

# **Comments on the Appropriate Balance of Fatty Acids in the Diet**

**MT Clandinin**

University Professor

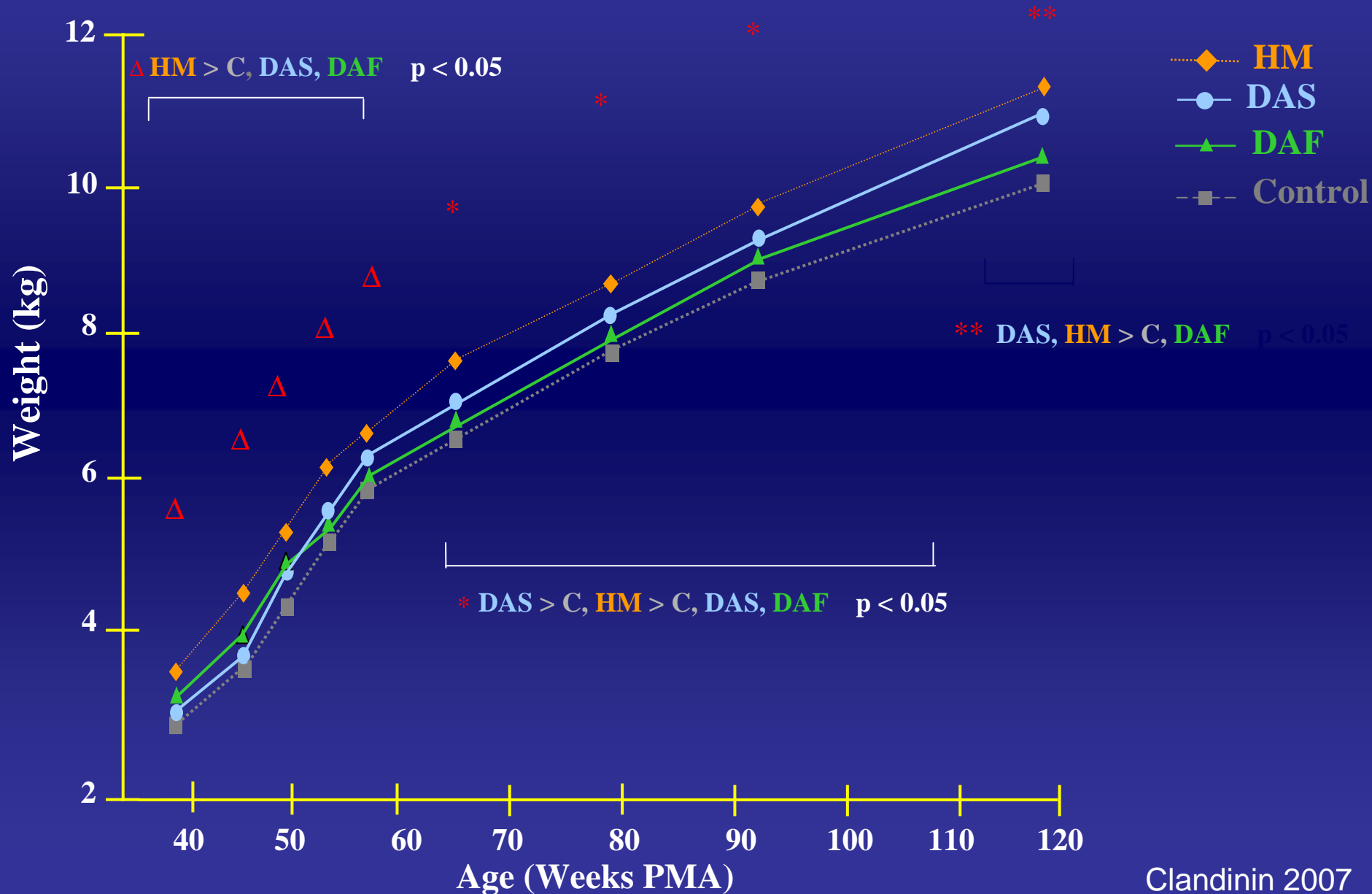
Department of Agricultural, Food and Nutritional Science and  
Department of Medicine, University of Alberta, Edmonton, Alberta

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# Outline

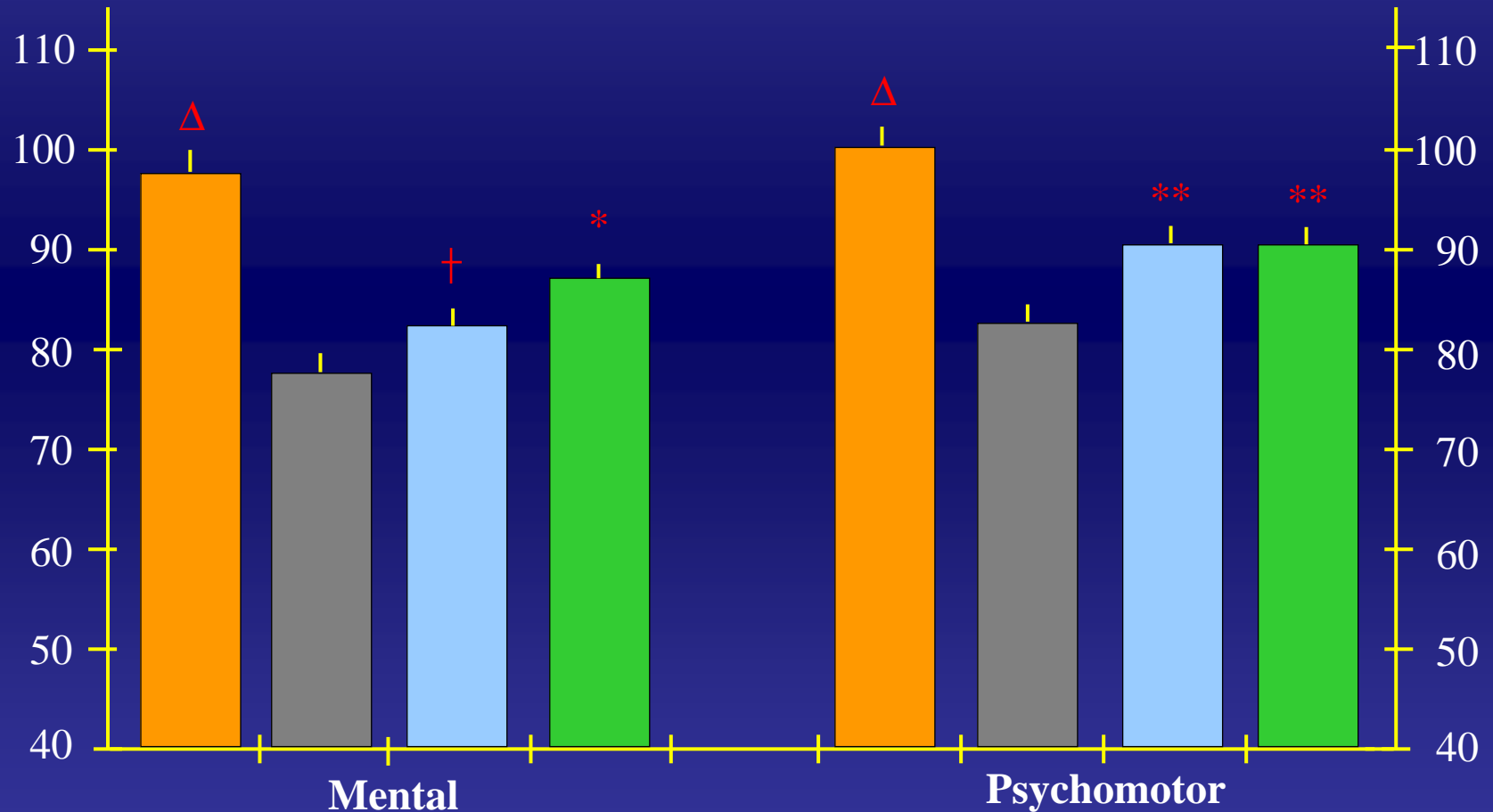
- Recognizing lessons from the past
  - Saturates, linoleic acid and trans
- Present understanding of Balance
- Understanding future directions
  - Impact of 'minor' dietary constituents
- Can we generalize the advice?
  - The new nutrition paradigm
  - Novel food sources of fatty acids
  - 'Natural' fat intakes

