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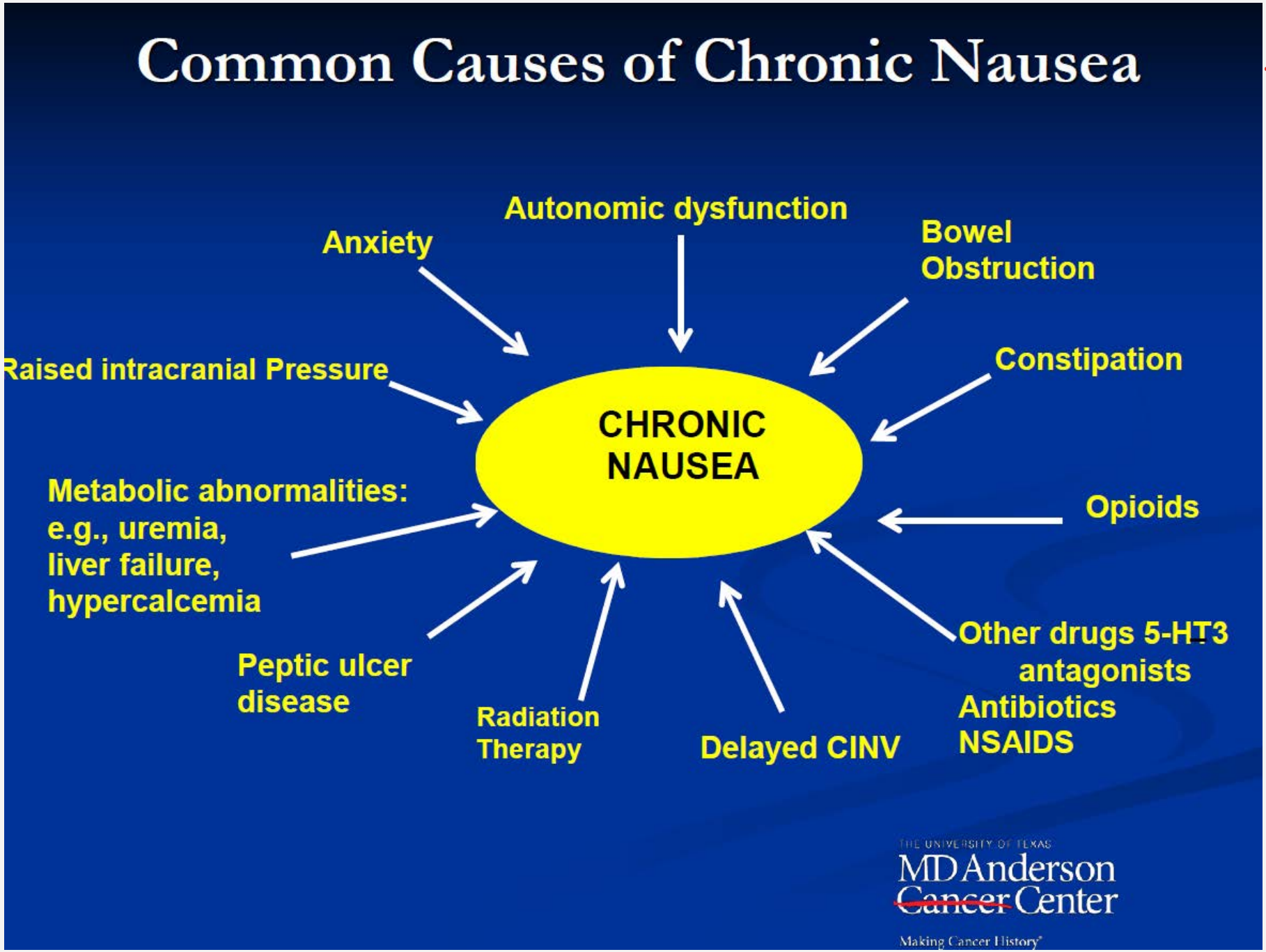
