Calorie Restriction, Fasting, Ketosis and Cancer

What you need to know ….

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Obesity, Chronic Disease, Cancer

Calorie Restriction

Fasting

Ketogenic Diet

Recommendations

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20% of all cancers diagnosed in the US are related to **lifestyle** and thus could be prevented

(WCRF)

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Obesity and Chronic disease

Associated with the following cancers:

- Thyroid
- Adenocarcinoma esophagus
- Stomach
- Pancreas, gallbladder, liver
- Multiple myeloma
- Post menopausal breast
- Ovarian, endometrial
- Kidney
- Colon
- Advanced prostate

- Inflammation
- Insulin resistance
- Metabolic dysregulation
- Oxidative stress

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Diabetes and Cancer

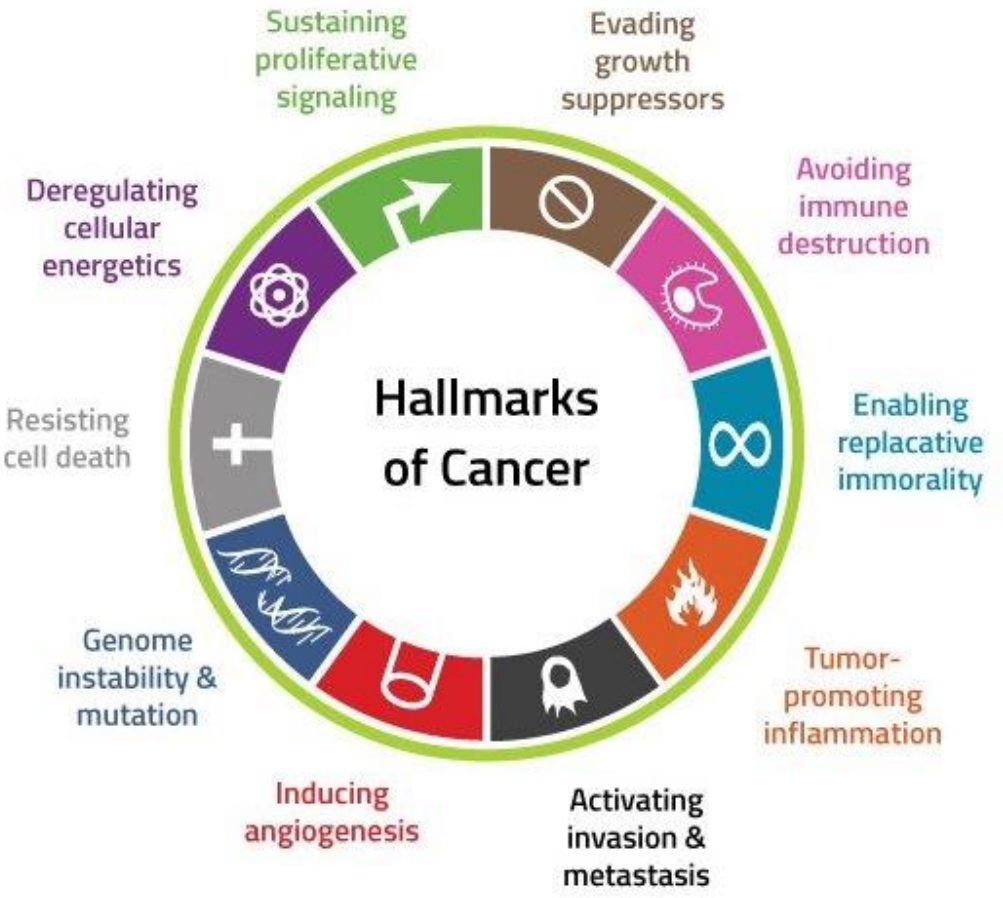
- Increases risk of developing cancer
- 8-18% prevalence of DM among newly Dx cancer pts
- Having DM at Dx of cancer increases mortality rate by 40%

The Hallmarks of Cancer

Obesity,
Hyperinsulinemia

Obesity
Warburg effect

Obesity
Altered macrophage function



Obesity
Reduced Apoptosis

Obesity
Inflammation

VEGF

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Calorie Restriction

Chronic reduction of energy intake by 20-40% without resulting in malnutrition

Metabolic effects:

- ↓ adiposity
- ↓ inflammation
- ↑ insulin sensitivity
- ↓ blood glucose
- ↓ growth factor signaling
- ↓ angiogenesis