# Mean Achieved Weights from 40 to 118 Wks PMA



# Bailey Score of Infant Development II: Scores at 118 Wks PMA

$\Delta$  HM > C, DAS, DAF p < 0.05  
† DAS > C p < 0.056  
\* DAF > C p < 0.05  
\*\* DAS, DAF > C p < 0.05



HM Control DAS DAF

# Fatty Acid Intakes

	<u>% Calories</u>
Saturates	12.5
18:1 n-9	17
18:2 n-6	6-9
18:3 n-3	1-2
AA and DHA	<0.4

# Identifying the Albertan Diet and what it could be

- Some initial assumptions:
  - Energy requirement approximately 2700 kcal for a male in mid teens or about 50 years old
  - Assume 30% calories as fat → 100 g fat/ day (or approximately 22 g/ day less for a female)
- Focus: The composition of the 100
  - Amazing lack of quantitative data
  - Why?

# Estimated Fatty Acid Intake of Americans

(1999-2000)

(Ervin et al., *Advance data*, 2004)

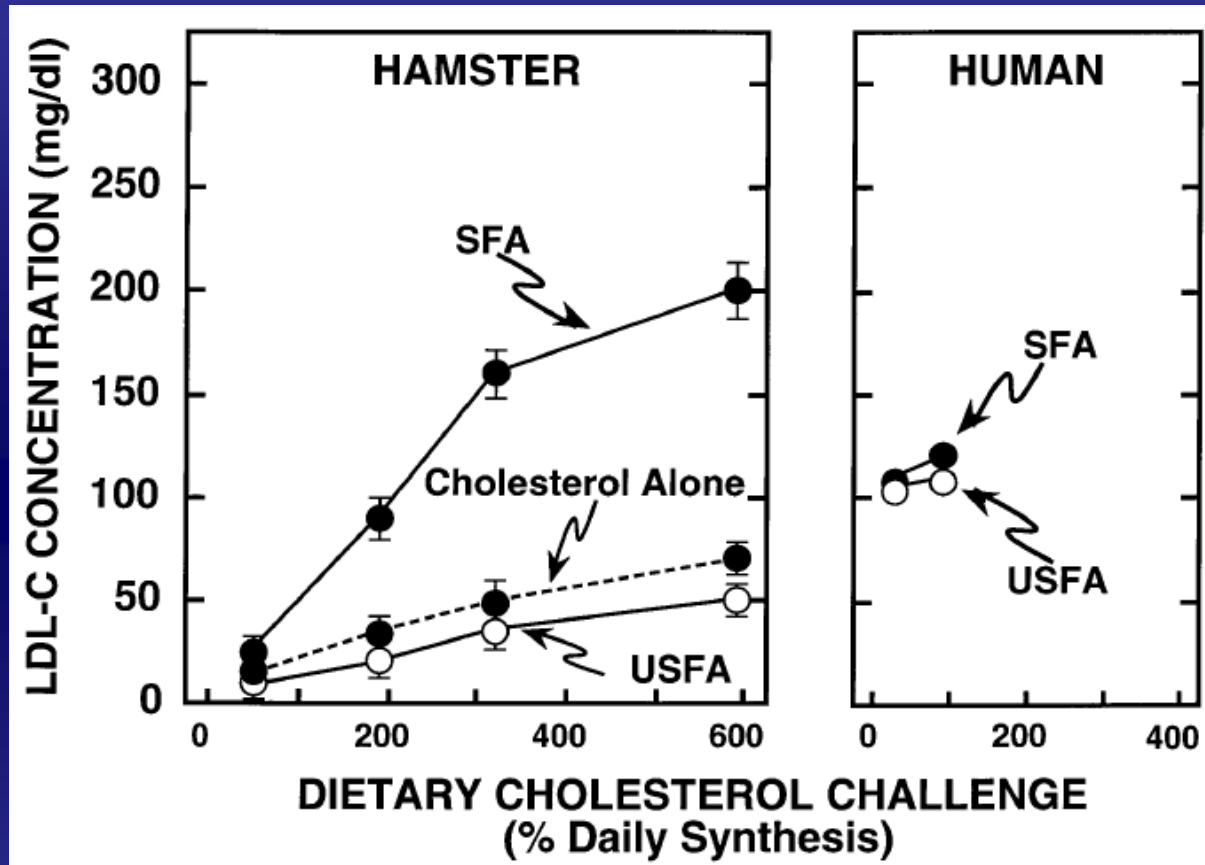
		16:0	18:0	18:2
Both sexes/All ages <sup>1</sup>		6.2	2.8	6.0
Men	20-39y	6.2	2.8	5.8
	40-59y	6.0	2.8	5.9
	60+y	6.0	2.8	6.1
Women	20-39y	6.1	2.8	6.2
	40-59y	6.0	2.8	6.3
	60+y	6.0	2.7	6.5

Values represent means as % of energy, assuming fat intake at 33% of energy.

<sup>1</sup>Excludes nursing infants and children.

Data from NHANES 1999-2000 for U.S. population based on 24h recall and coded to USDA's Survey Nutrient Database (versions 1994-96 and 1998).

# The Dependency of Fatty acid Effects on LDL-C Concentration on the Level of Dietary Cholesterol Intake



(Dietschy, *J Nutr*, 1998)

*Hamster:*

SFA = HCO + TP  
added to USFA

*Human:*

SFA = 4.5% en 18:2  
vs. 9.5% en 18:2

This diagram shows the absolute concentration of LDL-C achieved in hamsters or humans fed predominantly saturated fatty acids (SFA) or unsaturated fatty acids (USFA) under circumstances in which the amount of cholesterol in the diet was varied.

(Constructed using data from two sources: Fielding et al., *J Clin Invest*, 1995; Spady & Dietschy, *J Clin Invest*, 1988).

# The Historical Advice: 1980's

- Medical Professionals
  - High cholesterol results in CHD
  - Saturated fat causes high cholesterol
  - Polyunsaturates lower plasma cholesterol
- The Advice
  - Consumed > 10% of energy as linoleic acid
  - Reduce red meat, dairy fat, fat, animal fat, and egg consumption
- The Public “learned” and became fat on this advice
  - Saturates are bad
  - Higher fat foods are bad
  - Higher CHO foods not bad

