The Fat-to-Protein ratio: the missing link in Obesity and Diabetes?

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BACKGRD: How important is the basic macronutrient intake profile in shaping obesity and diabetes?

- Historical blame initially was placed on fat...

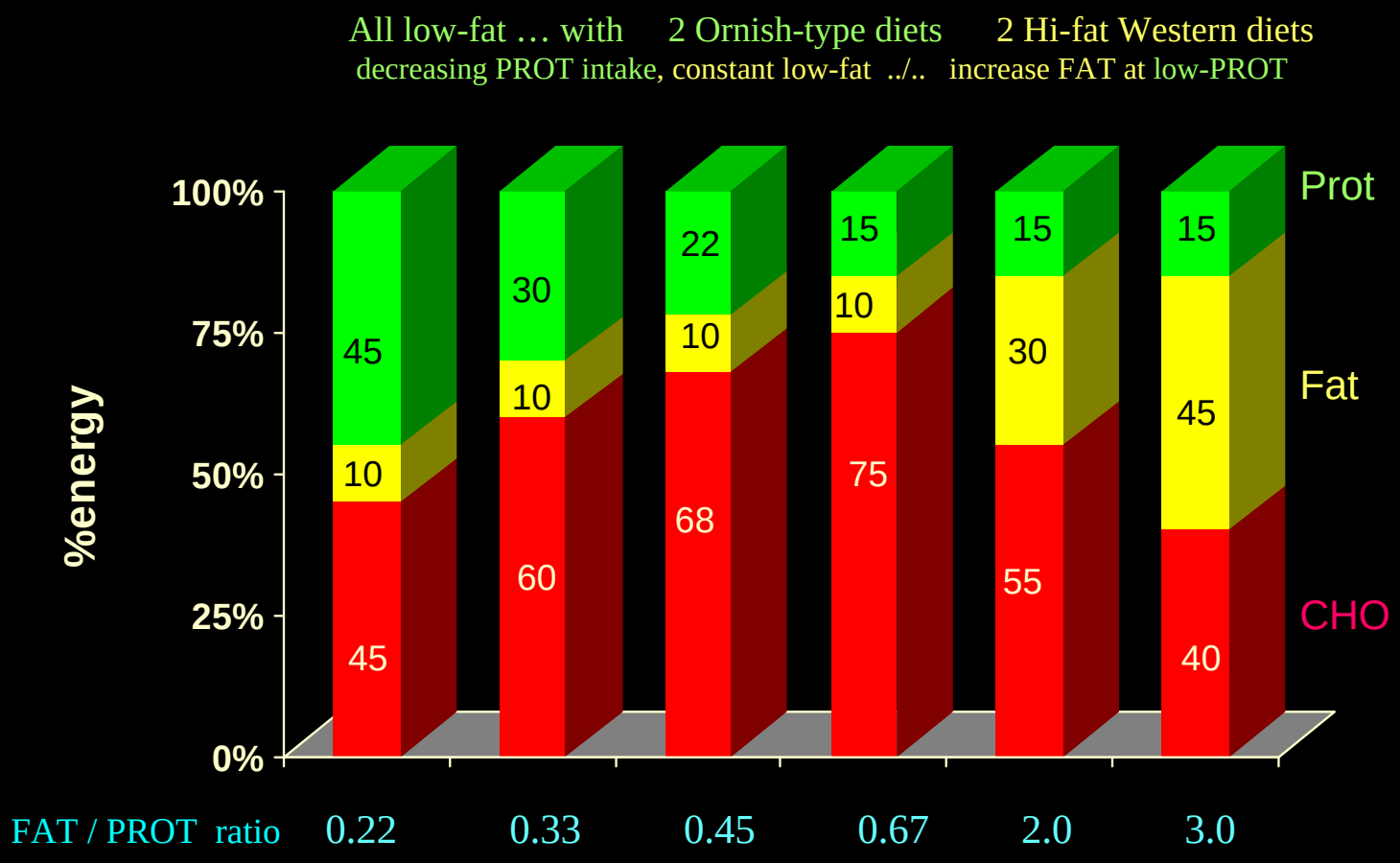
  "eat fat to become fat"…so the public health logic was to remove diet fat.

- So a hi-CHO, low-fat diet developed, and the obesity epidemic became even more rampant…

  "too much CHO causes obesity"…so now what?

- How important is diet PROT, the neglected energy source?

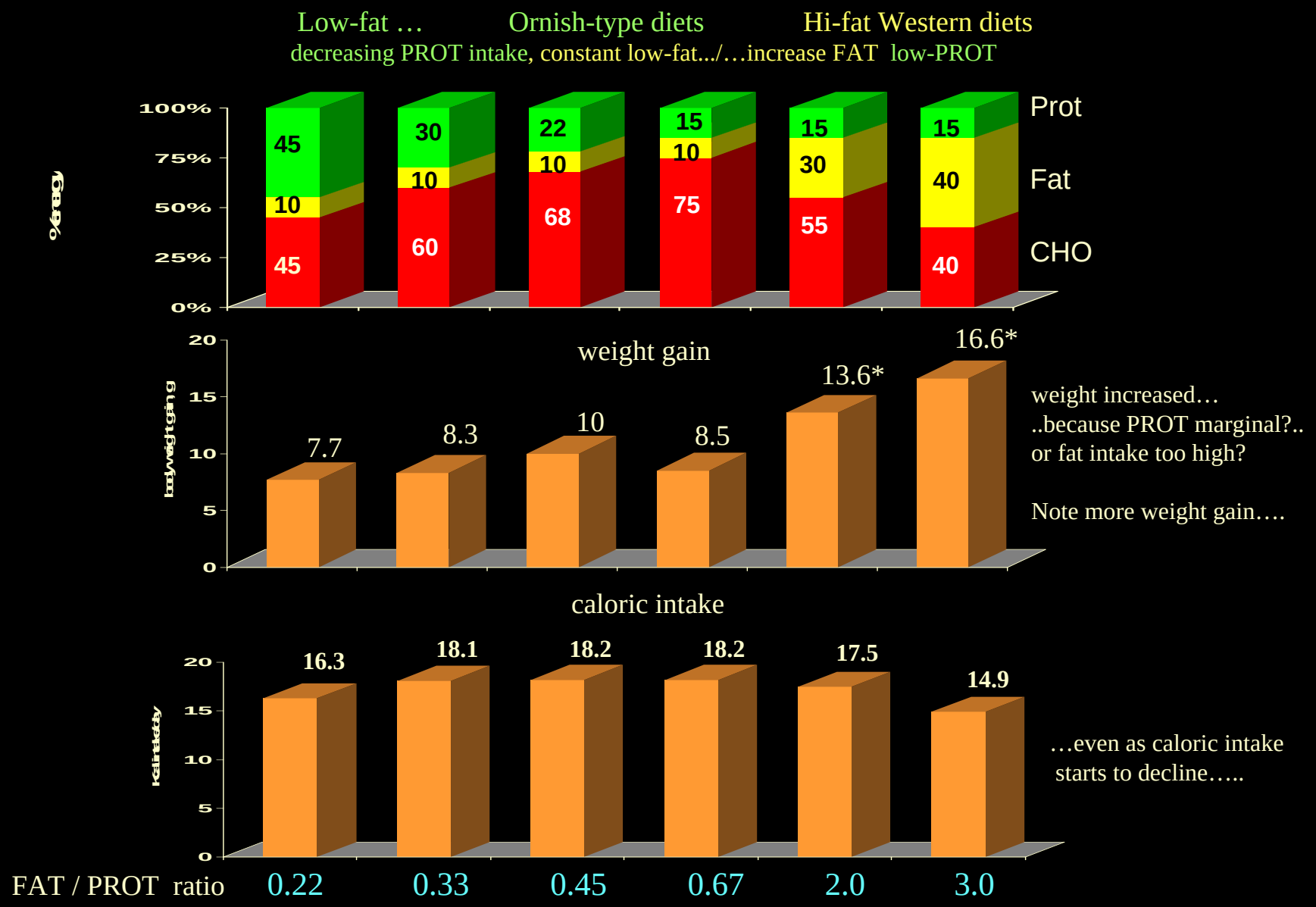
Study 13: Macronutrient Composition for diets fed to young male C57BL/6j mice (DIO mice)



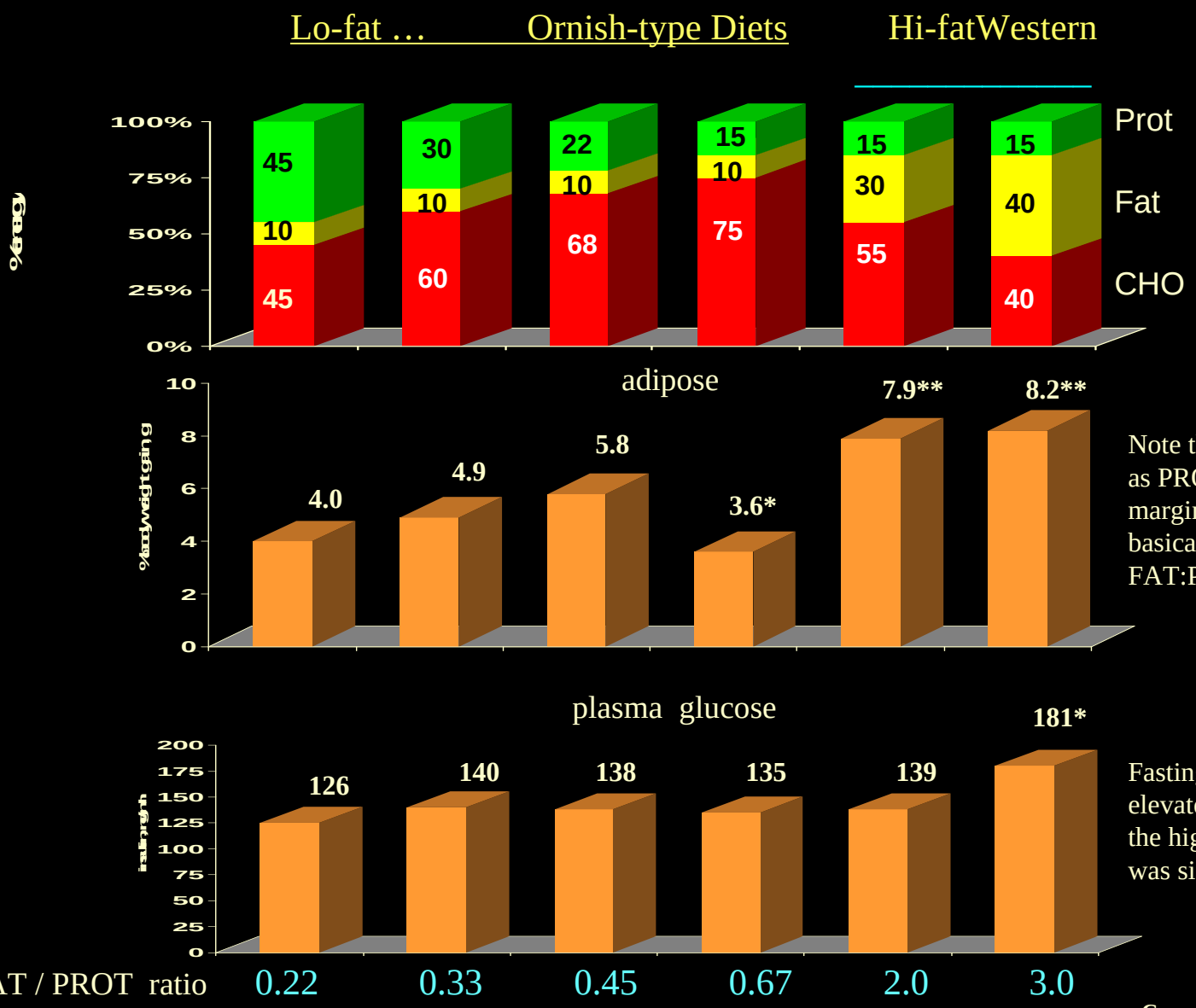
Q: How important is PROT at low-fat intake, and increased FAT at low-protein intakes?