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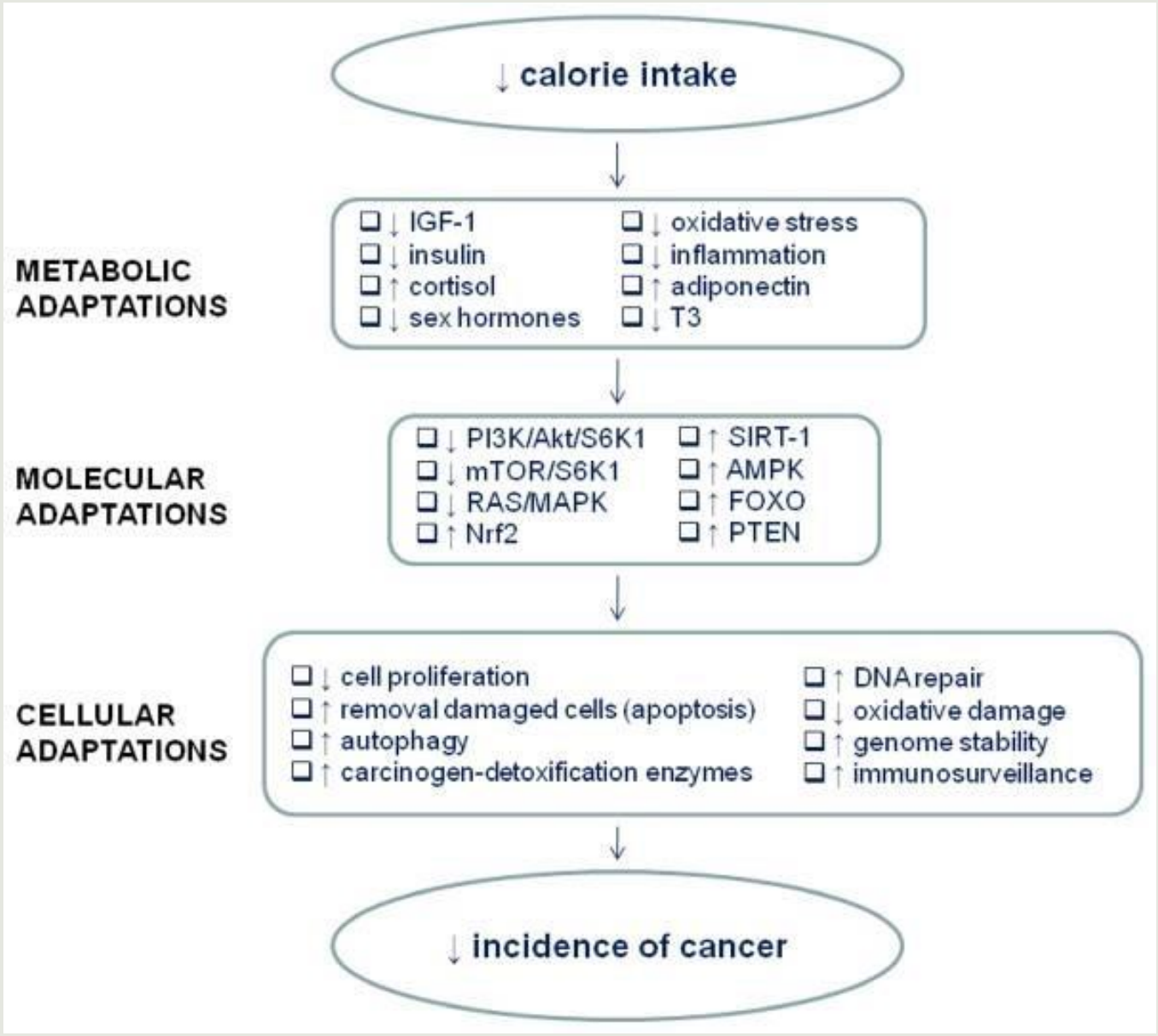