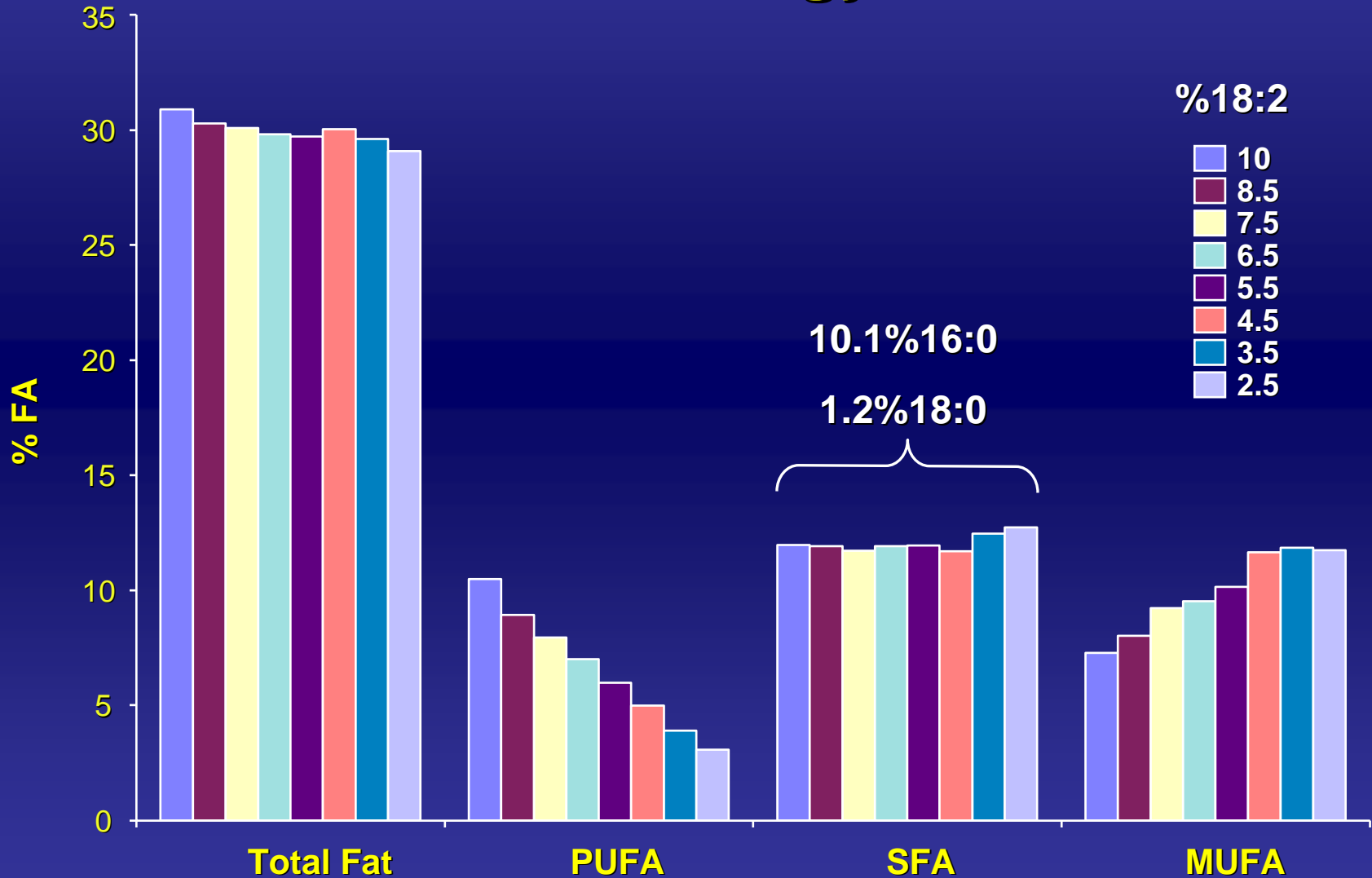
# The Solution:

- Polyunsaturates and a healthy lifestyle
- Lifestyle ads depicting 'good' fat products
- Various corn oil products high in trans fatty acids and devoid of n-3 fatty acids
- Whole pages of magazines and newspapers
- TV ads frying chicken
- 'Saturation' of the consumer

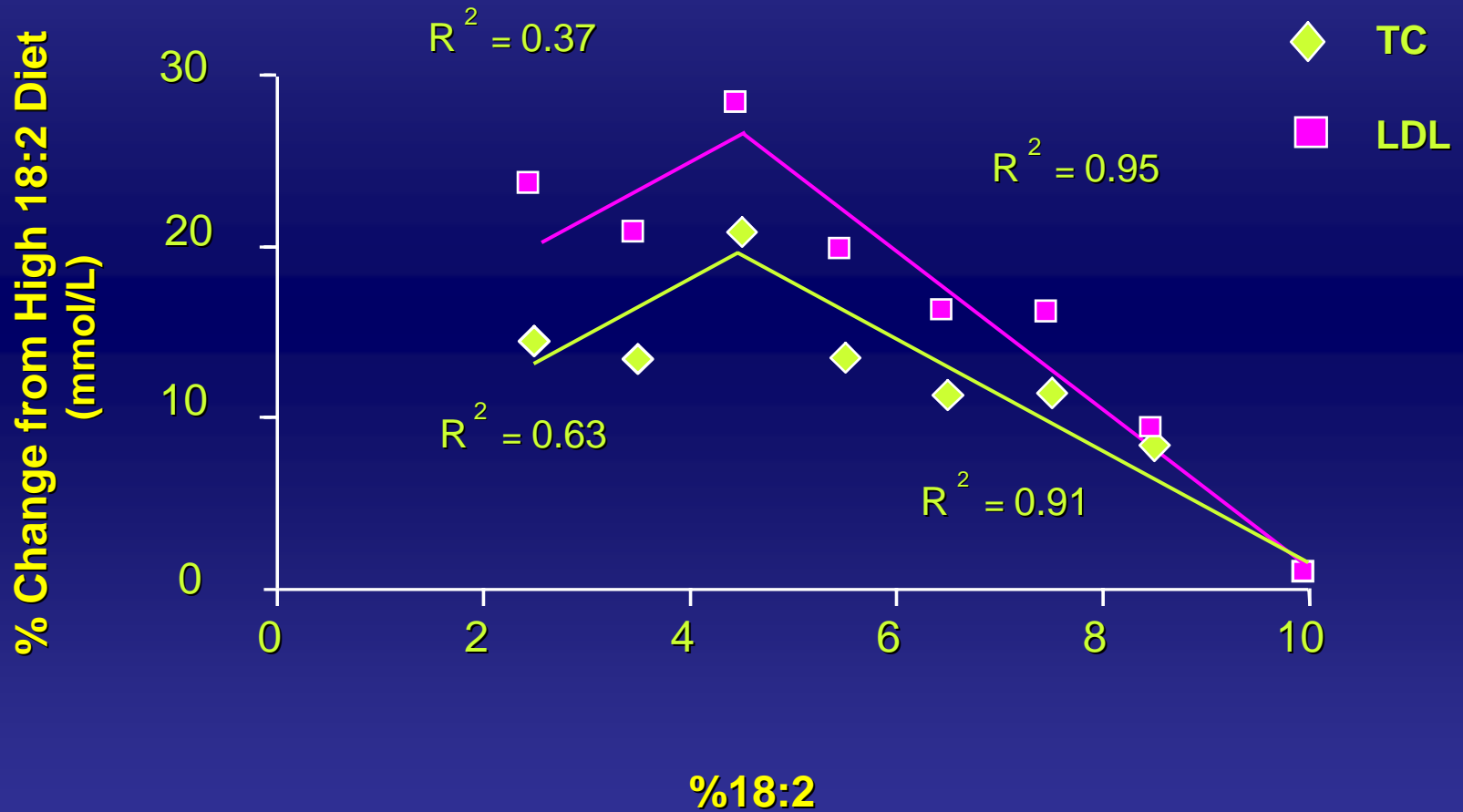
# Animal Variation in Cholesterol Response to Diet:

- Difficult to generalize to people
- Between species (i.e. monkeys, guinea pigs, gerbils, hamsters, rats, rabbits, pigs...)
- Between strains (i.e. monkeys: cebus, rhesus, cynomolgus, vervet...)
- Within strains (i.e. hamsters: F1B or CR Golden Syrian...)
- Differences:
  - Where FA synthesis occurs (& quantitative capacity)
  - Main carrier of cholesterol
  - Sensitivity to dietary FAs & cholesterol
  - Position of 16:0 & 18:2n-6
  - Lymphatic drainage