Cummings et al, unpublished

Study 13: Body weight and caloric intake for young male C57BL/6J mice over 17wks



Study 13: Adipose and plasma glucose for young male C57BL/6J mice

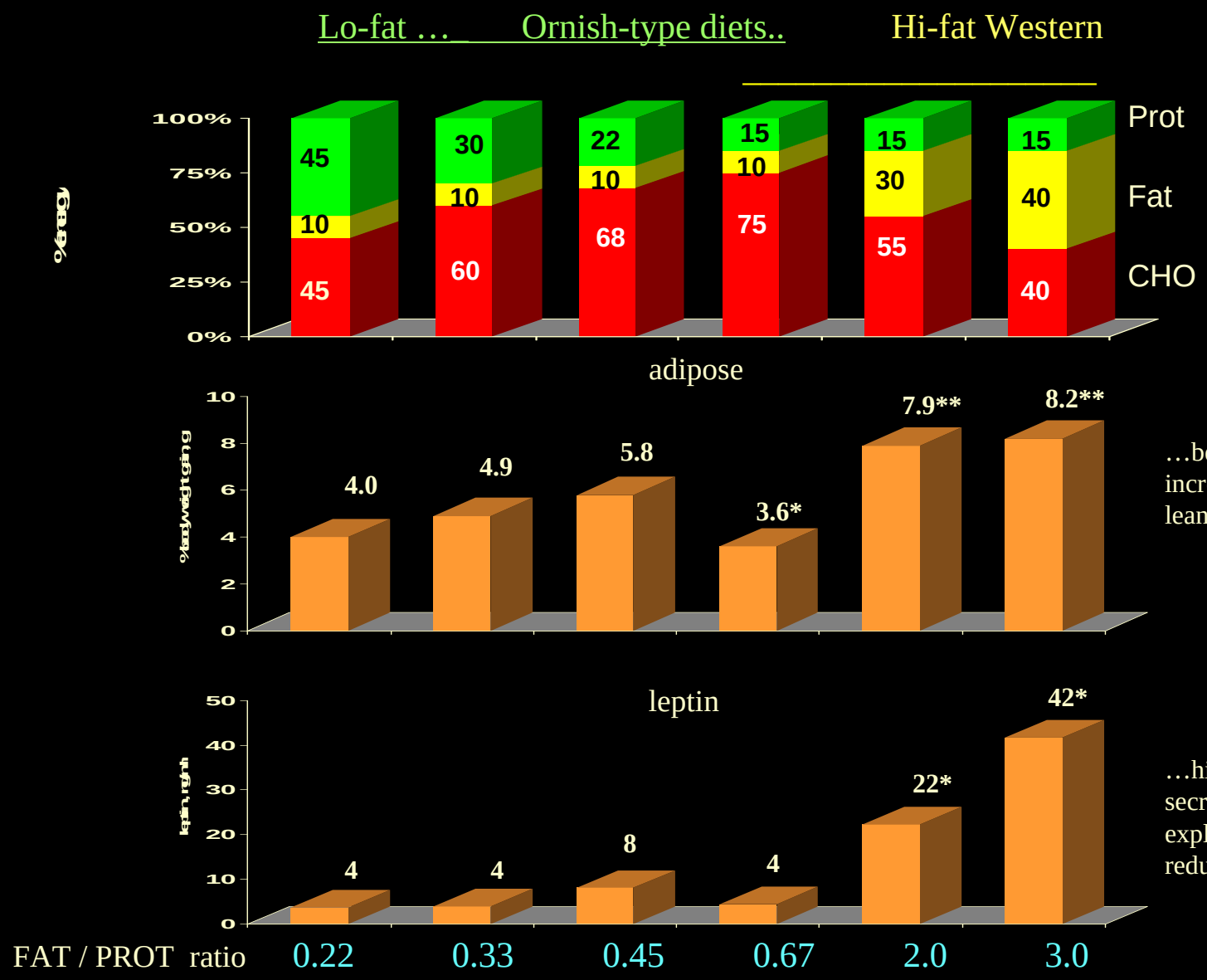


Note that adipose increases as PROT decreases, until marginal PROT intake…. basically follows the FAT:PROT ratio.

Fasting glucose was somewha elevated in all mice, but only the highest FAT:PROT ratio was significant from the rest.

Cummings et al., unpublished

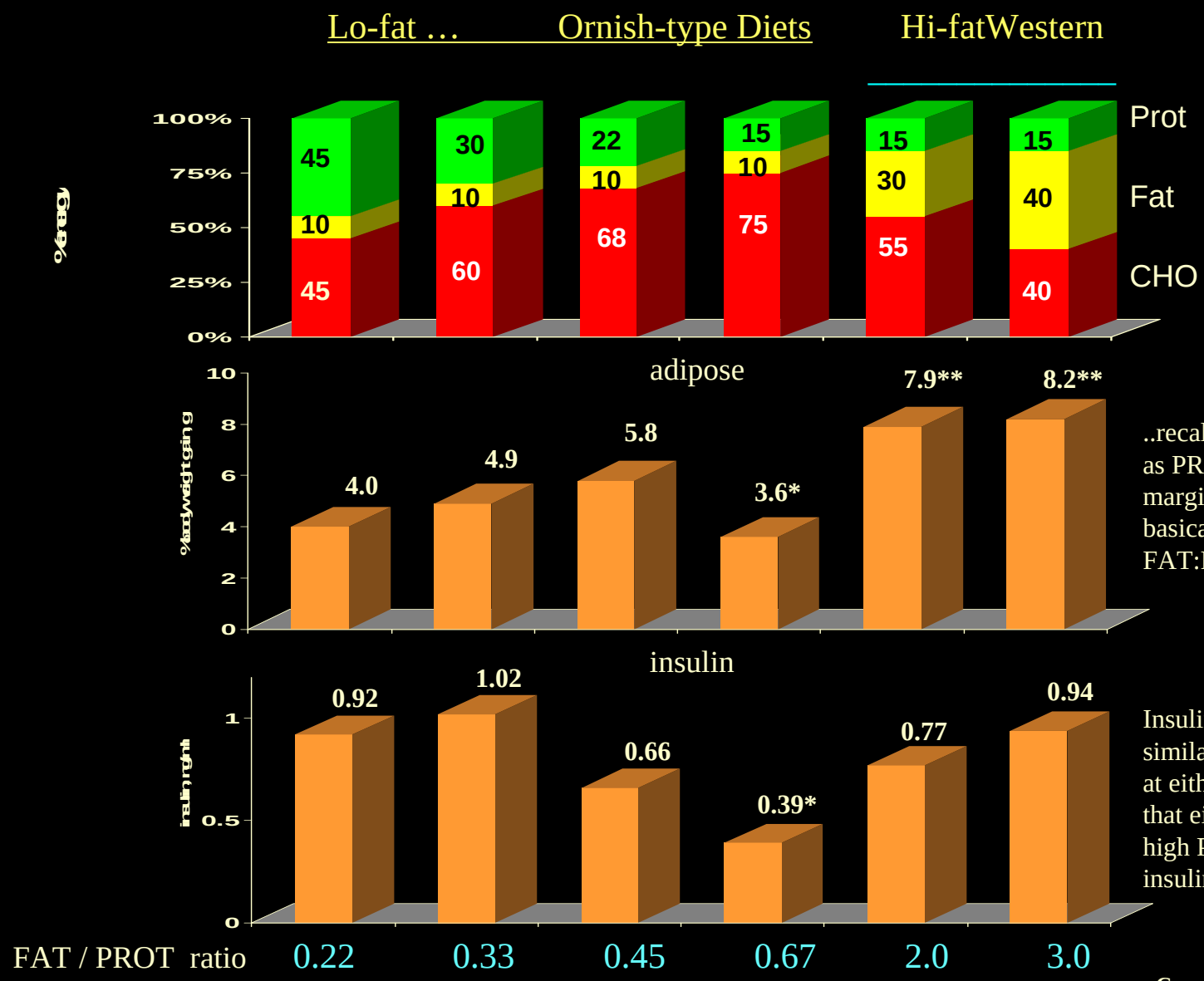
Study 13: Adipose and plasma leptin for young male C57BL/6J mice



…because adipose pool is increasing relative to lean body mass….

…high fat accumulation is secreting leptin, which explains the tendency for reduced caloric intake.

