



THE UNIVERSITY  
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Australian Government  
Rural Industries Research and  
Development Corporation



EQUINE  
CONSULTING • SERVICES

# The Relationship Between Insulin Status and the Occurrence of OCD in Thoroughbred Yearlings

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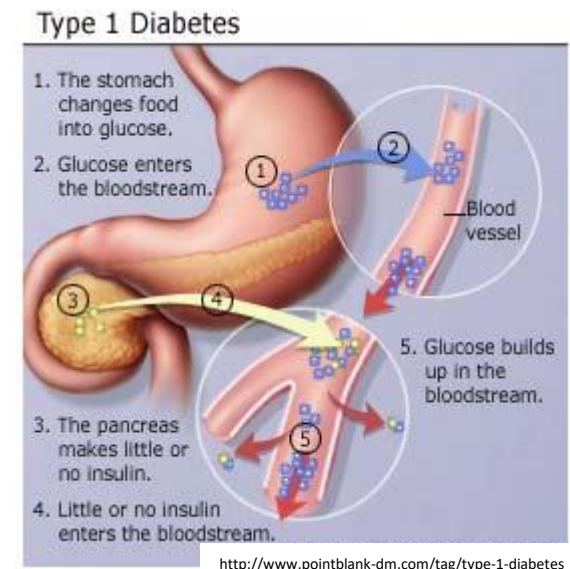
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# Overview

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- Summary of our current project
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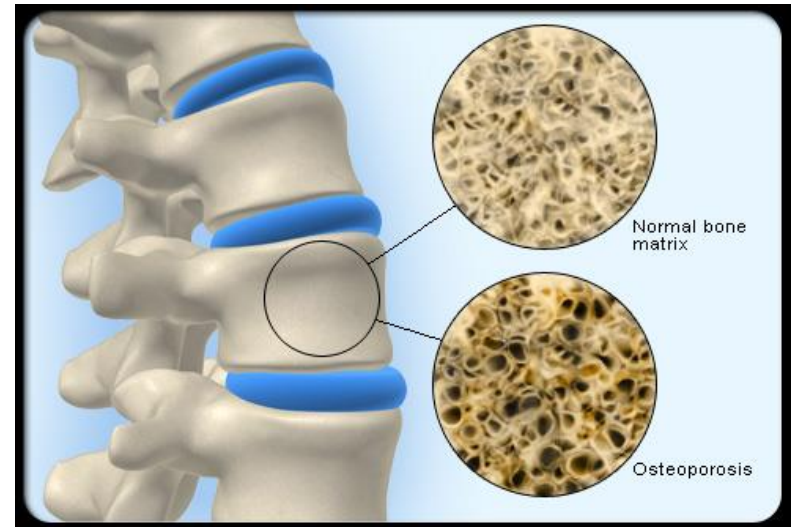
# Insulinopenia and bone

- Skeletal defects observed in conjunction with Type 1 Diabetes Mellitus (T1DM):
  - Diminished linear bone growth during pubertal growth spurt in adolescents;
  - Increased risk of fragility fracture;
  - Poor bone healing and regeneration characteristics



# Insulinopenia and bone

- T1DM associated with:
  - Decreased bone density  
(Hampson, G. *et al.*, 1998; Kemink, S.A. *et al.*, 2000; Muñoz-Torres, M. *et al.*, 1996; Tuominen, J.T. *et al.*, 1999);
  - State of low bone turnover  
(Kemink, S.A. *et al.*, 2000)



[http://www.rxlist.com/osteoporosis\\_slideshow/article.htm](http://www.rxlist.com/osteoporosis_slideshow/article.htm)

- Lower bone mass usually develops within the first few years of T1DM (Gunczler, P. *et al.*, 1998; McNair, P. *et al.*, 1981; Rosenbloom, A.L. *et al.*, 1977).
- Clinical relationship between bone mineral density and glycaemic control remains unclear

# Hyperinsulinaemia and bone

- Type 2 Diabetes Mellitus (T2DM) is associated with:
  - Increased bone mineral density, but
  - Decreased bone strength leading to an increase in the risk of fracture.
- Positive correlation between bone mineral density and fasting insulin levels (Barrett-Conner et al., 1996; Reid, I.R. et al., 1993).
- Positive correlation between bone mineral density and insulin dose among patients with T2DM (Fukunaga, Y et al., 1997; Weinstock, R.S. et al., 1989)
- Hyperinsulinaemia → preserve and maintain bone mass?