# Diet total fat, PUFA, SFA and MUFA as % of Energy



# Mean Change in Total Cholesterol and LDL-C when Consuming a High SFA Diet at Different 18:2 Intakes



# Nutrient Composition of Diets

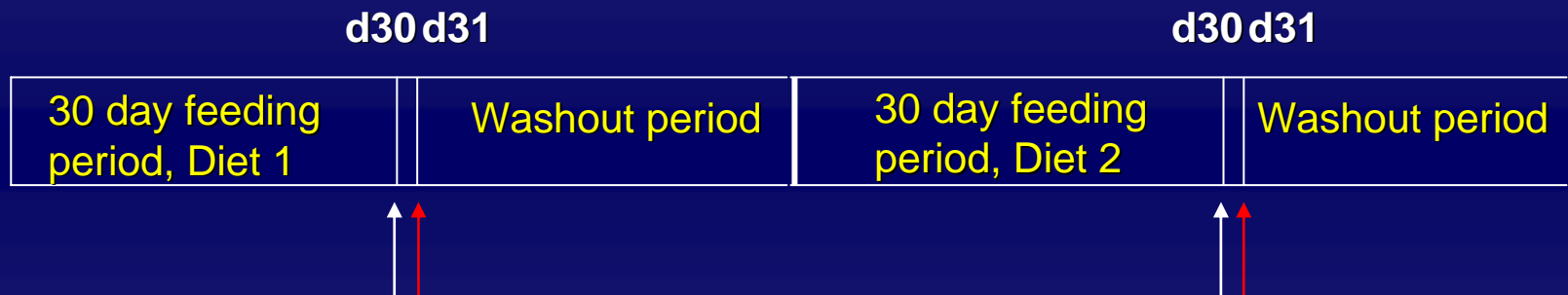
Nutrient	Low C16:0 Low C18:2	High C16:0 Low C18:2	Low C16:0 High C18:2	High C16:0 High C18:2
<b>Energy (cals)</b>	3073 ± 158	3027 ± 31	2991 ± 267	2988 ± 228
<b>Protein (%cals)</b>	15.7 ± 3.1	16.3 ± 0.4	16.9 ± 2.3	16.1 ± 2.1
<b>Carbohydrate (%cals)</b>	56.5 ± 4.8	57.8 ± 0.8	57.0 ± 3.3	53.5 ± 2.6
<b>Total fat (%cals)</b>	29.2 ± 1.7	27.8 ± 0.1	27.6 ± 1.1	31.1 ± 0.5
<b>SFA (%cals)</b>	4.8 ± 0.7	13.9 ± 0.6	4.7 ± 0.3	10.2 ± 0.7
<b>C16:0 (%cals)</b>	<b>3.2 ± 0.2</b>	<b>10.1 ± 0.4</b>	<b>2.9 ± 0.2</b>	<b>9.9 ± 0.2</b>
<b>C18:0 (%cals)</b>	0.8 ± 0.1	2.0 ± 0.1	1.1 ± 0.1	1.2 ± 0.1
<b>MUFA (%cals)</b>	18.8 ± 0.9	9.0 ± 0.2	7.5 ± 0.1	8.1 ± 0.3
<b>C18:2n-6 (%cals)</b>	<b>2.8 ± 0.6</b>	<b>2.0 ± 0.2</b>	<b>12.0 ± 1.4</b>	<b>12.1 ± 0.6</b>
<b>n-3 FA (%cals)</b>	0.5 ± 0.1	0.5 ± 0.1	0.5 ± 0.1	0.4 ± 0.0
<b>Cholesterol (mg)</b>	200 ± 21	208 ± 57	177 ± 77	149 ± 22
<b>Dietary fibre (g)</b>	27.1 ± 6.0	28.0 ± 5.1	32.7 ± 8.5	31.9 ± 5.3

Values represent means SEM; n=3 for each diet treatment.

Diet averages are based on the average nutrients calculated from each menu cycle for a given diet.

All values are derived from Food Processor II data.

# Experimental Design of Study

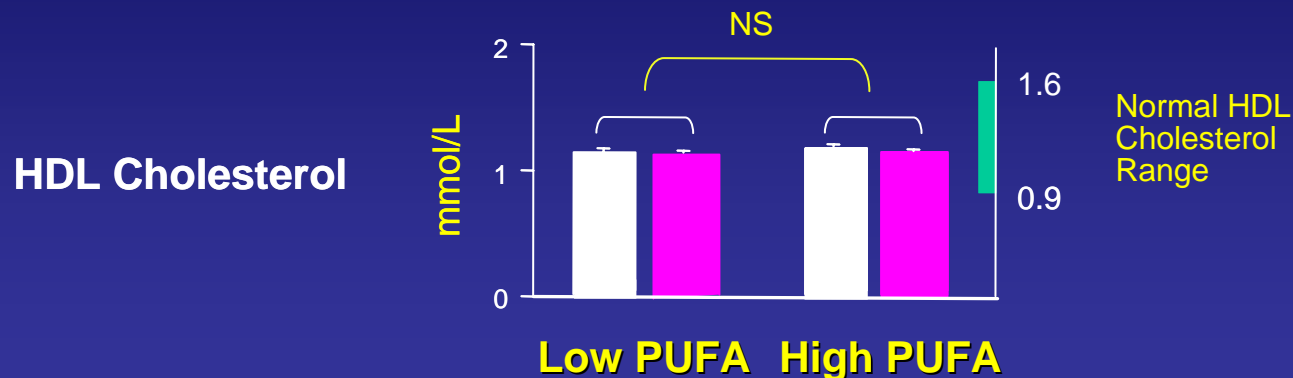
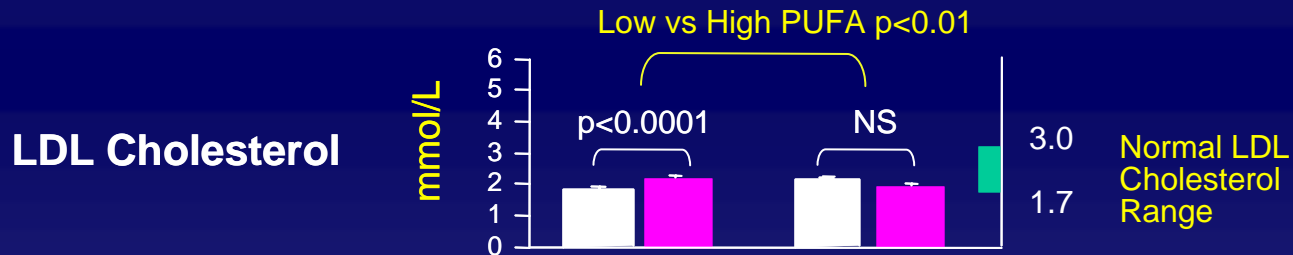
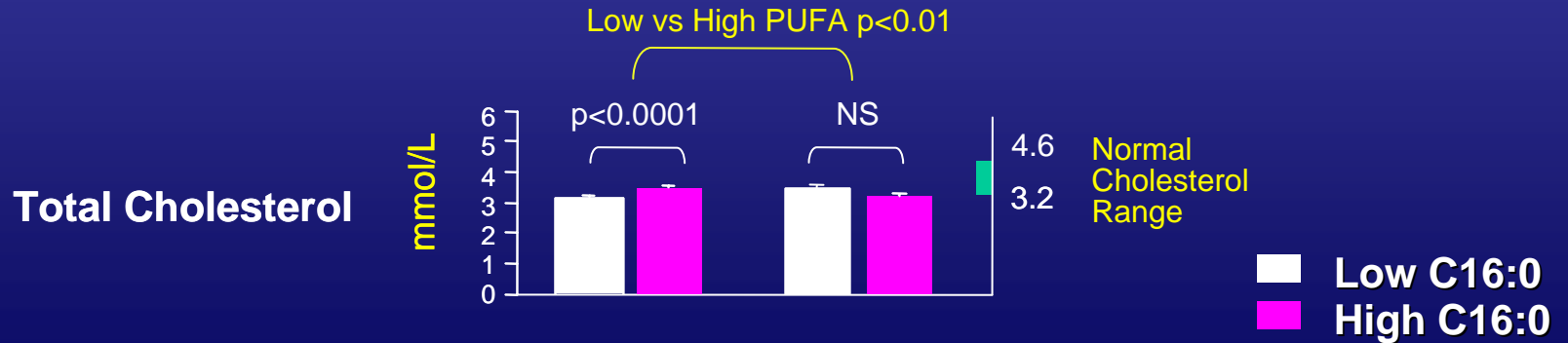