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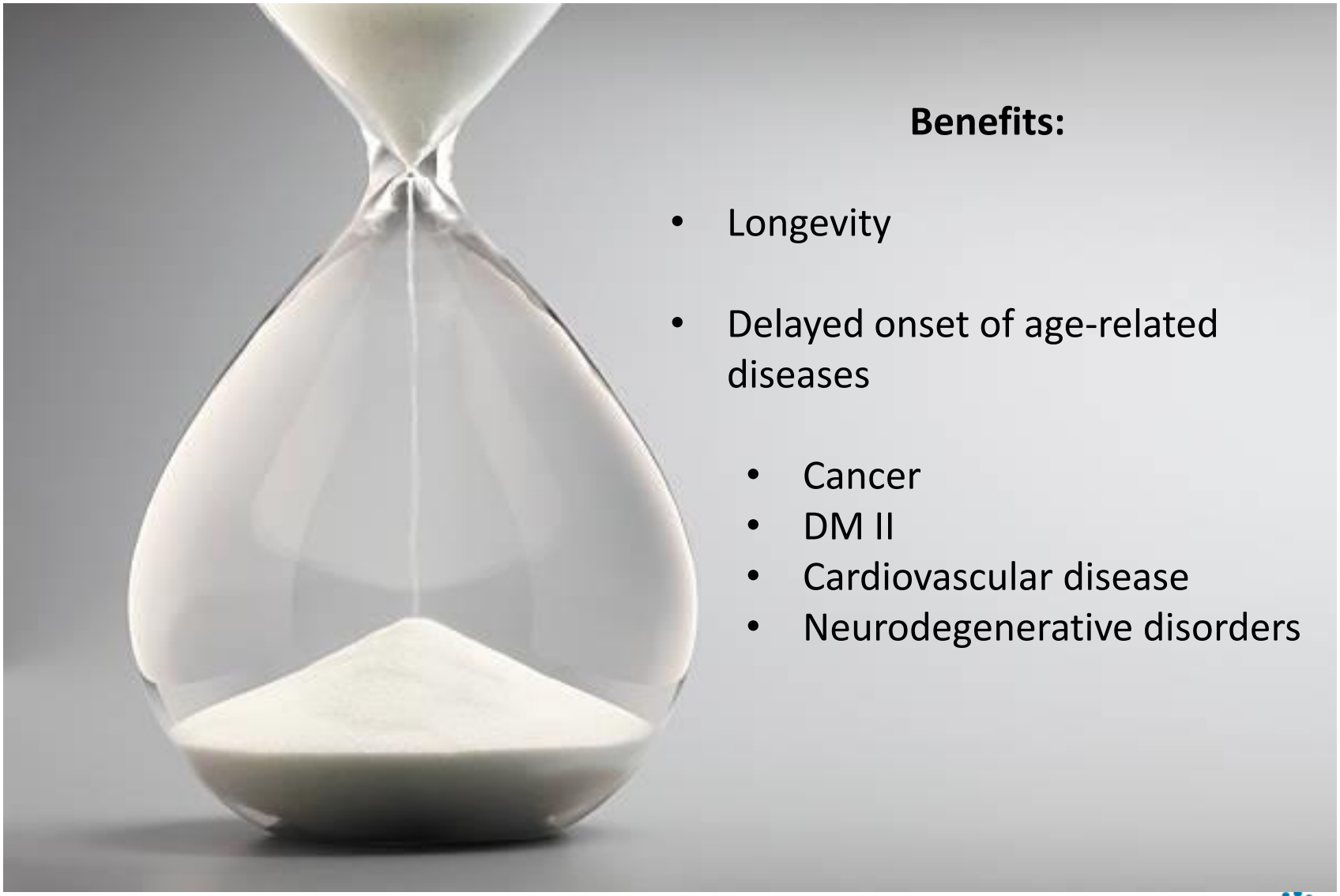
Calorie Restriction and Disease Prevention



Benefits:

- Longevity
- Delayed onset of age-related diseases
  - Cancer
  - DM II
  - Cardiovascular disease
  - Neurodegenerative disorders

Calorie Restriction and Cancer Tx

Limitations

- Duration to achieve metabolic benefits
- Weight loss/ malnutrition
- Sarcopenia/ cachexia

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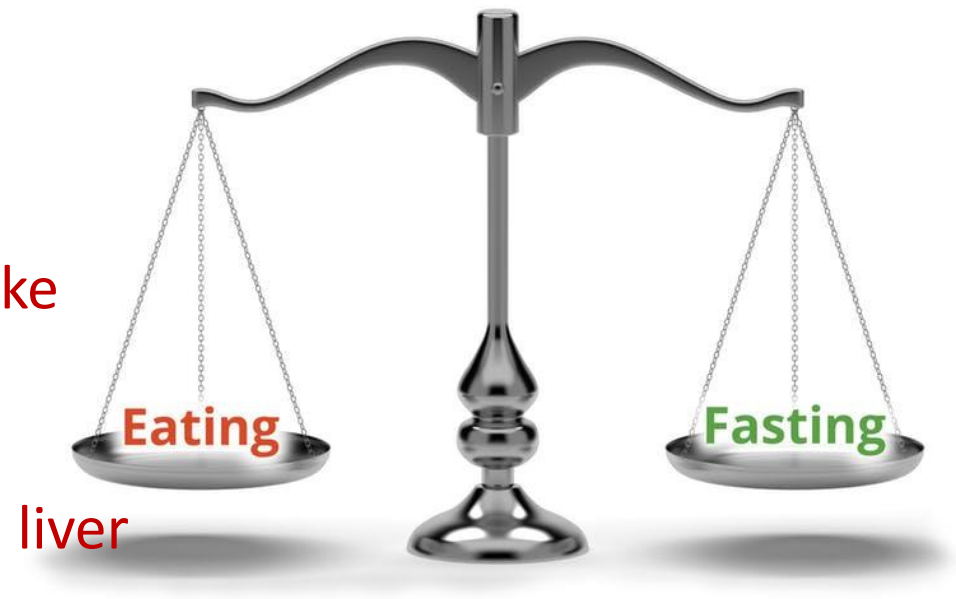
Fasting