Study 13: Adipose and plasma insulin for young male C57BL/6J mice

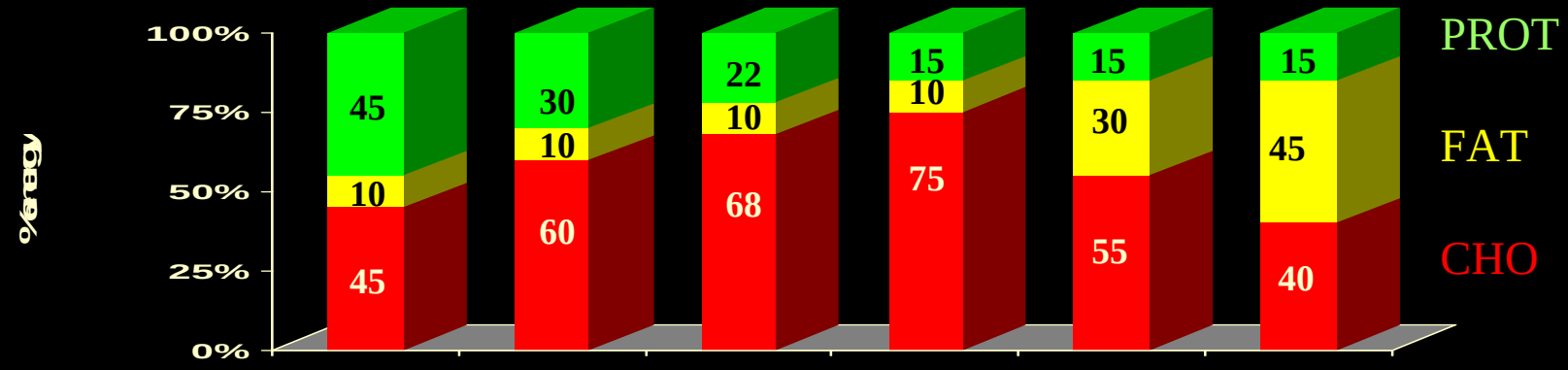


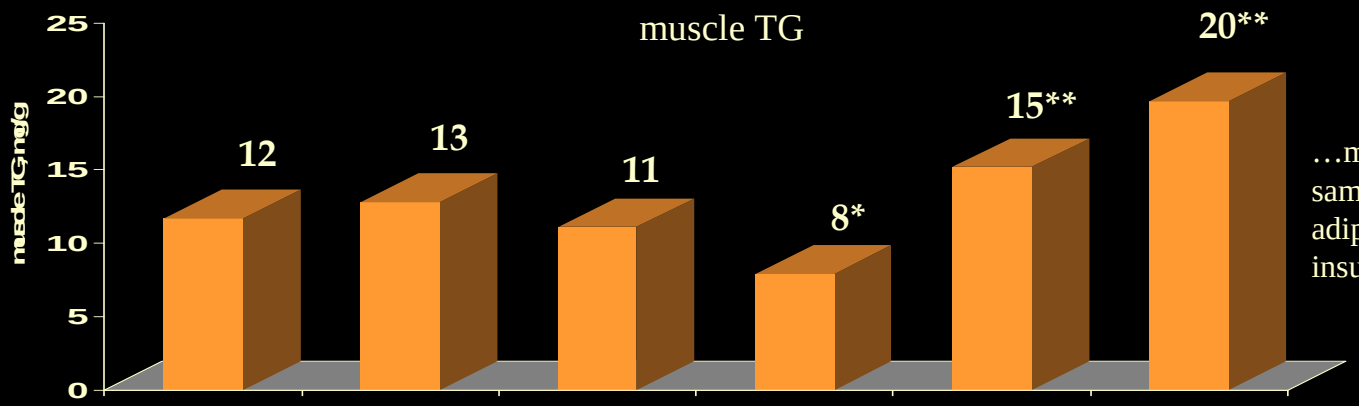
..recall that adipose increases as PROT decreases, until marginal PROT intake…. basically follows the FAT:PROT ratio.

Insulin does something similar, except it rises slightly at either end. This suggests that either high FAT or high PROT may promote insulin resistance?

Cummings et al., unpublished

Study 13 : Muscle TG in C57BL/6J mice after 14wk



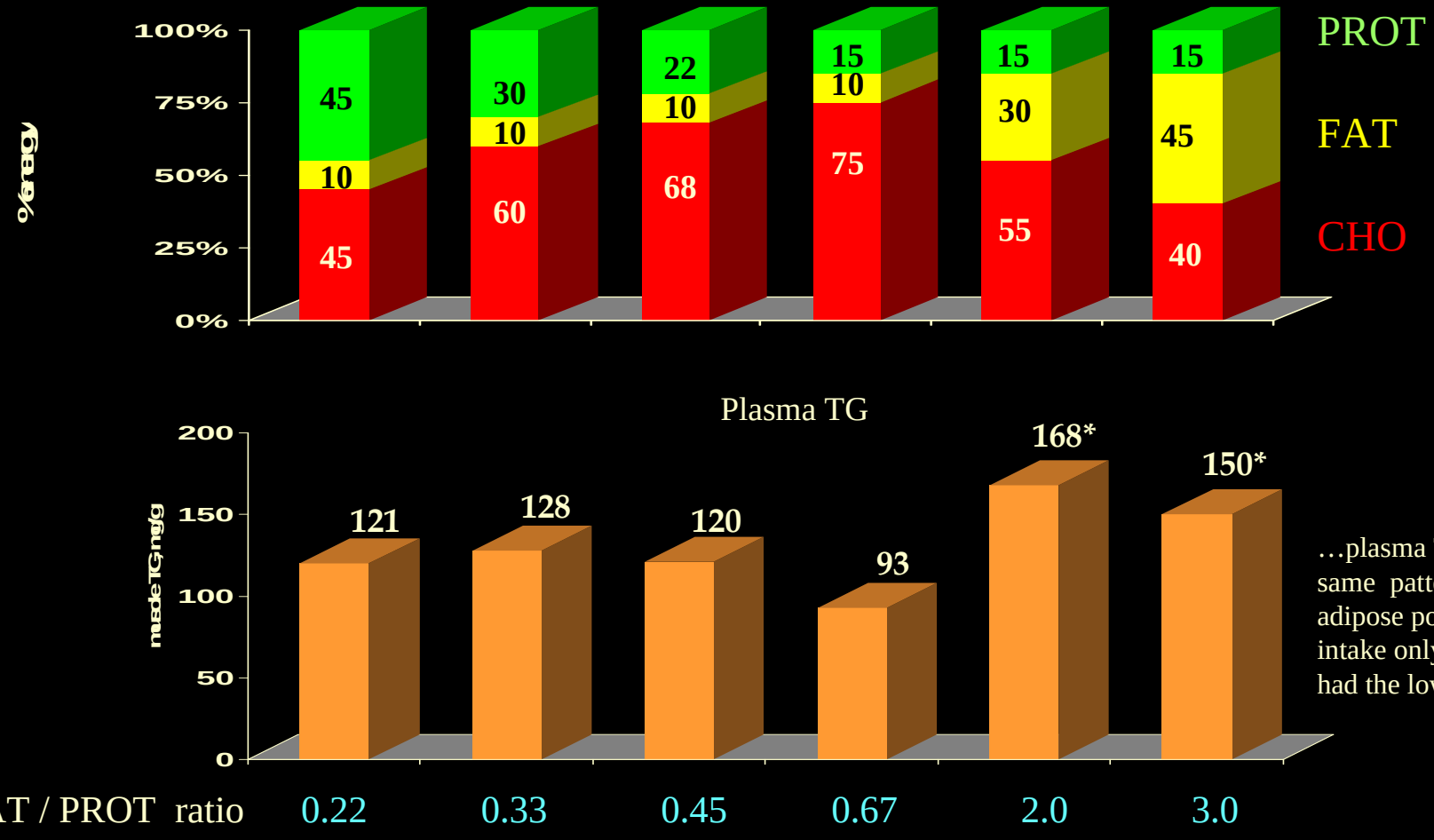


FAT / PROT ratio 0.22 0.33 0.45 0.67 2.0 3.0

…muscle TG follows same pattern of other adipose pools…may cause insulin resistance?

Cummings et al., unpublished

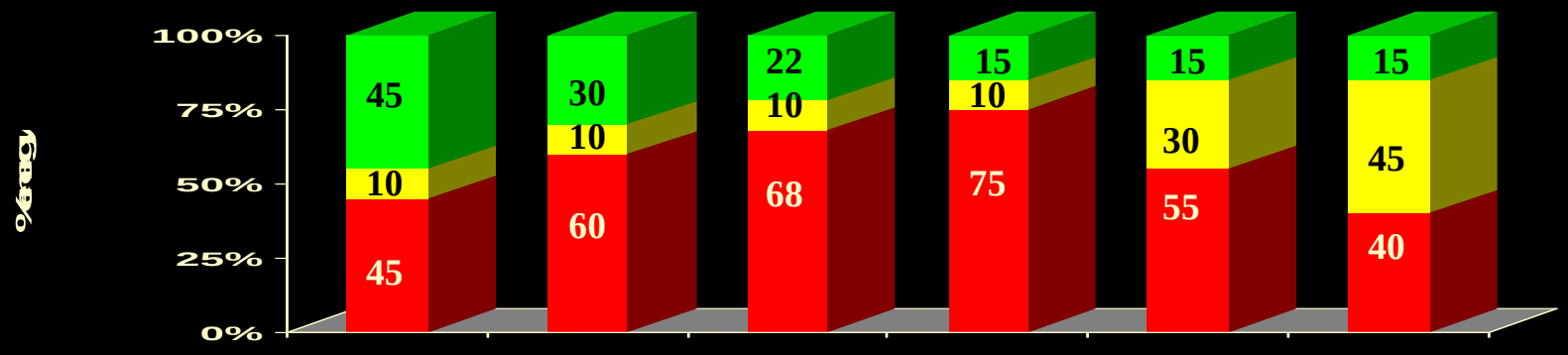
Study 13 : Muscle TG in C57BL/6J mice after 14wk