Background blood sample 24h blood sample

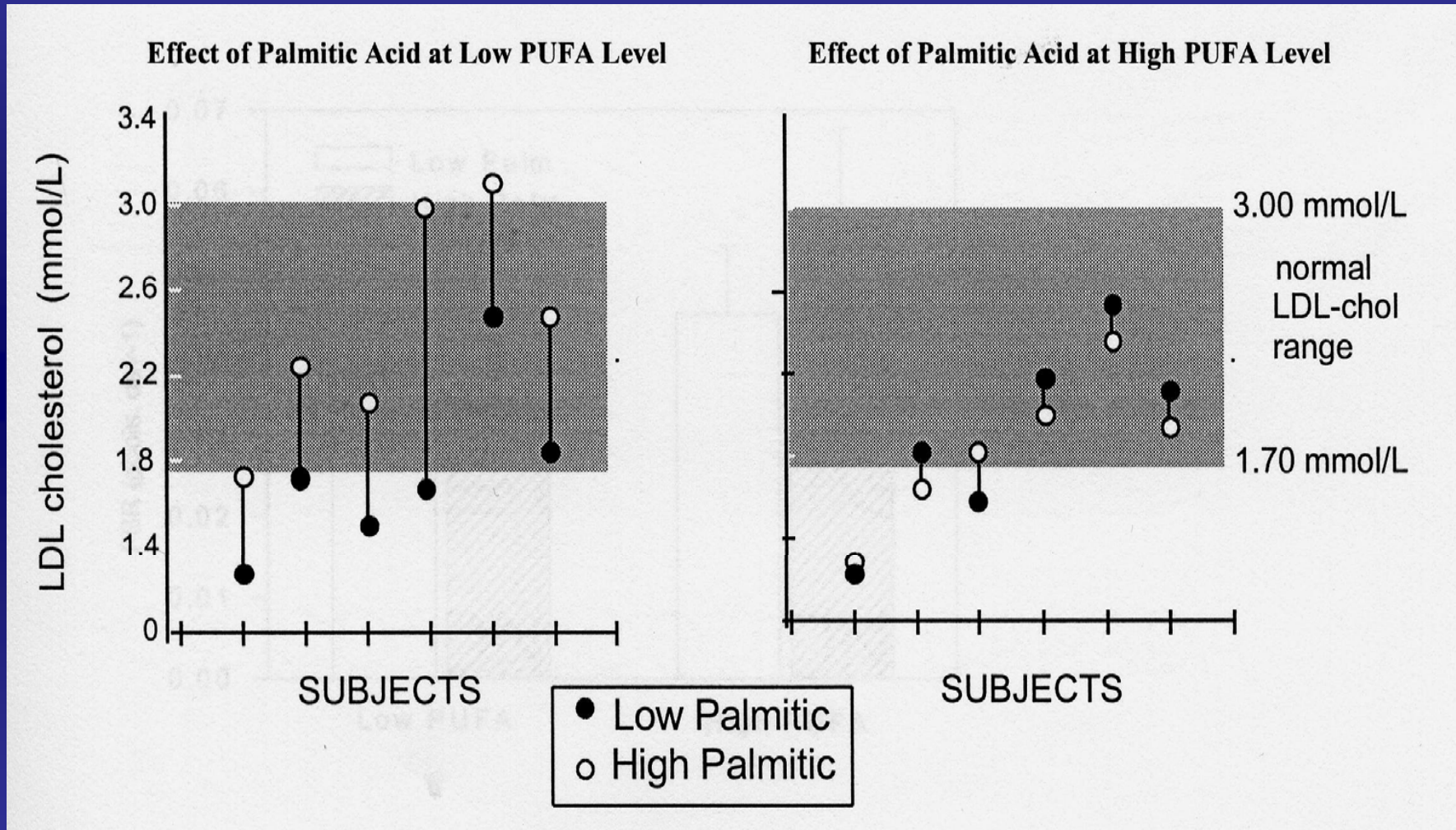
Priming dose of  $D_2O$

Maintenance dose of  $D_2O$

# Effect of 16:0 on Plasma Lipoprotein Cholesterol Values in Subjects Consuming Diets High or Low in 18:2

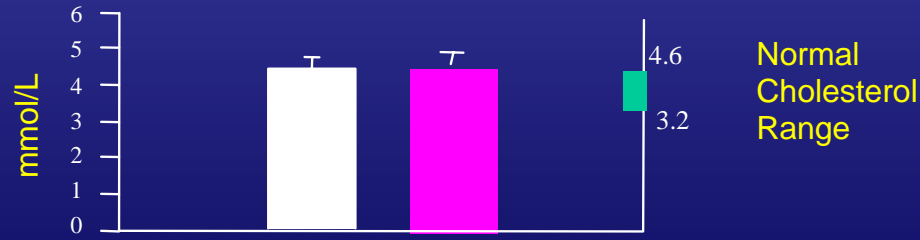


# Individual Variation in Response to Diet

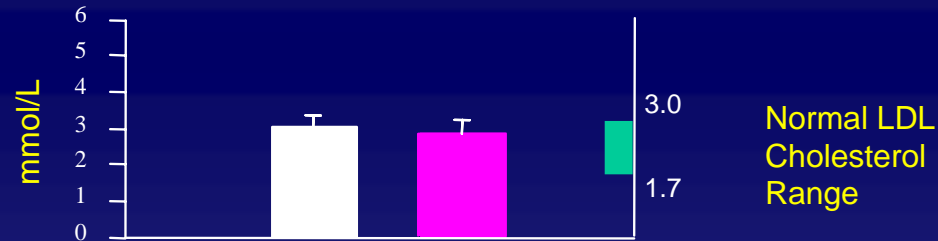


# Effect of 16:0 on Plasma Lipoprotein Cholesterol Values in Hypercholesterolemic Subjects Consuming Diets High in 18:2

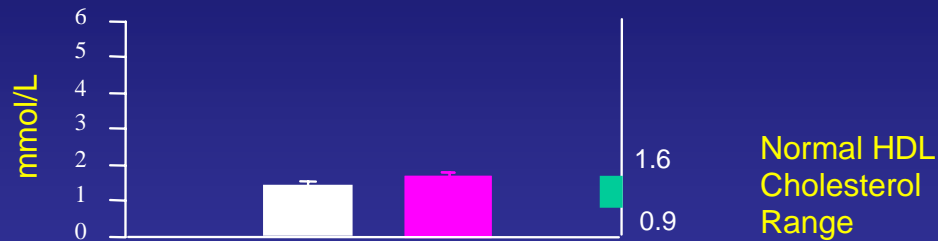
Total Cholesterol



LDL Cholesterol



HDL Cholesterol



Low C16:0      High C16:0

# Conclusions

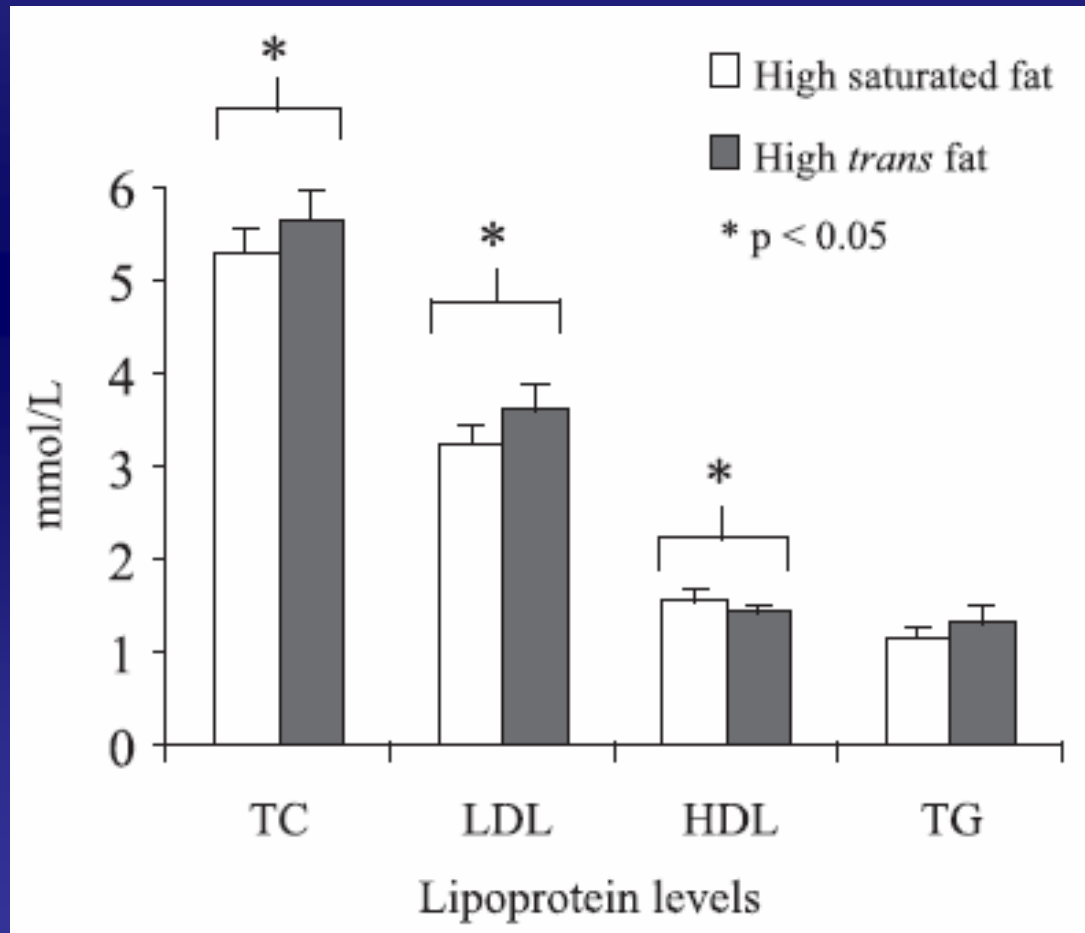
- Palmitic acid has relatively little effect on serum lipid profiles in the presence of higher intakes of linoleic acid