Voluntary withholding of food for spiritual, health and other reasons

Eat food
↓
Insulin
↓
Glucose uptake in cells
↓
Sugars stored in liver
Fatty liver



No food
↓
↓Insulin
↓
Burn stored sugars
↓
Burn fat

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Fasting regimens

Short fasts/ Intermittent fasting

- Generally <24 hours fasting
- Flexibility
- Can be done more frequently
- Eat 2-3 meals within the eating window
- Less time for snacking

Hydration during fasting is vital

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Fasting regimens

Longer fasts

- >24 hours fasting
- Alternate day fasting (5:2)
- Extended fasting

Hydration during fasting is vital

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Fasting

Glucose depletion → glycogen → amino acid (glucose)
fatty acids (ketones)

Metabolic effects:

- ↓ Blood glucose
- ↓ A1c
- ↑ Insulin sensitivity
- ↓ Triglycerides
- ↓ Inflammation
- ↓ Weight
- Cellular protection (healthy cells)
- Protection from oxidative stress (healthy cells)
- Greater changes in short term compared to CR

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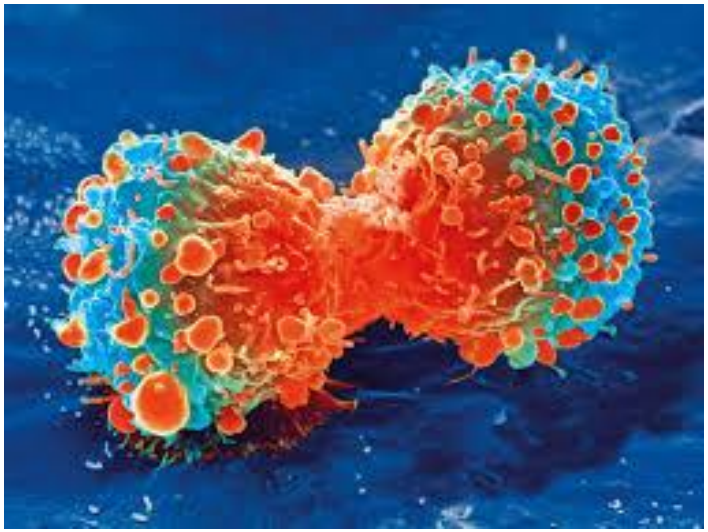
Fasting and Cancer



4 Studies in humans (2009-2015):

Durations: 24-180 hours fast
Various cancers and Breast cancer

- ↓ fatigue, weakness and GI side effects in fasting group (Safdie, 2009)
- ↑ erythrocyte, thrombocyte count 1w post chemotherapy in fasting group (de Groot, 2015)
- 72 hour fasting group showed N lymphocyte counts and maintenance of N WBC balance (not 24h group) (Cheng, 2014)
- ↓ fatigue, nausea, vomiting, constipation and CIPN (48-72h fasting group)
- ↓ DNA damage (48-72h fasting group), ↑ DNA damage in (24h fast group) (Dorff, 2016)