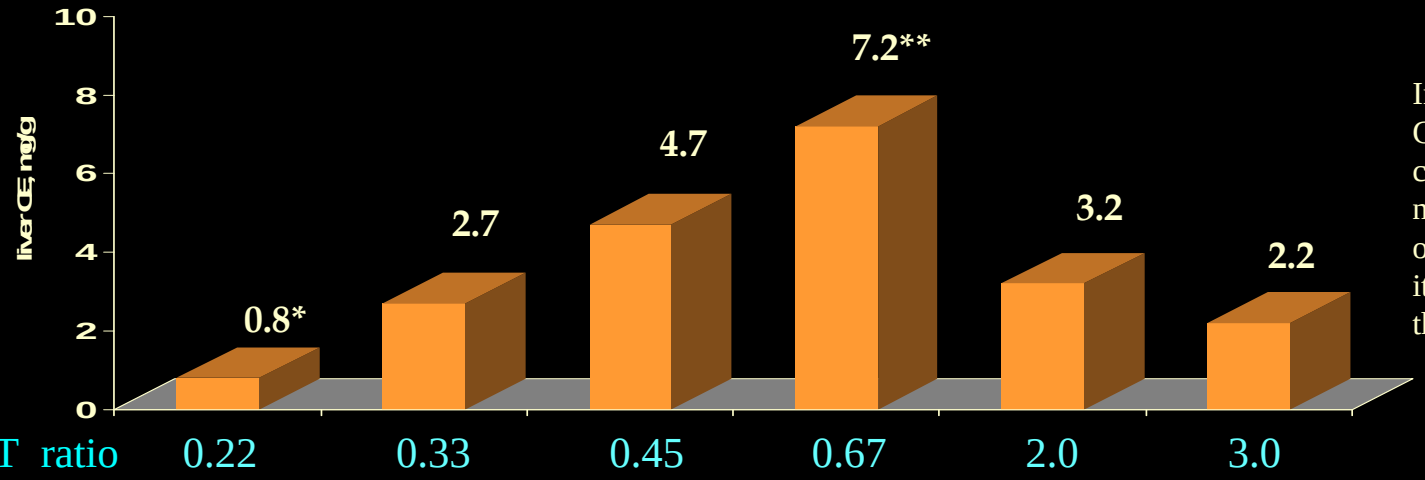
…plasma TG follows same pattern of adipose pools at high fat intake only….highest CHO had the lowest plasma TG!

Cummings et al., unpublished

Study 13: Liver CE in C57BL/6J mice after 14wk



liver CE

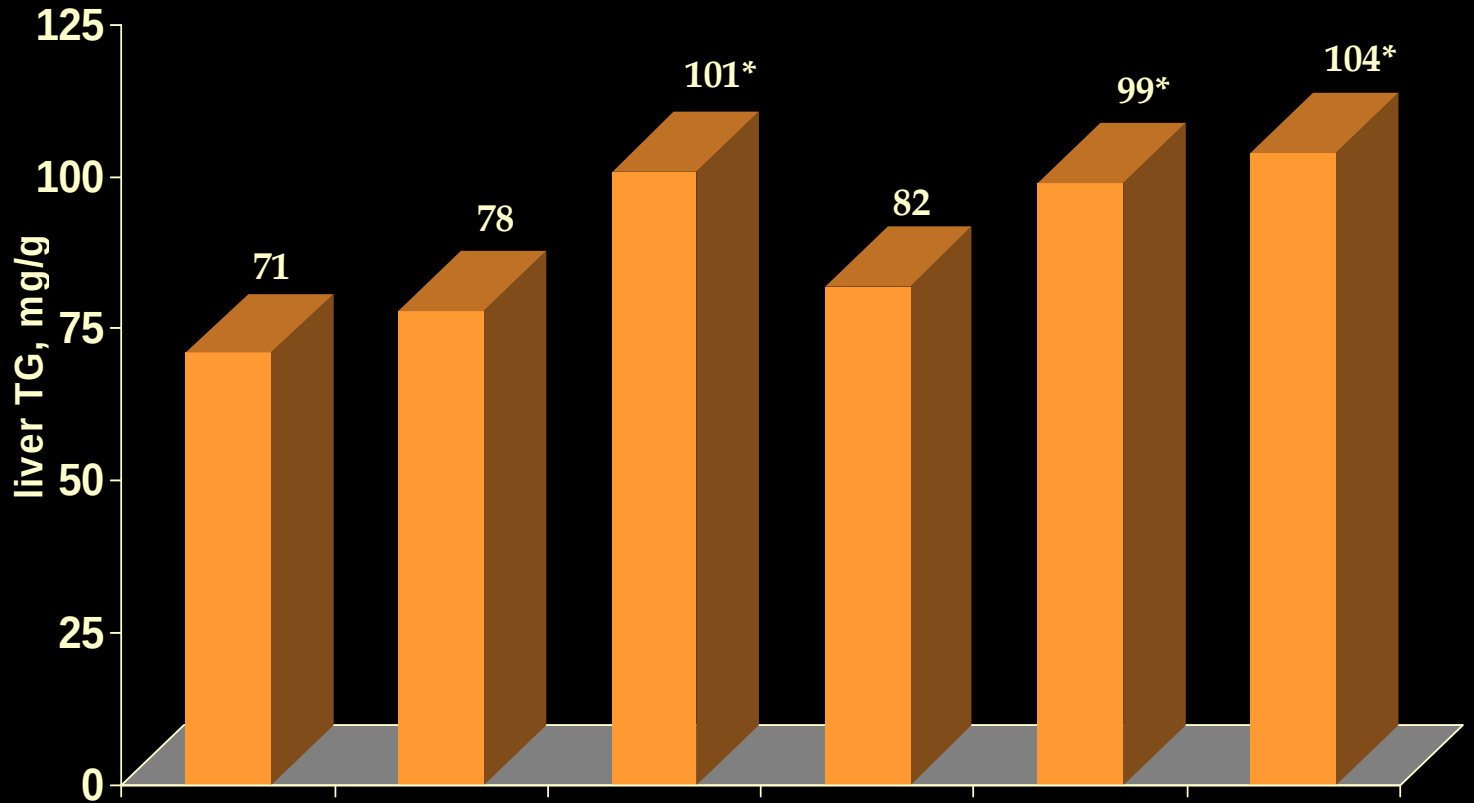


FAT / PROT ratio 0.22 0.33 0.45 0.67 2.0 3.0

Implies that high CHO induces liver cholesterol storage, no matter which other energy source it replaces…part of the Metab Syndr ?

Cummings et al., unpublished

Study 13 : Liver TG in C57BL/6J mice after 14wk

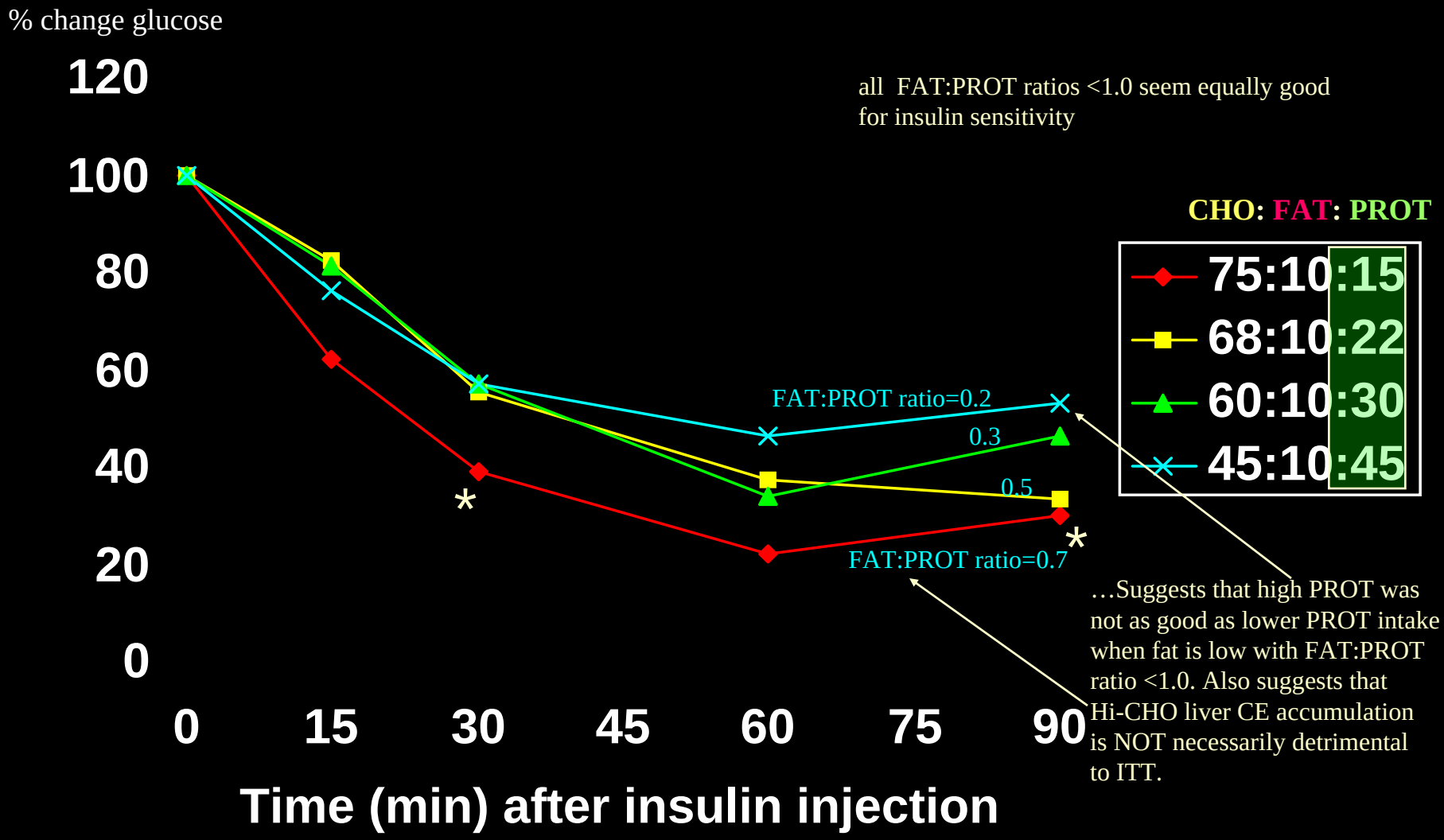


Fat energy	10	10	10	10	30	45
Protein energy	45	30	22	15	15	15
FAT / PROT ratio	0.22	0.33	0.45	0.67	2.0	3.0