# Nutrient intake per day (% energy)\*

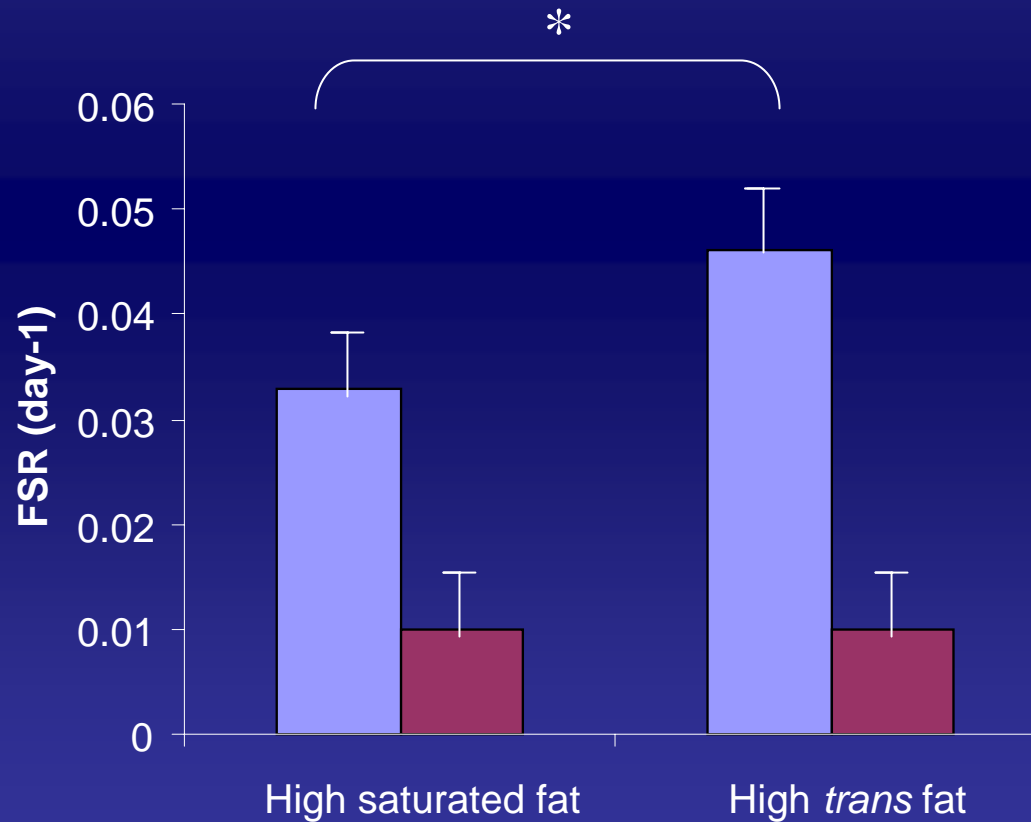
Nutrient	Baseline	High saturated fat	High trans fat
Total fat	29.3 ± 3.90	30.5 ± 1.59	29.9 ± 3.03
Cholesterol		213 ± 22	205 ± 19
16:0	9.77 ± 1.65	10.6 ± 1.51	4.54 ± 0.60
18:0	1.35 ± 0.25	1.31 ± 0.16	2.06 ± 0.33
18:1 (n -9)	11.42 ± 1.79	12.7 ± 1.45	7.75 ± 0.92
18:2 (n -6)	3.20 ± 0.58	3.54 ± 0.46	5.80 ± 1.11
18:3 (n -3)	0.14 ± 0.04	0.11 ± 0.08	0.49 ± 0.27
22:6 (n -3)	0.08 ± 0.12	0.14 ± 0.16	0.25 ± 0.17
Trans FA	n.d.	n.d.	5.59 ± 1.12
18:1 te	n.d.	n.d.	3.13 ± 0.67
18:1 (n -11t)	n.d.	n.d.	0.66 ± 0.20
18:1 (n13t)	n.d.	n.d.	1.14 ± 0.40
18:2 (n -6tt)	n.d.	n.d.	1.60 ± 0.10
18:2 (n -6tc)	n.d.	n.d.	0.25 ± 0.06