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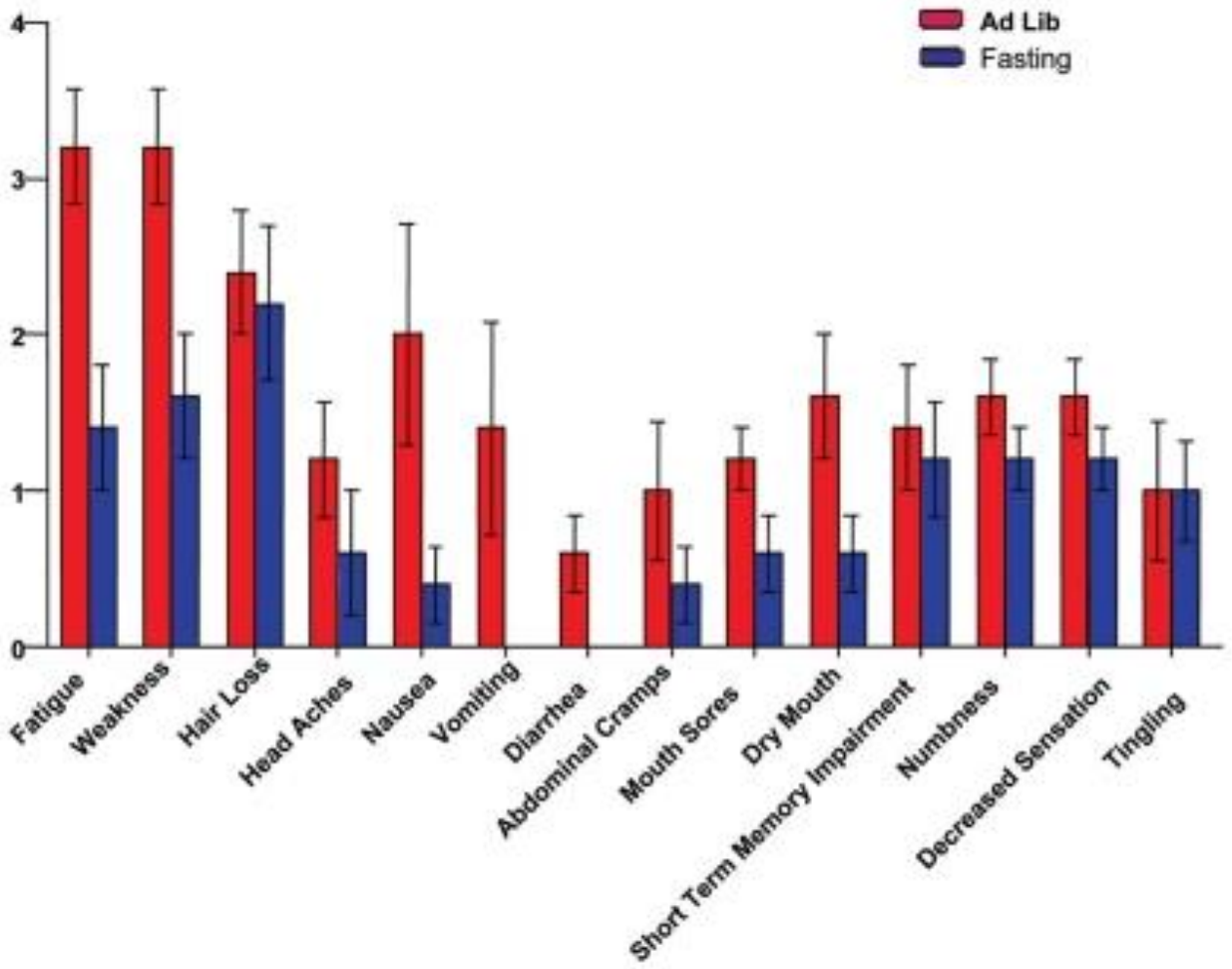

Average self-reported severity of symptoms in patients that received chemotherapy with or without fasting (Dorff, 2016)

Caution!

- Limited research in humans
- Small studies
- Mostly safety and feasibility studies
- Tumor growth, metastasis, prognosis not evaluated
- Diabetics?
- Elderly/ frail?
- Cachexia?
- Determine optimal duration
- Cancer types
- Chemotherapy protocols

MUCH MORE RESEARCH NEEDED!

Ketogenic diet

Very Low Carbohydrate High Fat diet

- Restricting CHO (<50 g/d), adequate Protein, high fat
- Encourage Whole Foods diet
- Metabolic approach using Ketone bodies as a principle energy source
- Combined with calorie restriction as indicated
- Administered under medical supervision