Cummings et al., unpublished

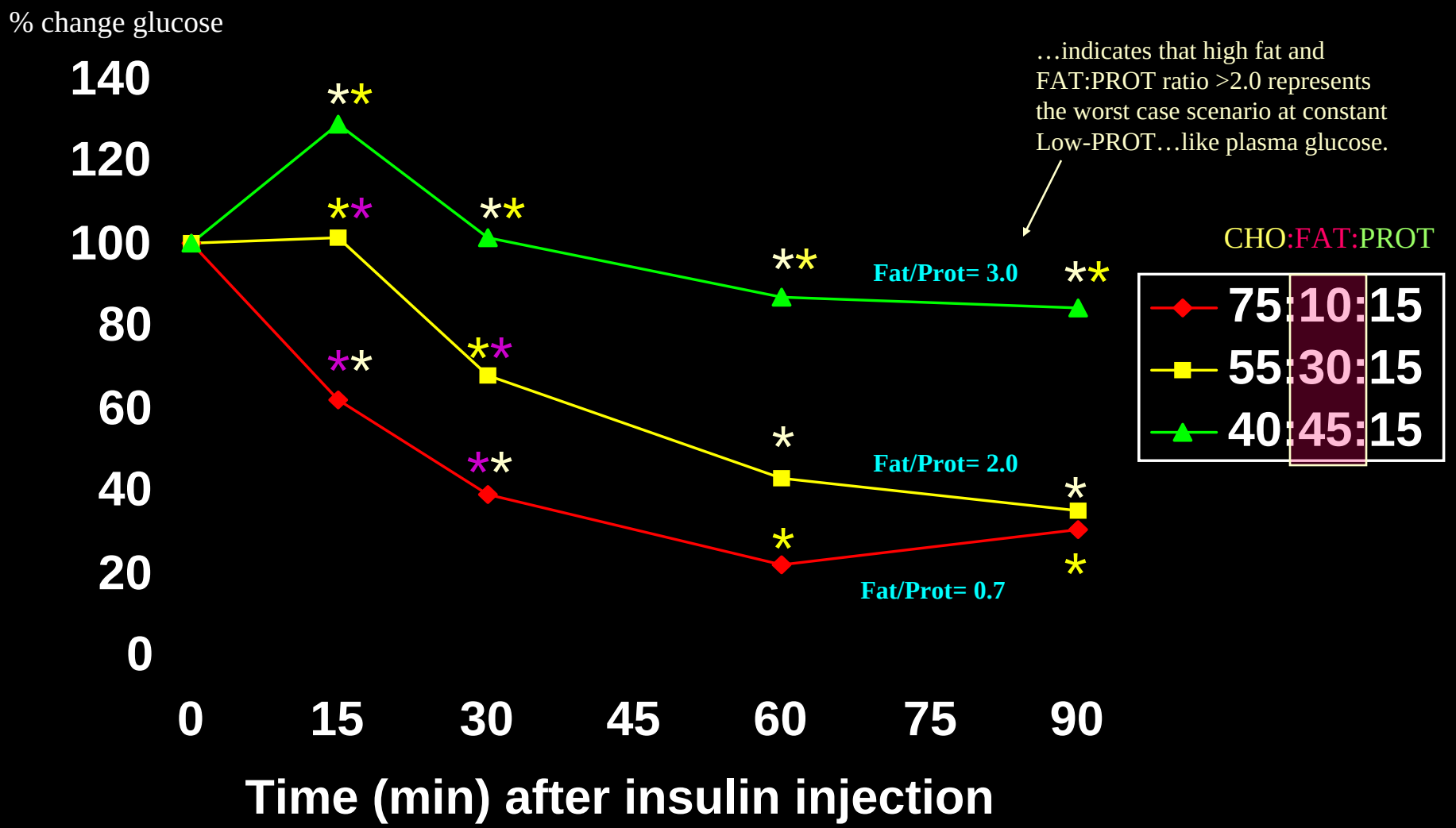
Study 13. Insulin Tolerance Test :

(increasing Protein at low Fat)



* significantly lower than 0.2 ratio ($p<0.05$) by one-way ANOVA and Fisher's PLSD test.

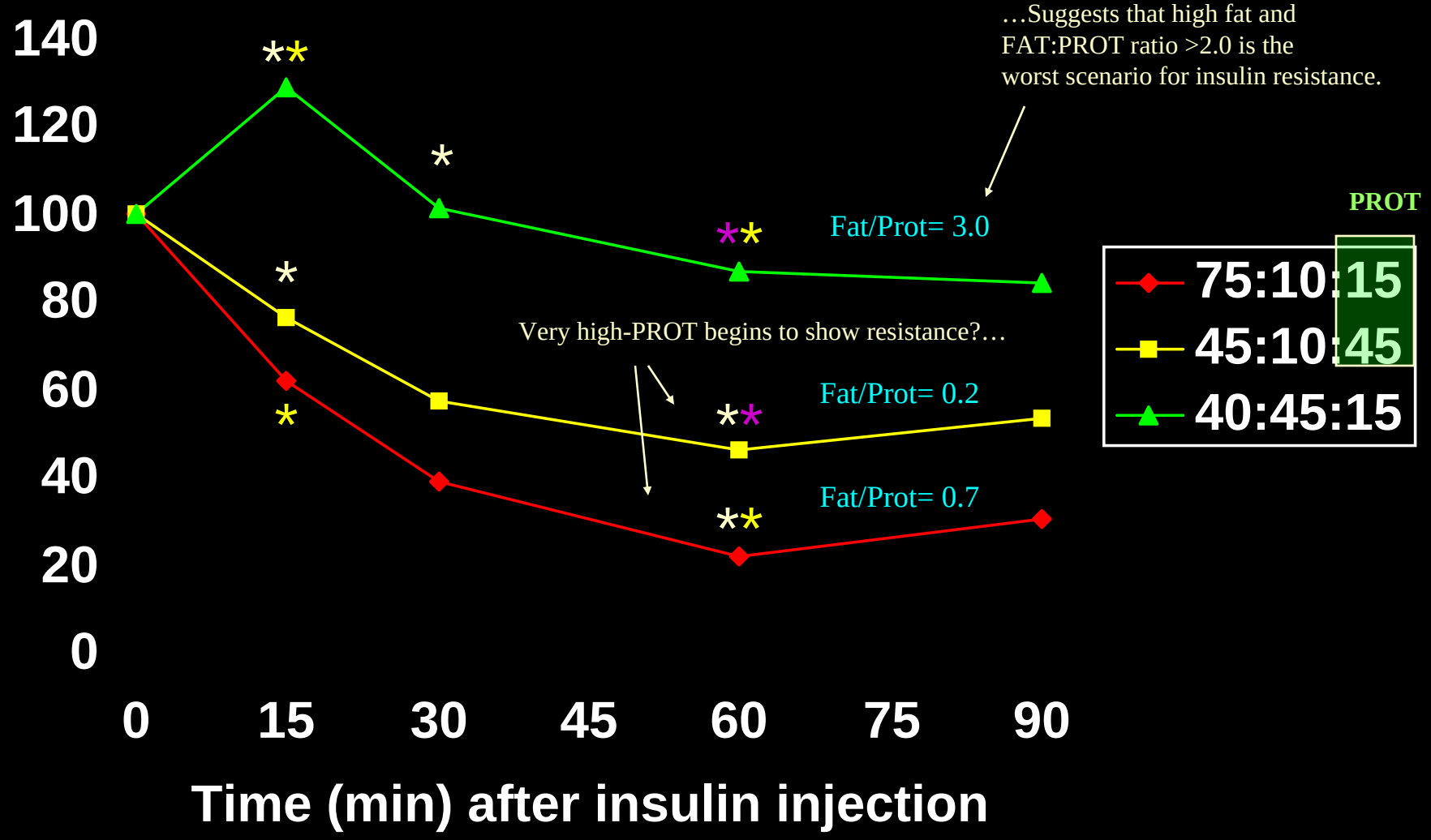
Study 13. Insulin Tolerance Test :
(increasing Fat at low Protein)



***means differ between diet Fat/Prot ratios ($p<0.05$) by one-way ANOVA and Fisher's PLSD test.

Study 13. Insulin Tolerance Test:

Comparing various Fat/Prot ratios in C57BL/6j mice



* * * means differ between diet Fat/Prot ratios ($p<0.05$) by one-way ANOVA and Fisher's PLSD test.

Conclude 1… *concerning obesity and insulin resistance*

- Increasing fat appears detrimental when PROT intake is low
- At low-fat intake PROT intake has minimal effect

(Question: does PROT protect against high-fat intake?)

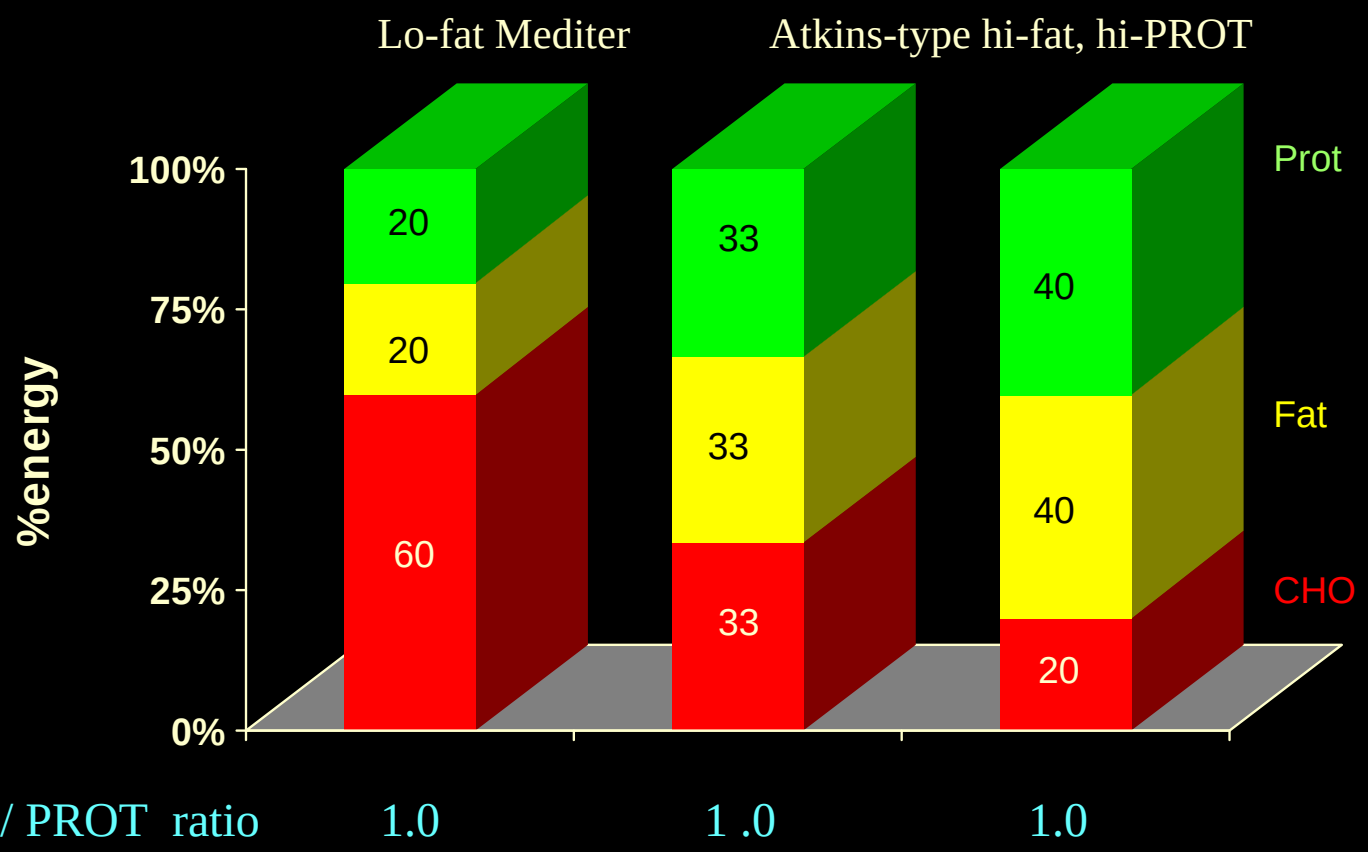
Study 2 *older obese male C57BL/6j mice*

- What happens if you increase FAT and replace CHO, but keep the FAT:PROT ratio constant at 1.0 ?