\* 18:1 te= *trans* elaidic acid, t=trans, tt=trans trans, tc= trans cis, n.d.= not detectable.  
 Nutrients analyzed from double portions of food consumed by volunteers (n=10)

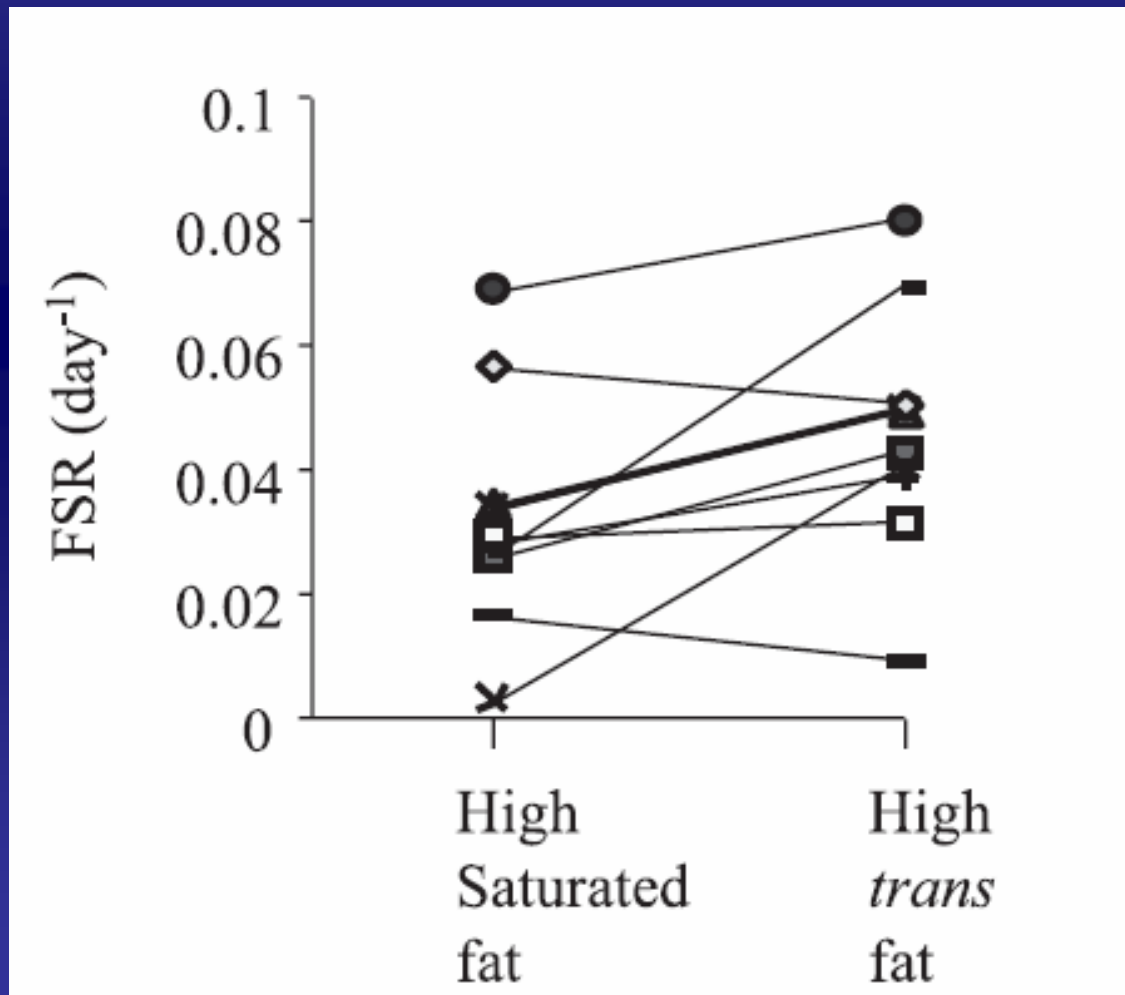
# Effect of consuming high saturated fat and high *trans* fat diets on plasma lipid and lipoprotein cholesterol levels (n=10). Values represent means $\pm$ SEM



# Effect of diet treatment on mean fractional synthetic rate (FSR) for cholesterol



# Individual subjects' fractional synthetic rates of total cholesterol after consuming a diet high in saturated faty and high in *trans* fat



# Plasma lipid and lipoprotein cholesterol concentrations (mmol/L) in subjects consuming 16:0 in the sn-1 vs. sn-2 position

## Diet Treatment

	Sn-2 16:0 low- 18:2n-6	Sn-1,3 16:0 low 18:2n-6	Sn-2 16:0 high 18:2n-6	Sn-1,3 16:0 high 18:2n	<b>Main effects</b>	
	<b>Mean</b>	<b>Mean</b>	<b>Mean</b>	<b>Mean</b>	Sn-2 vs. Sn-1, 3 16:0	Low vs. High 18:2n-6
TC	4.4	4.6	4.2	4.4	P=0.02	NS
HDL-cholesterol	1.0	1.0	1.0	1.0	NS	NS
LDL-cholesterol	2.8	2.0	2.7	2.7	NS	NS
TAG	1.2	1.6	1.2	1.5	NS	NS
TC: HDL ratio	4.3	4.8	4.2	4.4	P=0.0001	P=0.003

# Total cholesterol fractional synthesis rates in subjects consuming each diet treatment

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Diet treatment	Fractional synthesis rate (pools/d)	
	Mean	SEM
Sn-2 16:0 low 18:2n-6	0.054 <sup>a</sup>	0.005
Sn-1, 3 16:0 low 18:2n-6	0.040 <sup>b</sup>	0.004
Sn-2 16:0 high 18:2n-6	0.053 <sup>a</sup>	0.004
Sn-1, 3 16:0 high 18:2n-6	0.062 <sup>a</sup>	0.003

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<sup>A,b</sup> Mean values with unlike superscript letters are significantly different ( $p < 0.05$ ).

- 18:2n-6 is normally in the sn-2 position
- Cholesterol synthesis rate is lower when 16:0 is not in the sn-2 position at lower 18:2 intakes
- Does this mean that new interesterified fats having saturates in the sn-2 position normally occupied by 18:2n-6 will increase cholesterol synthesis?

# Average Daily Fatty Acid Intake for Children Aged 4-7 Assessed by 3-day Food Records

All subjects

(n=78)

Fatty acid intakes per day

$X \pm (SD)$

Median

Range

Linoleic acid 18:2 (g)

7.4 (3.3)

6.8

2.6-19

Linolenic acid 18:3 (g)

0.71 (0.5)

0.62

0.17-3.1

Arachidonic acid 20:4 (mg)

57 (35)

51

1.2-180

Eicosapentaenoic acid 20:5 (mg)

17 (36)

4.6

0.0-200

Docosahexaenoic acid 22:6 (mg)

37 (63)

16.5

0.0-350

N-3 (g)

0.75 (0.5)

