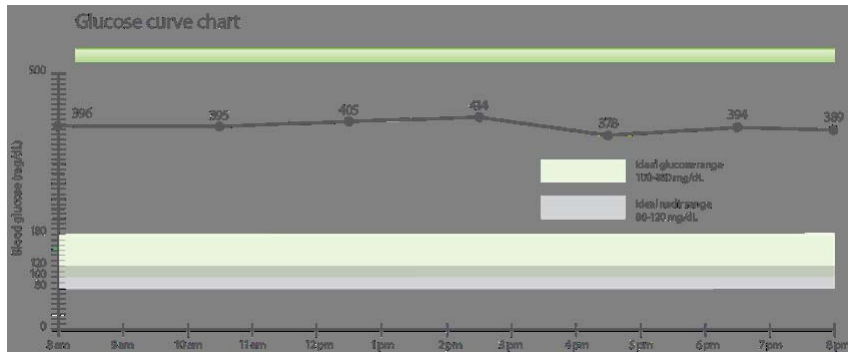
## BG curve on PZI VET®



## Cassanova

- Did well until stock of PZI VET dwindled in late 2009
- Switched to glargine
  - 1.5 IU SID
  - Cat did well for 2 months
- Became PU/PD again - developed glycosuria
- BG curve: above 400 throughout the day
- Fructosamine 460

## BG on Glargine



## What is your next step?

1. Increase glargine dose
2. Switch insulin
3. Question owner on administration
4. Quit practice and move to Spain

## Case Study

- Veterinarian increased dose to 2.5 IU SID
- One month later - curve was exactly the same
  - Clinical signs persisted
- Increased dose to 2.5 IU BID
- Cat returned to clinic
  - Weak
  - Dilated pupils
  - BG 498 mg/dL
- What's your diagnosis?



## Case Study

### Diabetic ketoacidosis (DKA)

- Treated and stabilized within 48 hours
- Cat remained in hospital for 5 days
- Urine culture: concurrent UTI was present



## What's your next step?

1. Increase dose of glargine.
2. Switch to a different insulin.
3. Question owner on administration technique.
4. Quit practice and become a BI vet.

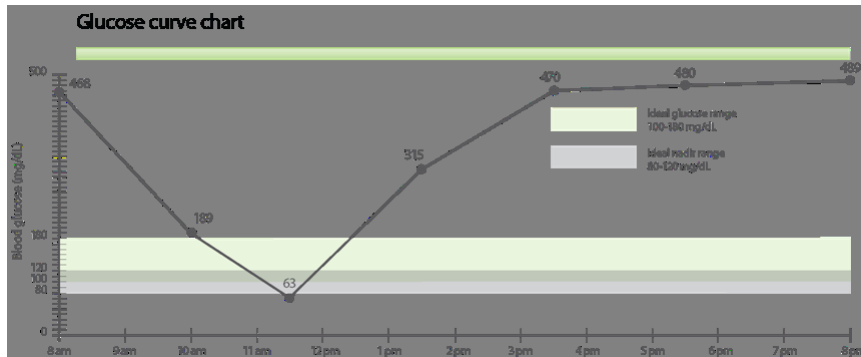
## Cassie

Owner was questioned further on administration technique

- Owner stated that she had given 16 year old son responsibility for insulin administration a couple of months ago
- Son later admitted he was not giving insulin consistently
- Owner took over care and continued cat on 2.5 IU/BID
- Clinical signs continued
- Blood glucose curve...



## BG Curve



## Somogyi Effect

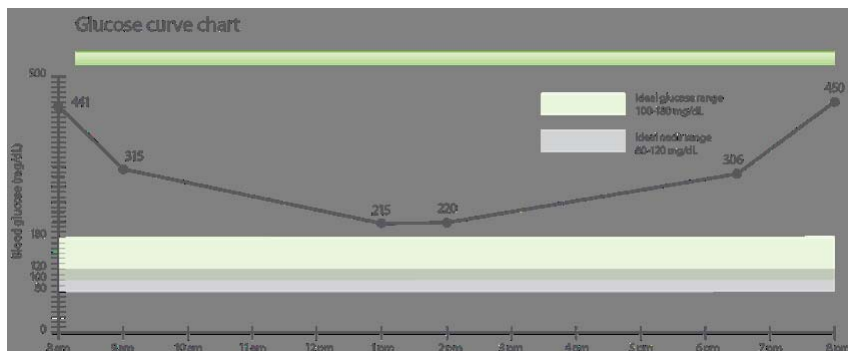
- Overcompensation for low blood glucose levels
- Protective mechanism against hypoglycemia
- Insulin dose too high
- Not eating well around time of administration<sup>7</sup>

## Next Steps

- Cat was switched to PROZINC
- 1.5 IU BID
- Clinical signs improved
- Still some glucosuria
- Glucose curve 2 weeks later