... ie. increase FAT and PROT together at expense of CHO.

Study 17: Macronutrient Composition fed to obese adult male C57BL/6J mice

(question: would increasing PROT calories be important for weight control?)

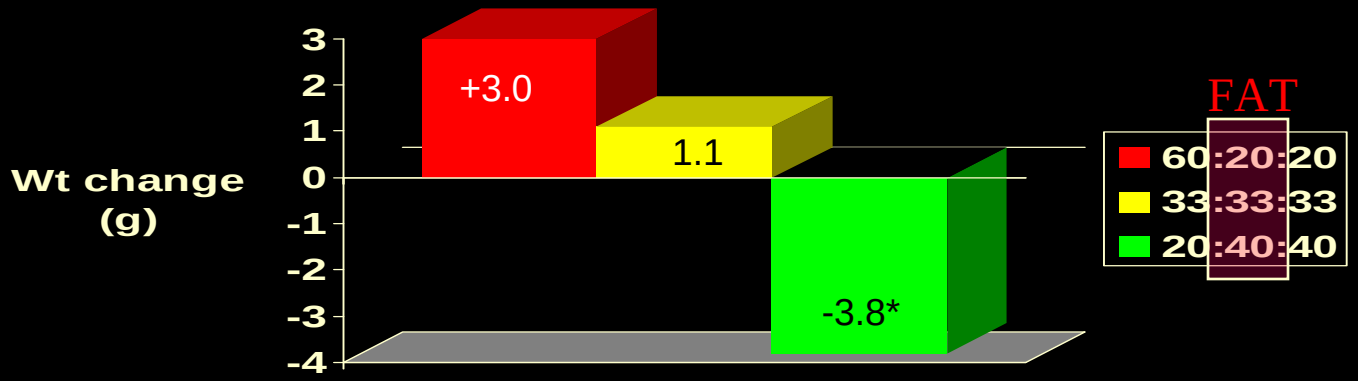


FAT / PROT ratio 1.0 1 .0 1.0

(ratio held constant, ie as FAT calories increased, the PROT calories increased in step so both replace CHO)

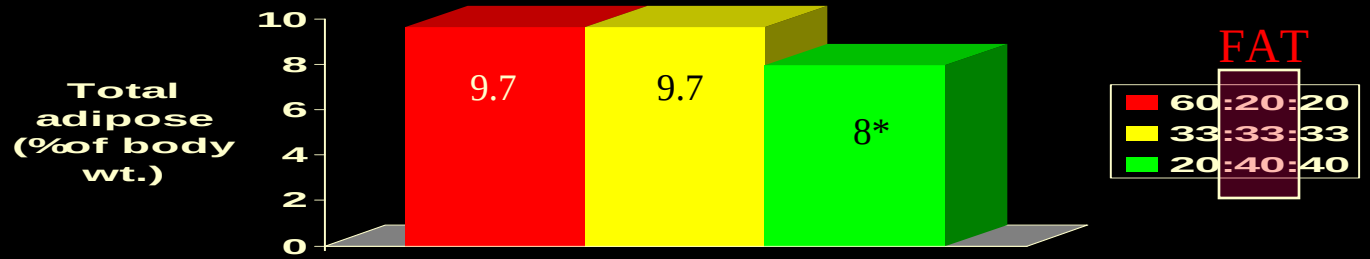
Study 17: Weight Gain/Loss in 14wks

in overweight male C57BL/6J Mice fed diets with increasing protein content



Caloric intake, kcal/d 14.9 14.3 12.6

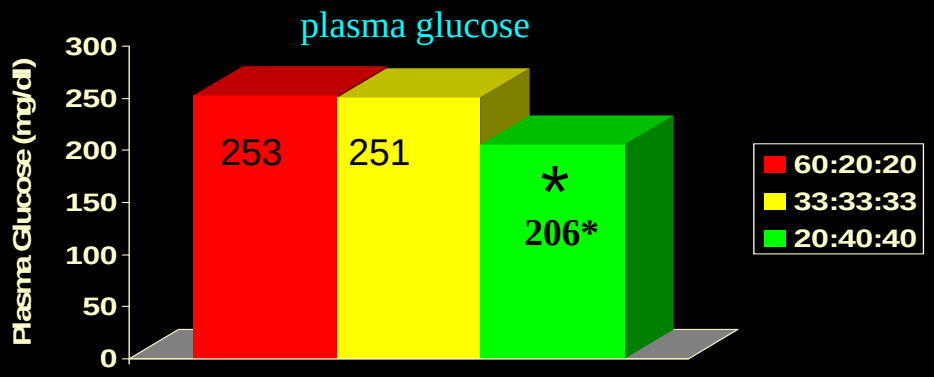
Point is that high-fat is not bad with sufficient protein intake.

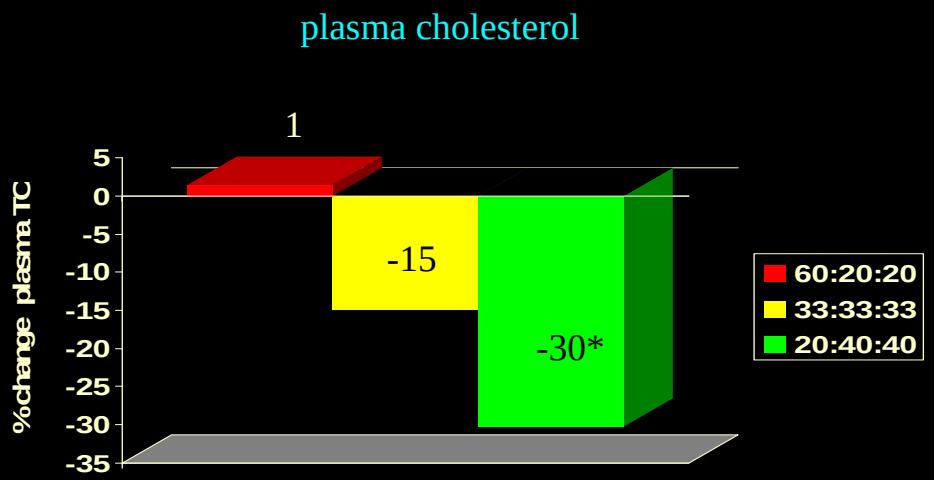


all Fat/Protein ratios constant at 1.0

*** Significantly lower ($p<0.05$) by one-way ANOVA and Fisher's PLSD test**

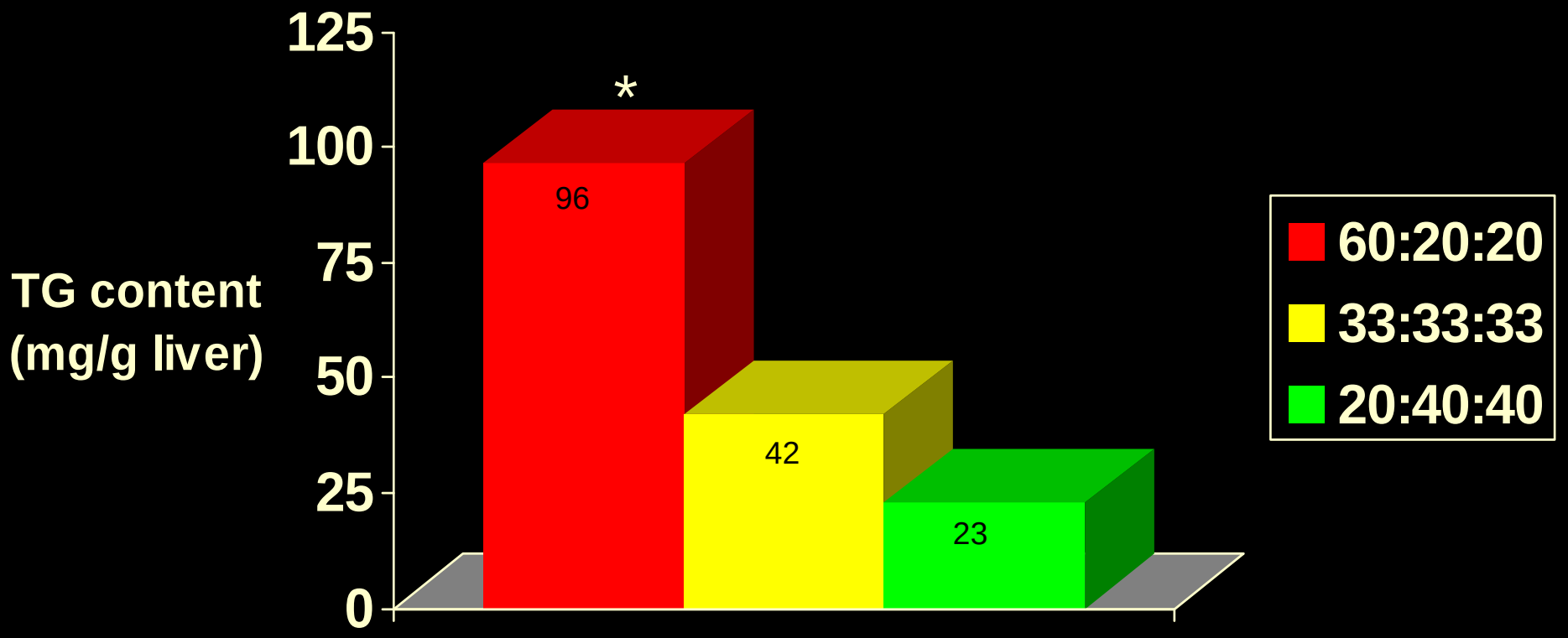
Study 17. Terminal fasting plasma glucose, cholesterol, and triglycerides for overweight male C57BL/6J mice fed diets of increasing PROT content





* significant ($p<0.05$) by one-way ANOVA and Fisher's PLSD test.