0.72

0.18-3.1

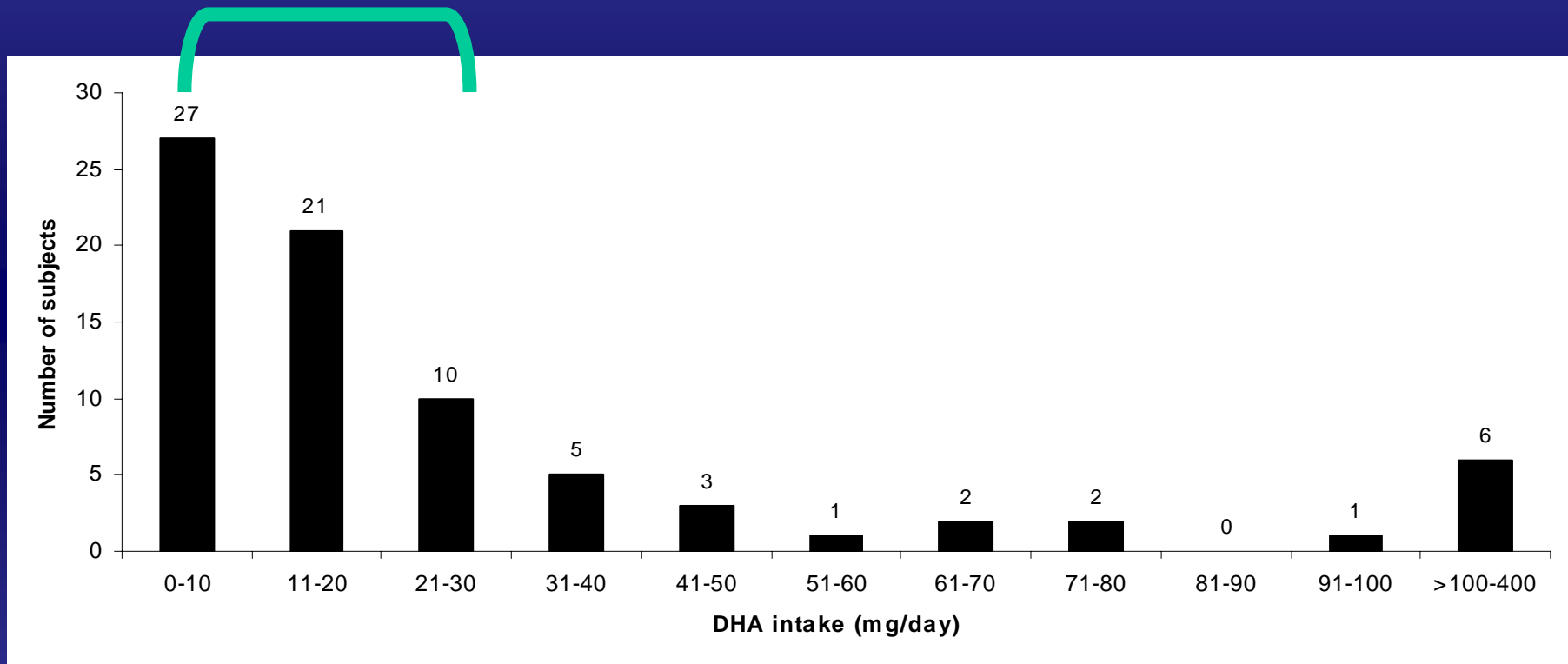
N-6 (g)

7.4 (3.3)

6.7

2.6-19

# Distribution of DHA intake (mg/day) assessed by 3-day food records for children aged 4-7 years



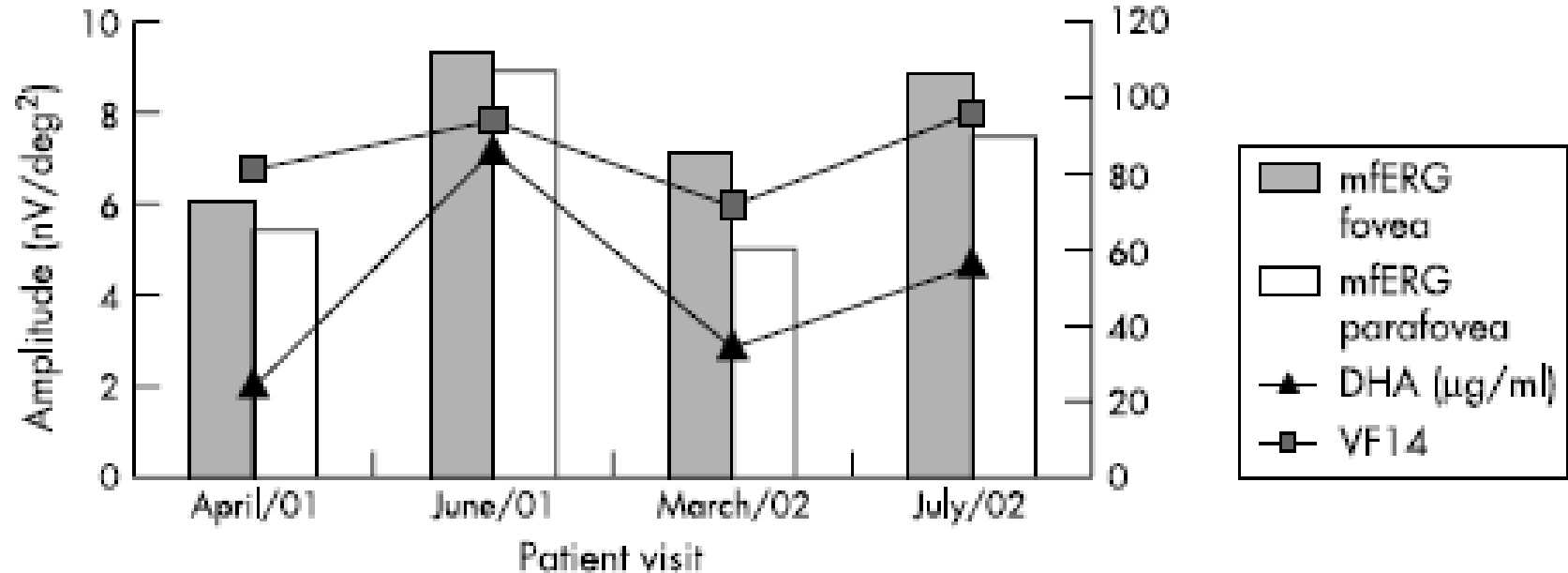
- Mean: AA:  $57 \pm 37$  mg/d; DHA  $37 \pm 63$  mg/d
- Median: AA 51 mg/d; DHA 17 mg/d

# The Main Balance in the Albertan's 100 grams

Other Sats	0-2	% Calories
16:0	25	8
18:0		
18:2n-6	18-25	6-8
20:4n-6	~0.5	0.2
18:3n-3	1-2	0.3-0.6
20:5n-3	2	0.6
22:6n-3		
Minor constituents	1-2	
18:1n-9	The balance	The balance

- Can we generalize the advice?
  - Effective public/ food policy
  - Take note of the history
  
- The New Nutrition Paradigm
  - Proteomics
  - Metabolomics
  - Suggests we need to better individualize the advice with the genotype
  - An example

# Effect of DHA on retinal function in patient with reduced ELOVL4 function



# The Future:

- Genetically defined differences in:
  - Rates of conversion of precursor essential fatty acids to metabolites
  - Fatty acid elongation
  - Affected by diet in ways that alter disease risk and disease progression

# Food Sources of Fatty acids

- Novel sources
- GMO sources
- DHA grown in the field or plantation
- Risk and safety assessment

Before we repeat the sort of history  
acknowledged earlier

# Concluding Remarks

- Difficult to assess effect of one FA
  - Change in one FA must be at expense of others
  - Testing abundance of one FA or absence of another?
- FAs exert effects at cell membrane (Clandinin, *FEBS Letters*, 1976)
  - FAs in diet → FA membrane composition
- FA balance important
  - Test within range of human intake

# What is the Big Current Issue?

- How to reduce trans intake
- Source of saturates
  - Palm oil                      Hydrogenation
  - Dairy fat      *versus*      Interesterification
  - Other SFA

I'M WORRIED. HOW CAN MANKIND SURVIVE WITHOUT HUNDREDS OF SCIENTIFICALLY FORMULATED DIETARY SUPPLEMENTS AND A CAREFULLY PLANNED EXERCISE PROGRAM?