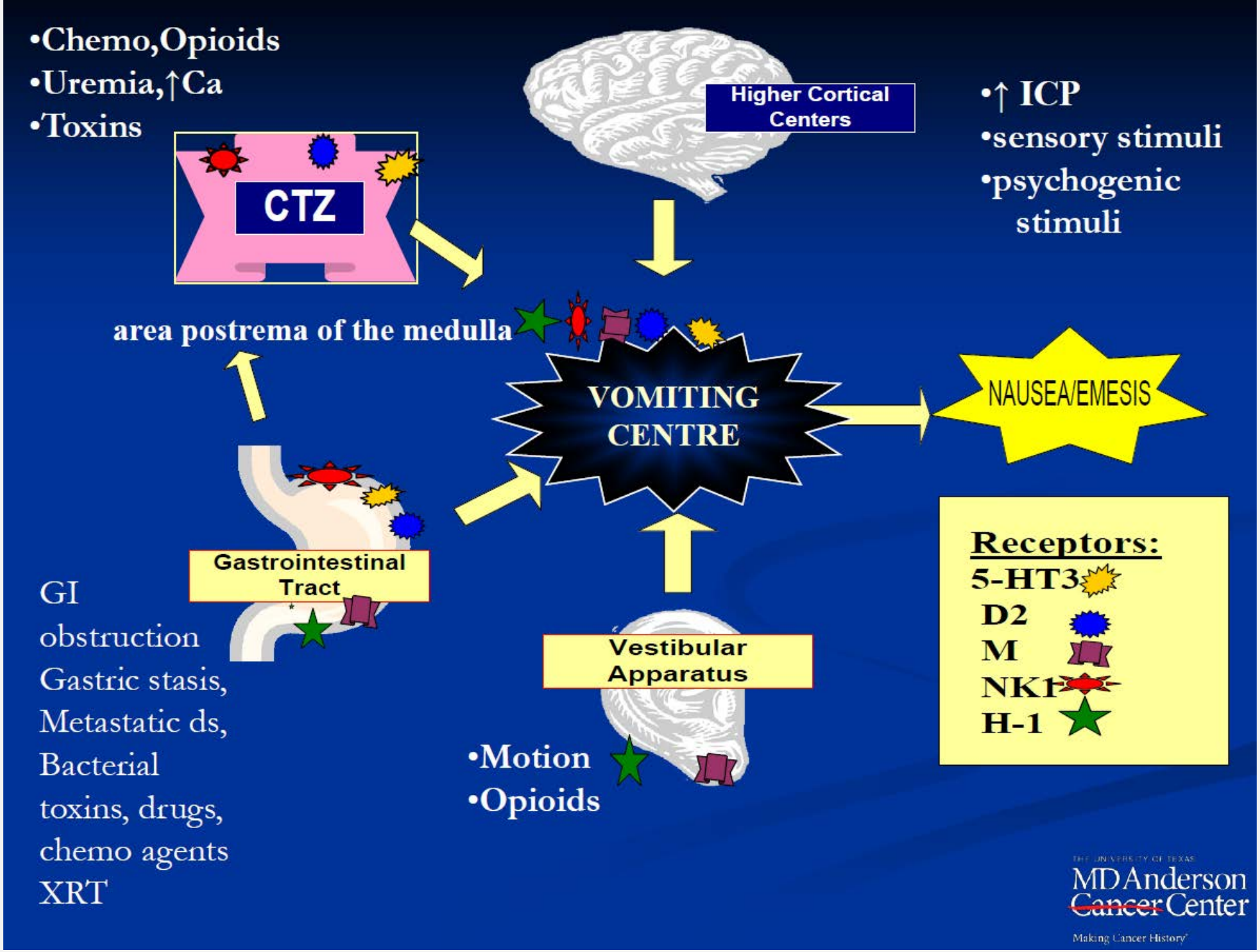
CHRONIC NAUSEA