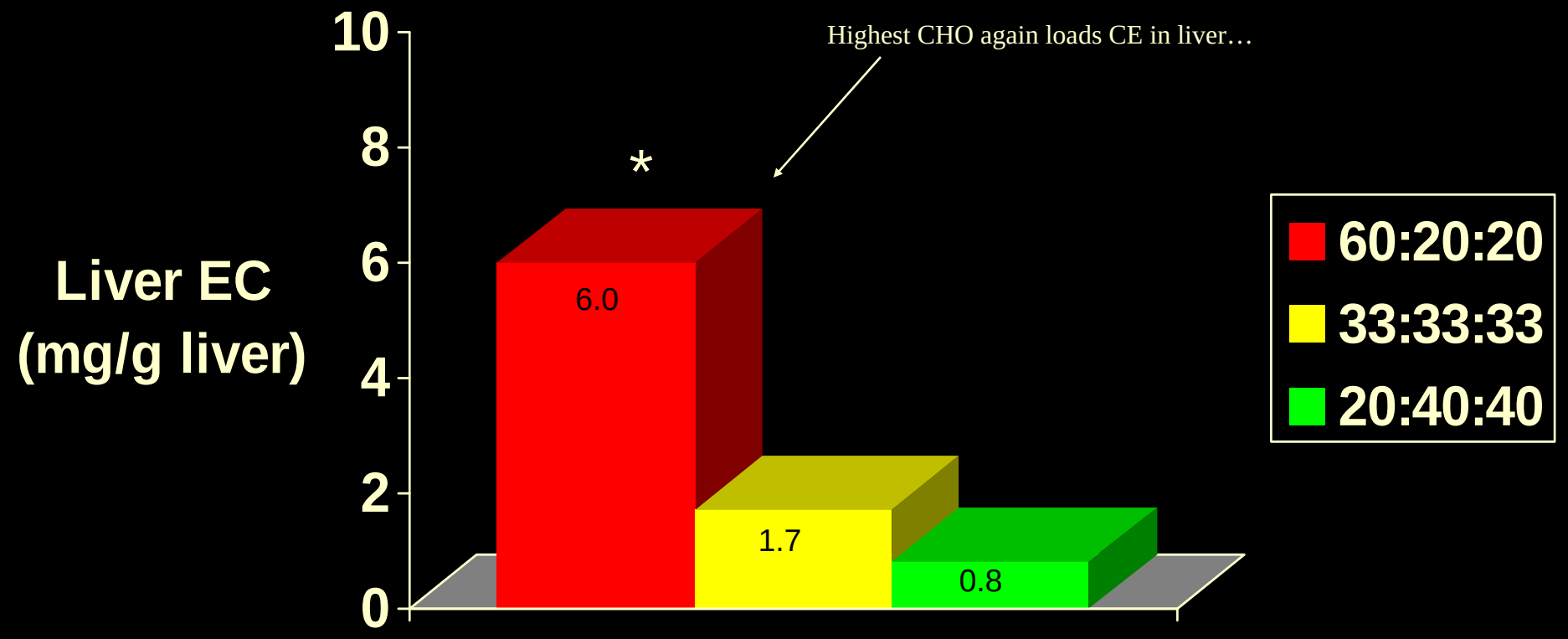
Study 17. Liver Triglycerides in Overweight Male C57BL/6J Mice fed diets of increasing PROT and Fat/Prot ratio of 1.0



* Significantly increased ($p<0.05$) by one-way ANOVA and Fisher's PLSD test.

Study 17. Liver Esterified Cholesterol

in Male C57BL/6J Mice Fed Diets of Increasing PROT Content



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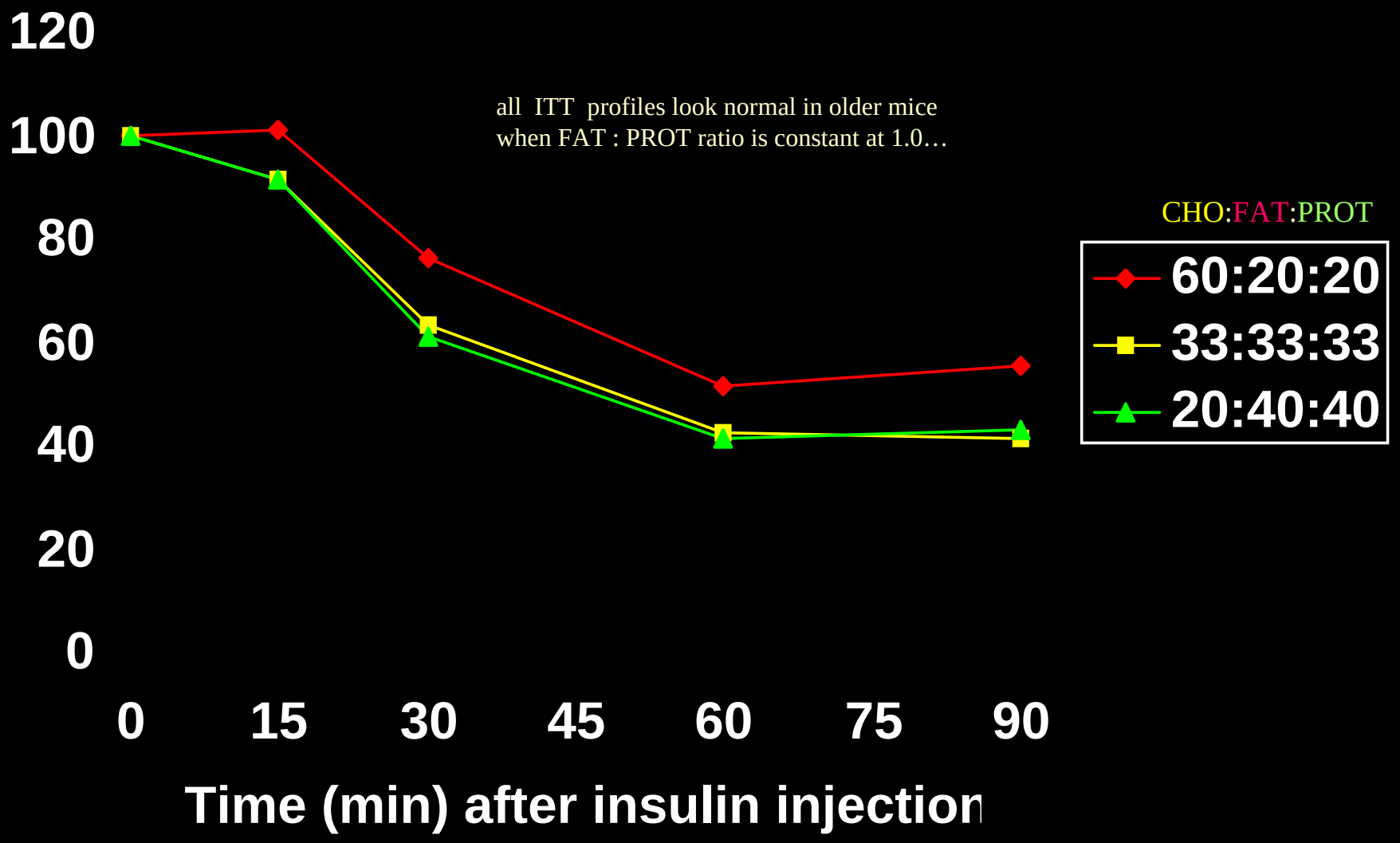
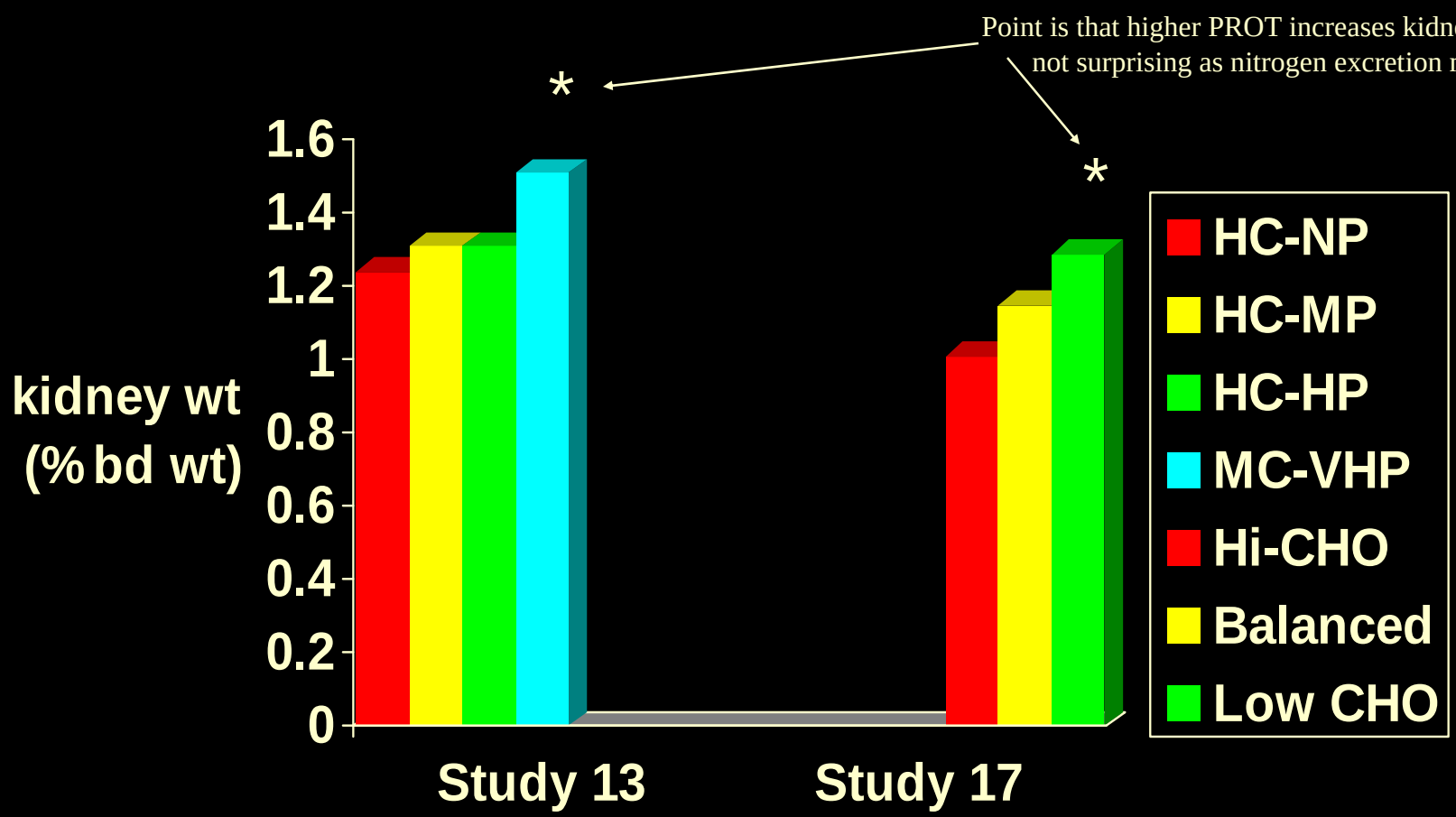
Study 17. Insulin Tolerance Test in Overweight Male C57BL/6J Mice fed diets with increasing fat-protein content