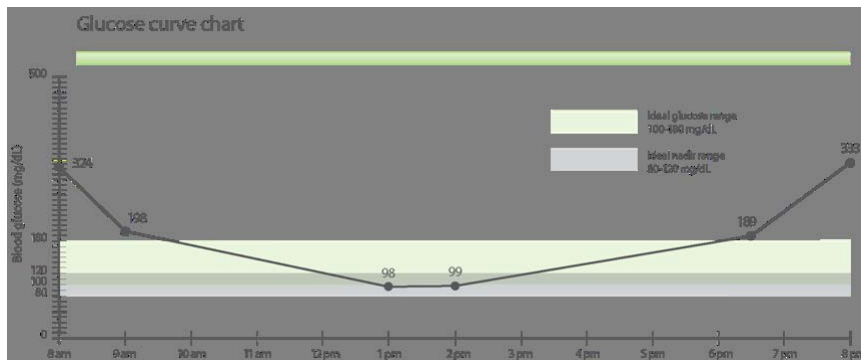
## Glucose Curve on PROZINC



## Case Study

- Insulin dose too low
- Increased to 2 IU BID
- All clinical signs resolved within 5 days
- Blood glucose curve...

## BG curve on PROZINC



## Diabetic Complications

### Causes of diabetic complications

- Poor owner compliance
- Concurrent disease
- Insulin resistance or poor efficacy of product<sup>3</sup>

## Diabetic Complications

### Poor owner compliance

- Always check administration history and technique first
- Owner education is key

### Concurrent disease

- UTI
- Pancreatitis
- Gastrointestinal - IBD
- Renal/cardiac conditions
- Others...<sup>2,3</sup>

## Diabetic Complications

### Therapeutic insulin resistance

- Rule out concurrent conditions first
- Variable absorption - injecting into inflamed tissue
- Diet and feeding schedule

### Inefficacy of product

- Expired product
- Not refrigerated/dropped
- Variability of product response in individual<sup>3</sup>

## Current Treatment Options

## Goals of Therapy

- Eliminate owner-observed clinical signs
- Maintain healthy interactive pet
- Avoid acute and chronic complications
  - Hypoglycemia
  - Diabetic ketoacidosis
  - Weight loss (gain)
  - Diabetic neuropathy<sup>2</sup>

## Current Diet Recommendations

- Still a matter of personal opinion
  - Academics cannot fully agree
- Cats and carbs....where are we now?
- Current data suggests<sup>7</sup>
  - Feeding cats a high protein/low carb diet is best
  - Helps to maintain glycemic control
  - Not ideal for all cats - renal/pancreatic issues benefit from high carbohydrates

## Oral Hypoglycemics

### Glipizide (Glucotrol®) - sulfonylurea class

- Studies in early '90s showed some promise in cats
- May work in 1 in 5 cats<sup>2</sup>
- Option when insulin is not
  - Many owners eventually convert to insulin<sup>2</sup>

Glucotrol is a registered trademark owned by Pfizer Inc.



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## Insulin Choices

- NPH
  - Considered too short-acting for cats<sup>2</sup>
- Vetsulin®
  - Purified porcine insulin zinc suspension
  - Lente insulin: intermediate-acting<sup>2</sup>
- Glargine (Lantus®)
  - Microprecipitates form on injection
  - Off label use in veterinary medicine
  - Short shelf life (4 weeks)
  - Remission in cats?<sup>7</sup>

Vetsulin is a registered trademark owned by Intervet, Inc. Lantus is a registered trademark owned by Sanofi-Aventis.



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## Glargine

The remission story...

- Based on a single study in a small handful of cats
  - *Marshal RD, Rand JS. Insulin glargine and a high protein-low carbohydrate diet are associated with a high remission rate in newly diagnosed diabetic cats. J Vet Intern Med. 2004;18(3):401.*
- Subsequent study disputes results
  - Showed more remission twice daily lente insulin better than once daily glargine
  - *Weaver et al. Use of glargine and lente insulins in cats with diabetes mellitus. J Vet Intern Med 2006;20(2):234-238.*

## Remission

What really determines remission in cats?

- Presence of pancreatitis - important factor<sup>4</sup>
- Degree of insulin resistance<sup>2</sup>
- Presence of concurrent disease<sup>2</sup>
- Type of insulin???