•Chemo,Opioids
•Uremia,↑Ca
•Toxins
Higher Cortical Centers
•↑ ICP
•sensory stimuli
•psychogenic stimuli
CTZ
area postrema of the medulla
VOMITING CENTRE
NAUSEA/EMESIS
Gastrointestinal Tract
GI obstruction
Gastric stasis,
Metastatic ds,
Bacterial toxins, drugs, chemo agents
XRT
Vestibular Apparatus
•Motion
•Opioids
Receptors:
5-HT3
D2
M
NK1
H-1
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Specific Treatment

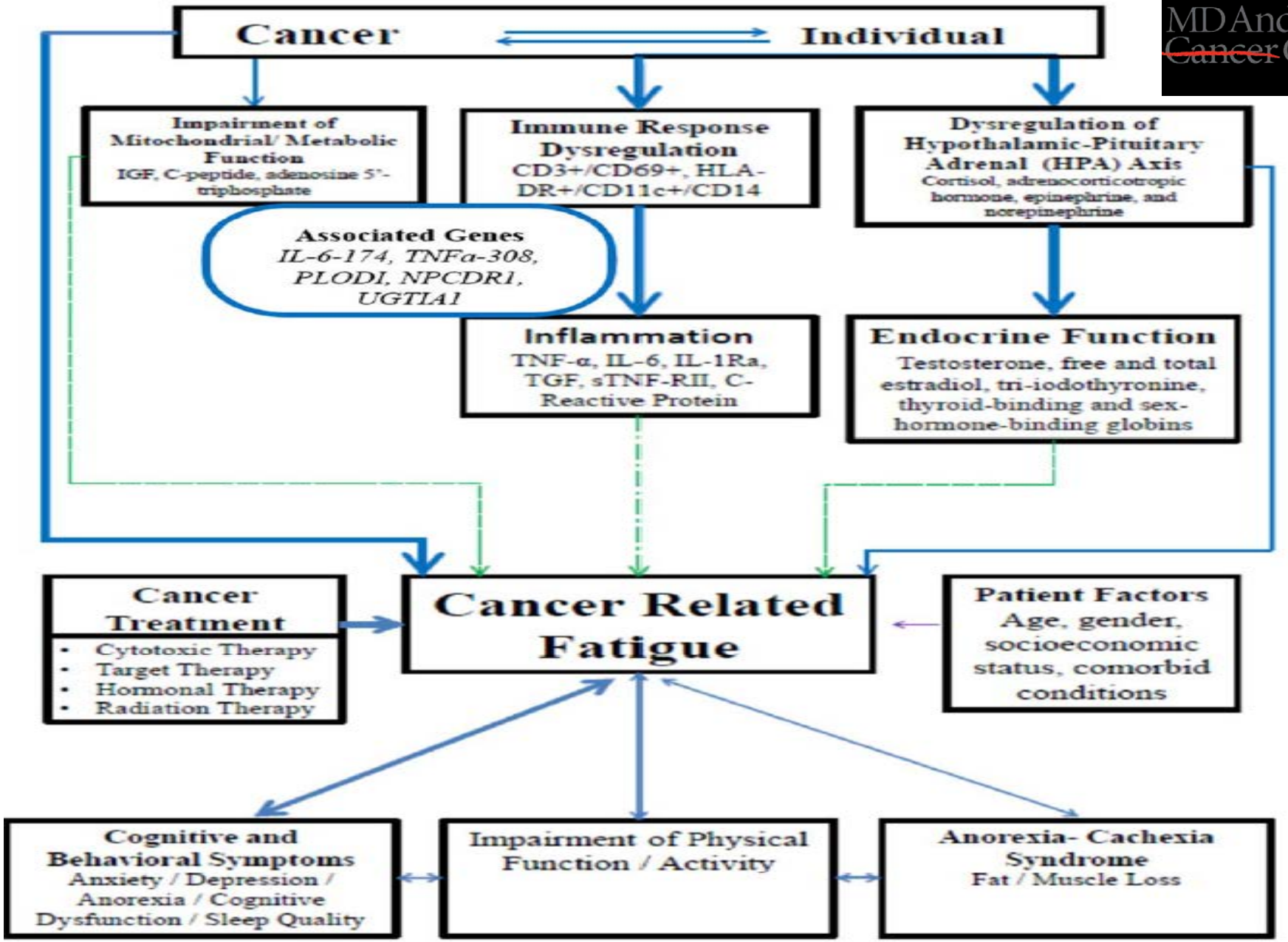
Treat underlying etiology…….Are there multiple etiologies ?