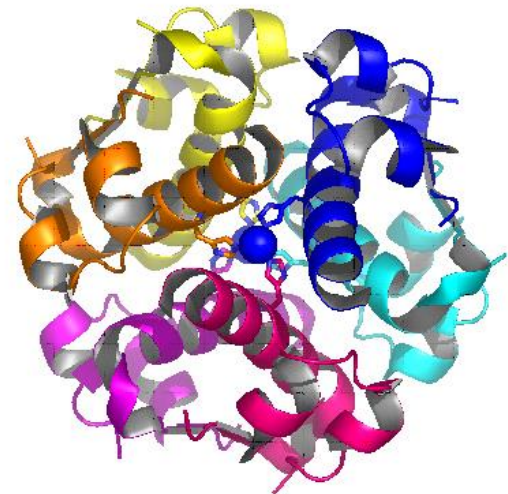
# Experimental models

- Rosiglitazone (anti-diabetic drug) administration to mice
    - Significant decrease in bone mineral density, bone volume and bone formation rate (Rzonca, S.O. et al., 2004);
  - Insulin administration
    - Stimulates osteoblast activity and mineral apposition rates (Verhaege, J. et al., 1992)
- *Bone regeneration is impaired in insulin deficiency;*
- *Regeneration can be restored by insulin treatment*



# Cell Cultures

- In response to physiological doses of insulin, cultured osteoblasts show increased rates of
  - Proliferation (Hashizume, M & Yamaguchi, M., 1993; Wergedal, J.E. & Baylink, D.J., 1984)
  - Collagen synthesis (Canalis, E.M. et al., 1977; Pun, K.K. et al., 1989; Rosen, D.M. & Luben, R.A., 1983)
  - Alkaline phosphatase production (Canalis, E., 1983; Kream, B.E. et al., 1985)
  - Glucose uptake (Hahn, T.J. et al., 1988; Ituarte, E.A. e
- Synergistic effects with other anabolic agents in bone such as IGF-1 and PTH?



# Current knowledge...Insulin and skeletal disease in horses

- Do diets high in soluble carbohydrates cause of OCD?
  - Glucose intolerance caused by insulin resistance?
- In one study: strong positive correlation found between serum glucose and insulin post feeding and OCD across farms (Pagan et al., 01)
  - Does diet-induced hyperglycaemia or hyperinsulinaemia predispose weanlings to OCD?





# Insulin and skeletal disease in horses

- Other studies investigated influence of starch intake on skeletal development (Ott, E.A. et al., 2005)
  - Bone osteochondrotic lesions not related to diet
  - Weanlings require some glucose to support normal growth
- IGF-1 not found to differ between fat supplemented and conventional carbohydrate-supplemented foals (Ropp, J.K. et al., 2003)



# Our study: Maternal metabolic status and the occurrence of OCD in Thoroughbred foals

## Aims:

- To investigate the effect of maternal nutrition/metabolism on skeletal disease in growing foals.
- To study the role of insulin resistance in the mare on skeletal development in the foal.
- To gain a greater understanding of the nutritional requirements of broodmares and growing foals



# Insulin status and occurrence of skeletal defects in Thoroughbred yearlings

- 52 yearlings
- Stabled overnight
- Blood sample collected prior to feeding (6.30am)
- Bloods tested for basal glucose and insulin
- Information on skeletal abnormalities obtained from survey radiographs



# Preliminary results – yearlings-07

- Fasting insulin significantly lower in yearlings with OCDs and other skeletal abnormalities ( $P < 0.01$ )
- Fasting glucose not significantly different between groups ( $P = 0.13$ )
- NSD birthweight

TUBE #	INSULIN mIU/L	Comments
12	1.0	L HOCK OCD
11	1.8	NSA
13	1.9	L HOCK OCD
26	2.2	L & R STIFLE OCD
43	2.3	L & R HOCK OCD
10	2.7	NSA
17	3.2	NSA
42	3.3	NSA
29	3.3	R HOCK OCD
8	3.4	NSA
41	3.4	NSA
30	3.4	L & R HOCK OCD
52	3.4	L & R HOCK OCD
35	3.8	NSA
51	4.4	NSA
25	4.4	NSA
33	4.5	NSA
46	4.6	L HOCK OCD
23	4.7	NSA
36	4.8	NSA
49	4.8	NSA
18	4.8	L HOCK OCD
3	5.2	NSA
24	5.2	NSA
7	5.4	NSA
38	5.4	NSA
1	5.7	NSA
37	6.4	NSA
6	6.9	NSA

# Supportive Results

- Same farm, yearlings-08
  - Smaller population (30 yearlings)
  - Fasting insulin lower in yearlings with skeletal abnormalities ( $P = 0.09$ )
- Second farm, yearlings-07
  - Yearlings,  $n=15$
  - Fasting insulin significantly lower in yearlings requiring surgery for skeletal abnormalities ( $P<0.05$ )





# Preliminary results...

- Studies suggest correlation between insulin and skeletal abnormalities in growing foals
  - Yearlings with OCD and other skeletal abnormalities had a lower fasting insulin compared to yearlings with NSA
- On-going work:
  - IGF-1, osteocalcin levels, response to glucose challenge or feeding, BMD, fat mass, body weight, insulin threshold?