## What's Missing

We need a long-acting insulin  
approved for cats



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## A New Insulin

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# PROZINC

PROZINC is the first veterinary approved long-acting protamine zinc insulin specifically designed for use in cats<sup>8</sup>



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# PROZINC

## PROZINC - The right choice for feline diabetic patients

- The first FDA approved long-acting protamine zinc insulin<sup>8</sup>
- Predictable glycemic control - comparable performance to PZI VET<sup>10</sup>
- Specifically for cats - largest prospective study in diabetic cats<sup>9</sup>
- Recombinant technology<sup>8</sup>



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## PROZINC

- PROZINC is indicated for the reduction of hyperglycemia and hyperglycemia associated clinical signs in cats with diabetes mellitus<sup>8</sup>
- Long duration of action<sup>8</sup>
- Long shelf life: 2 years
- Recombinant human DNA technology



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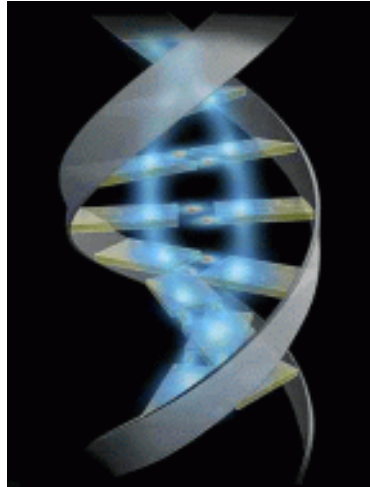
## PROZINC

- Protamine zinc insulin formulation
  - Classified as long-acting
  - Duration of effect: 10-14 hours in cat
- Provides consistent and reliable regulation of blood glucose
- Backed by extensive clinical studies



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## Recombinant Technology



## Recombinant Technology

What are the advantages of using a recombinant insulin?

- Animal-sourced raw materials - not required
- This means.....

**Reliable supply**



## PROZINC - Predictable Control

### Clinical Efficacy Studies and Peer Reviewed Publications



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## PROZINC Clinical Efficacy Trials

### The largest prospective study ever conducted on a feline insulin

- 19 veterinary clinics across the US
  - 14 general practices
  - 4 referral clinics
  - 1 university
- 176 cats received PROZINC over 45-day
- 151 included in effectiveness evaluation
- Results published in the Nelson paper



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## Safety

- 71 cats experienced glucose nadir < 5

### Most had no clinical signs

- Only 17 cats required oral glucose sup
- All cats recovered

- Other adverse events...

- Lethargy, vomiting, diarrhea<sup>8</sup>



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## Dosing PROZINC

- U-40 syringe
- Starting dose: **0.1 - 0.3 IU per pound q 12 hours**
  - (0.2 - 0.7 IU/kg)
- Give with or immediately after a meal
- Further dose adjustments may be required
  - Diet changes
  - Weight changes
  - Concurrent illness
  - Remission<sup>8</sup>



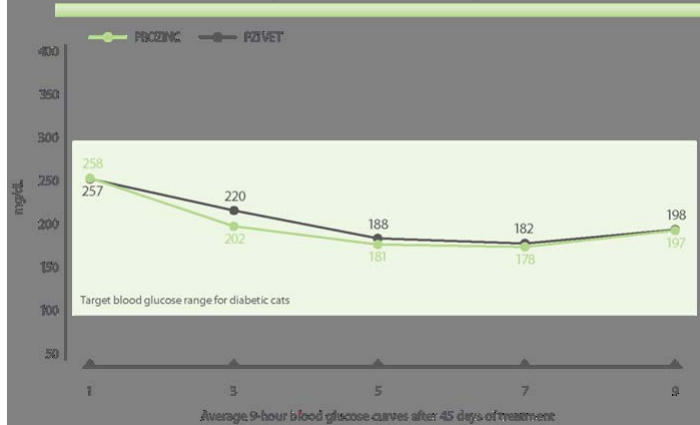
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## What about switching from PZI VET to PROZINC?

Comparison of mean 9-hour glucose curves of cats receiving PROZINC<sup>®</sup> vs. PZI VET<sup>®</sup> (protomine zinc insulin)



## PROZINC

### Fair balance statement

As a class, the use of any insulin when regulating a diabetic cat may be associated with side effects. The most common side effect reported in field studies was hypoglycemia. This is usually mild (lethargy, weak, trembling, uncoordinated, groggy, dazed), but may be serious and life-threatening (seizures, coma). If side effects occur, cat owners should contact their veterinarian immediately.

### Fair balance statement con't

Cats should be evaluated for pre-existing conditions and currently prescribed medications prior to treatment with PROZINC. Routine monitoring (blood parameters such as glucose and fructosamine and clinical signs) is essential to maintain a regulated cat. PROZINC insulin is contraindicated during episodes of hypoglycemia. Please refer to the package insert for complete product information.



## Conclusions

### We discussed...

- Why cats become diabetic
- Insulin resistance
- Non-insulin-dependent vs. insulin-dependent diabetes mellitus
- New and current monitoring options



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## Conclusions

- Case study of Cassanova
  - Demonstrating how diabetic complications arise in case and how to deal with them
- A new insulin...

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(protamine zinc recombinant human insulin)



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## The Call to Action

- Talk to your clients
  - Client communication is key to successful diabetes control
- Look at your patient
  - Clinical signs - your most important monitoring tool
- Start your new diabetic cats on **ProZinc™**



# Thank you

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# Questions?