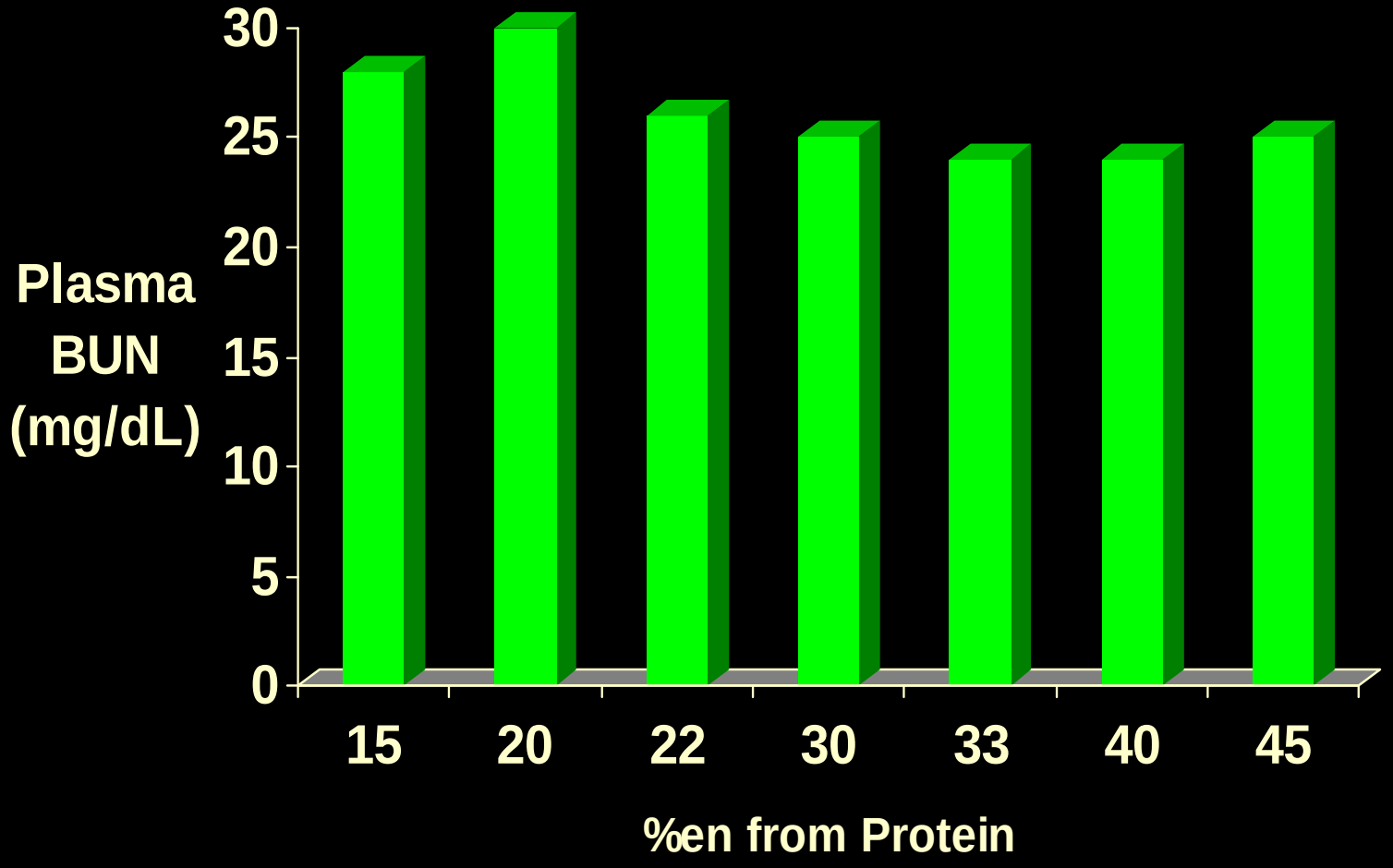
Study 17. Effect of increasing dietary protein on kidney weight in growing and adult male C57BL/6j Mice



* Significantly greater ($p<0.05$) by one-way ANOVA and Fisher's PLSD test

Plasma BUN

at Different Levels of Dietary Protein

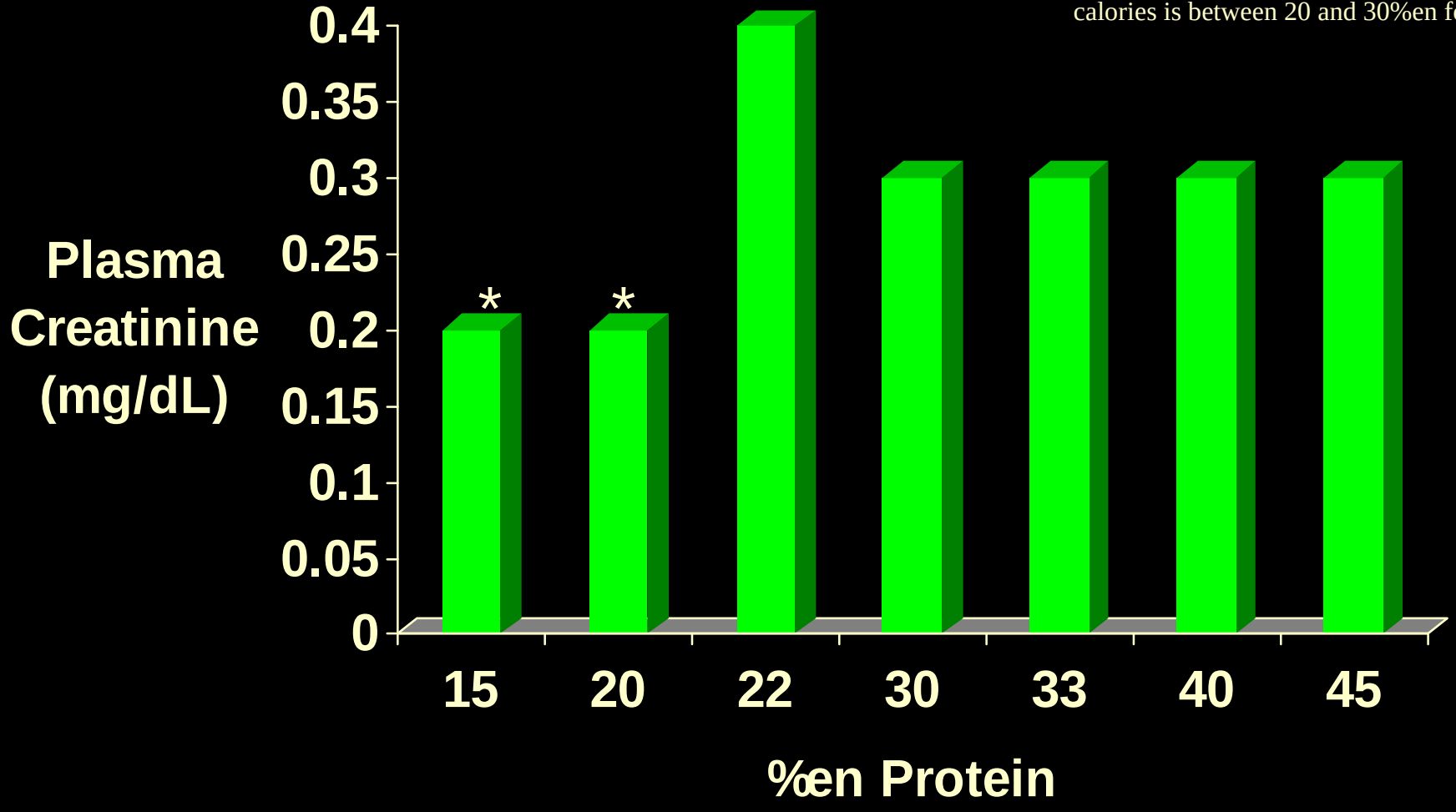


…but PROT had no effect on BUN…

Plasma Creatinine

at different levels of dietary protein

…suggests that the optimal level of PROT calories is between 20 and 30%en for mice.



*value is below published normal range for male C57BL/6J mice.

Conclude 2

- Increasing PROT calories (to 40%en) along with FAT calories while maintaining 1:1 ratio, led to similar 15-18% reduction in energy intake and body weight (as fat).
- Maintaining the FAT:PROT ratio at 1.0 was without effect on insulin sensitivity, which was normal at all intakes.
- Feeding up to 40%en as PROT (and FAT) to mice had no adverse effects on PROT utilization or turnover, and had a favorable effect on lipid and glucose metabolism.
- Feeding high-fat to mice is not problematic if protein accompanies the fat.