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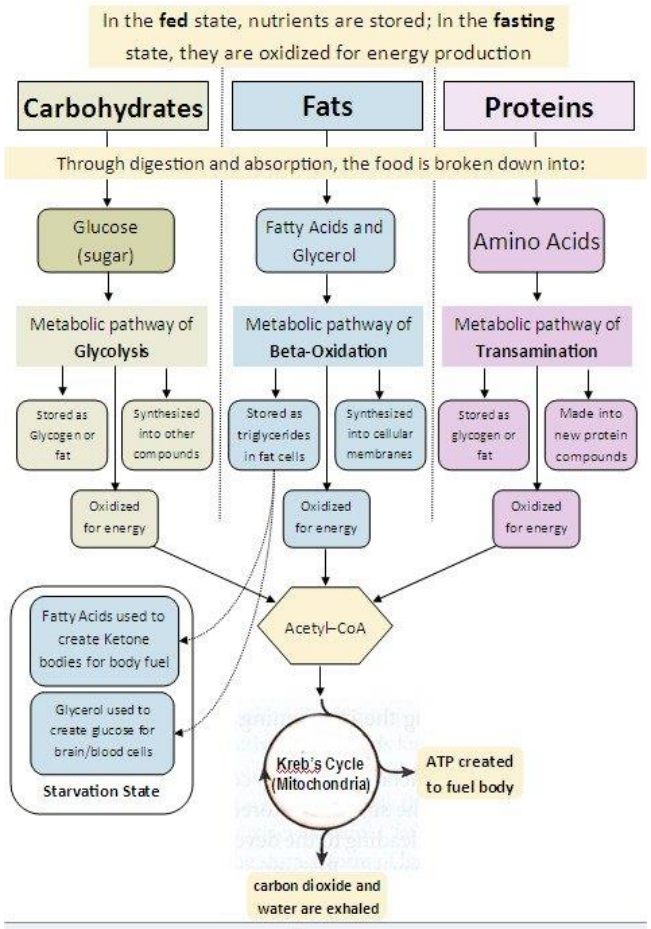
Metabolic response to Macronutrients

"Feasting"

CHO > Glc (Insulin response)
- ATP formation
- Glycogen (storage)
- Excess (adipose tissue)

Fats > Lipoprotein (LDL/ HDL)
- Excess (adipose tissue)

Protein > Amino acids
- Protein synthesis
- Amino acid pool
- Excess (urea or keto acids > energy source, gluconeogenesis, adipose tissue)



"Fasting"

CHO, fat, protein metabolized to Acetyl CoA (ATP in mitochondria)

"Starvation"

Glycogen depletion > ↓Insulin levels drop > body mobilizes stored fat
- Fatty acids in circulation
- Liver forms ketones
- Brain oxidizes ketones as E source > ↓ Glc demand > ↓gluconeogenesis
- Preservation of muscle

KETOSIS = Starvation without hunger

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Benefits of Ketosis

- Anti-seizure effect
- Adequate protein intake maintain LBM
- Adipose tissue utilized in ketone production > weight management
- Ketone bodies = appetite suppressing effect
- Improved metabolic markers
    - ↓ TG, ↑ HDL
    - ↓ insulin resistance
    - ↓ Glc levels
    - ↓ markers of inflammation

Careful consideration

TEAM APPROACH

- History of pancreatitis
- Active gallbladder disease
- Impaired liver function
- Impaired fat digestion
- Poor nutritional status
- Gastric bypass surgery
- Abdominal tumors
- ↓gastrointestinal motility
- History of kidney failure
- Pregnancy and lactation

Ketosis is NOT Ketoacidosis

Ketoacidosis

- ↓ Insulin → ↑ BG → release of fats from fat cells → ↑ ketone production
- ↑ BG + ↑ketones → disruption of the normal acid/ base balance
- Life threatening

Ketosis

- Fasting → ↓ BG →↓ Insulin→ ↑ fatty acids mobilization → ↑ ketone body
- Controlled process
- Beneficial metabolic results

Ketosis is NOT Ketoacidosis

	Normal diet	Ketosis	Ketoacidosis
BG	80-120 mg/dL	65-80 mg/dL	300 mg/dL
Insulin	6-23 microU/L	6.6-9.4 microU/	~/= 0 microU/L
BHB	0.1 mM	7/8 mM	>25 mM
pH	7.4	7.4	<7.3

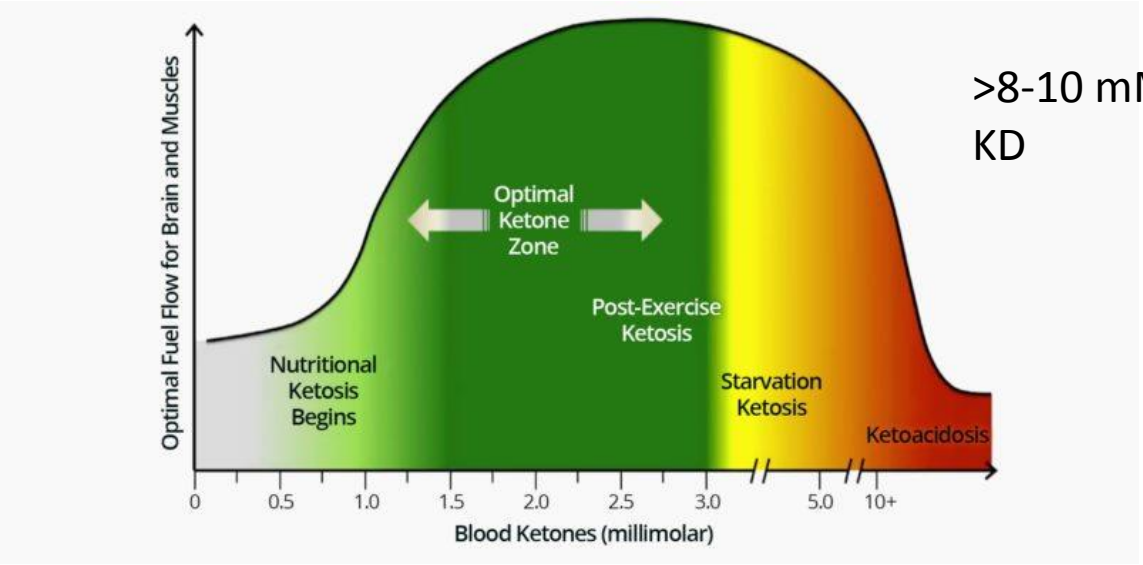
Monitoring Ketosis and Ketosis goals

Measuring:

Urine ($)	Ketostix
Breath ($$)	Ketonix
Blood ($$$)	Precision Xtra
	Keto-Mojo

Therapeutic goals:

0.5-1.5 mM/L ketosis	Light nutritional
1.5-3.0 mM/L	Optimal Ketosis
>3 mM/L	Generally no necessary to achieve these levels (GBM, seizure d/o)
>8-10 mM/L KD	Unlikely to achieve on



GKI can also be used if desired

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THE KETOGENIC FOOD PYRAMID

Carbohydrates

Keep carbohydrates to a maximum of 5% of your total daily calorie intake. Making up of mostly green cruciferous vegetables. **Avoid all sugars, starches, grains, bread, pasta, fruits** (except avocado).

5%

Protein

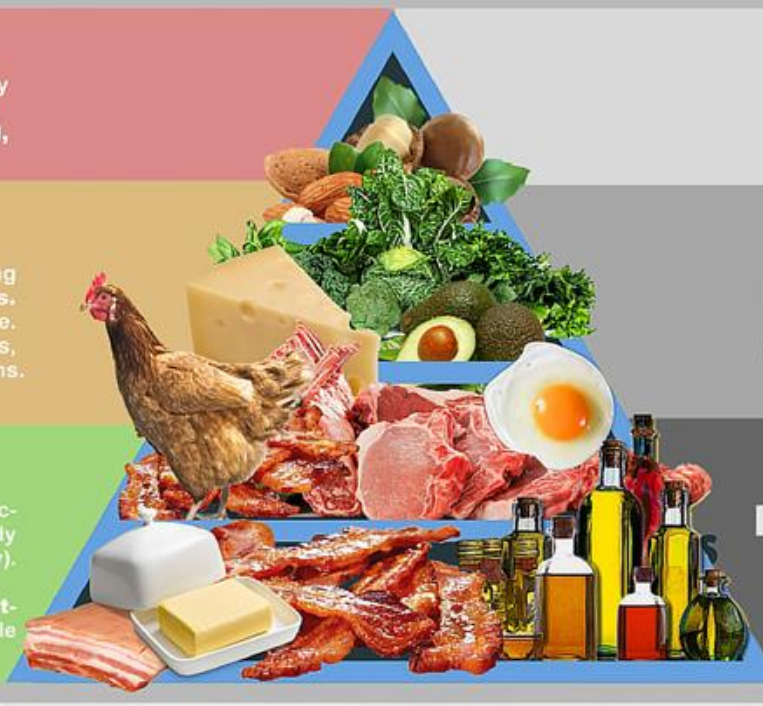
Protein is essential for muscle retention and muscle building but **too much protein can keep you out of Ketosis.** Limit your protein intake to 25% of your daily calorie intake. Excellent sources of protein are: Fatty cuts of meat, eggs, full fat cheeses. Avoid milk, fat reduced chesses and creams.

25%

Fat

Fats will make up a dominant portion of a Ketogenic Diets macronutriets. When fat intake is high and carbs are low the body will resort to using fat as fuel through **Ketosis** (put simply). When possible your fat intake should come from **Saturated Fats** (Butter, Coocnut Oil etc) & **Monounsaturated Fats** (Avocado, Macadamia Nuts etc). Ensure you get ample Omega-3's in your diet as well.

70%



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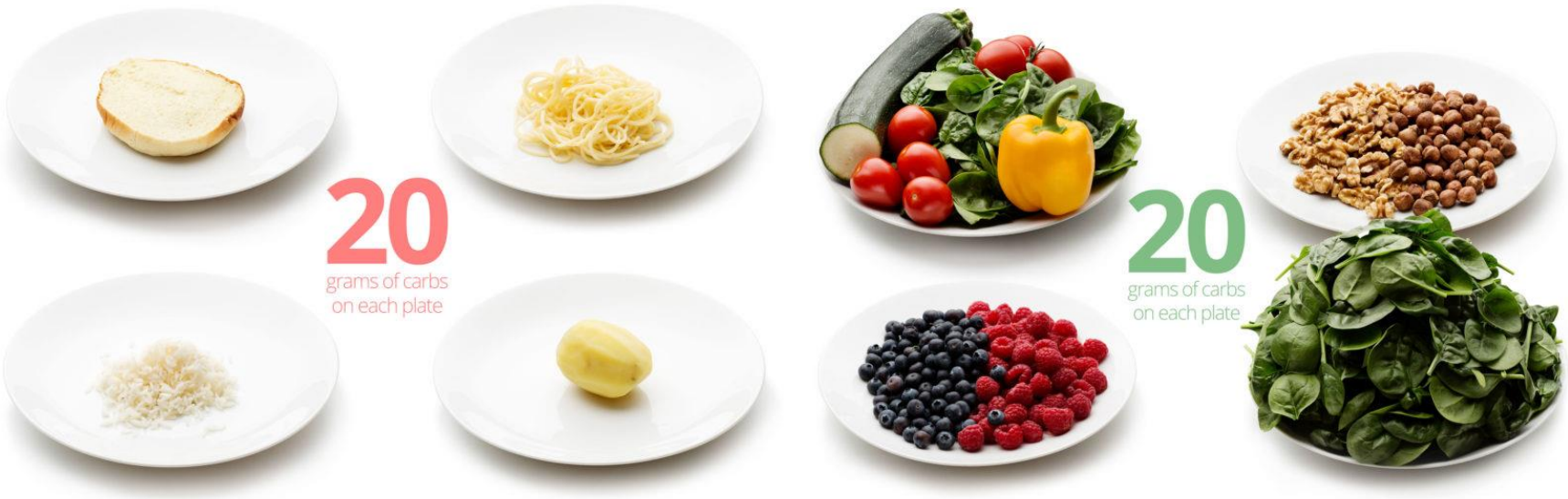
20 grams of CHO



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Common and manageable side effects

Keto flu (2-3 d after starting KD)

- Headache
- Fatigue
- Dizziness
- Light nausea
- Irritability, “brain fog”
- Sugar cravings

Adequate hydration
Electrolyte replacement (K, Mg, Na)

Leg Cramps	Hydration, Mg supplementation, adjust CHO
Constipation	Hydration, Fiber, MOM/ Miralax
Keto breath	Hydration, adequate Na, oral hygiene, adjust CHO
Palpitations	Hydration, Na
Gout	Hx of gout?, Limit ETOH, Allopurinol

Ketogenic Diet

- Is patient motivated/ Ready for change
- Goals of ketosis
- Baseline nutrition knowledge
- Support
- Short term intervention vs lifestyle change
- Diet expansion (portion control, fiber rich nutrient dense choices)
- Reassess

Keto
<20 g/d

Moderate low CHO
20-50 g/d

Liberal low CHO
50-100 g/d

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BEST RECOMMENDATIONS

CANCER PREVENTION and CANCER SURVIVORS

1. Achieve a healthy weight through diet and regular physical activity
2. Whole foods
3. Anti-inflammatory diet
4. Healthy fats with every meal
5. 2-4 oz protein protein from a variety of sources with every meal
6. Extend fasting time between dinner and breakfast >13 hours
7. Limit intake of added sugars and processed foods

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BEST RECOMMENDATIONS

PATIENTS UNDERGOING Tx

- Work with a knowledgeable provider if considering CR/ Fasting/ KD
- Maintain weight if underweight or desirable weight
- Controlled weight loss if overweight
- What you eat matters
- Optimal blood glucose levels
- Nutrient dense foods
- Whole foods
- Healthy protein sources
- Avoid processed foods
- Limit added sugars
- Hydrate
- Keep moving

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What and how we eat matters!

All the time!

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