Hypercalcemia	Hydration,bisphophonates
Opioid toxicity	Opioid rotation/decrease dose
Constipation	Agressive bowel regimen. ? Xrays
Gastric ulceration	PPIs,H2-antagonists
Infection	Antibiotics
Tense ascites	Paracentesis, consider IP cathetor
Anxiety	Counseling, Anxiolytics
Brain metastases	Radiation therapy, Sterioids
Malignant bowel obstruction	? Pt prognosis; Resection, bypassing, or stenting, venting gastrostomy

Anti-emetic Agents

Class	Medication
Dopamine antagonist ***Mainly acts CTZ***	▪ With prokinetic effects ▪ Metoclopramide ▪ Without prokinetic effects ▪ Haloperidol, Prochlorperazine, Chlorpromazine, Promethazine
H1 receptor blockers	Promethazine, Diphenhydramine, Meclizine, Hydroxazine,
Ach antagonist	Scopolamine (transdermal), Hyoscyamine, Glycopyrrolate
5HT3 antagonists	Ondansetron, Granisitron, Dolasetron
Other useful agents…	Dexamethasone, Dronabinol, Lorazepam

CANCER RELATED FATIGUE



MASCC Biomarker Group
Saligan et al JSCC 2015

Investigations

Medical Condition	Assessment Modality
Anemia	Complete blood count, serum vitamin B_{12} , folate, iron, transferring saturation, ferritin levels, fecal occult blood tests, and, if positive, further evaluation for blood loss
Medication side effects and polypharmacy	Anticholinergics, antihistamines, anticonvulsants, neuroleptics, opioids, central α antagonists, beta-blockers, diuretics, SSRI and tricyclic antidepressants, muscle relaxants and benzodiazepines
Cognitive or functional impairment	Assessments such as ADL, IADL, MMSE, and "get up and go" test
Mood disorders	Assessment of depression and anxiety following the DSM IV criteria
Side effects of primary disease treatment	Recent radiation therapy, chemotherapy, surgery
Malnutrition	Serum albumin, pre-albumin, cholesterol
Infections	Blood cultures, urine culture, chest radiography, HIV antibody, RPR, PPD skin test
Other contributing medical conditions	Directed based on clinical finding

Yennu & Bruera JAMA 2007

CRF Management

Specific treatment of underlying causes

- Cachexia
- Autonomic failure
- Anemia
- Infection
- Hypoxia
- Hypogonadism
- Depression
- Others

Symptomatic Treatment

Pharmacological & Complementary

- Corticosteroids
- Psychostimulants(?)
- New agents
  -Ginseng?

Non-pharmacological

- **Energy conservation**
- **Physical Activity (Aerobic or Resistance)*; Yoga***
- **Psychosocial:**
  - **Cognitive Behavioral therapy* (CBT-BT-CBT-I)**
  - **Mindfulness based stress reduction**
  - **Psycho-educational**
  - **Supportive Expressive Therapy**
- **Massage?**
- **Acupuncture?**
- **Qigong?**

* Level 1 evidence

ANOREXIA -CACHEXIA

International Consensus Definition

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- Two group:

1. Cachexia (>5% WL < 6 months OR >2% + BMI <20)
2. No cachexia

- Four group:

1. No cachexia
2. Pre- cachexia (<5%)
3. Cachexia (>5% OR >2%+BMI <20)
4. Refractory (>15%+BMI<23 OR >20% + BMI <27)

Cachexia: Clinical Significance

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Prevalence in Cancer:

- 50-80%; 4 of 5 pts in adv stages
- GI >lung > breast 80%/60%/40 %

Clinical Outcomes: "Bad Condition"

- Shortened survival
  - leading cause of death; 20-30%
- Impacts Rx decisions, and outcomes of cancer Rx
- ↑ Morbidity
- ↓ QoL
- Psychological distress ~35-75%.

DeWys 1980; Vigano 2000; Wigmore 1997, Andreyev 1998; Bruera 1997

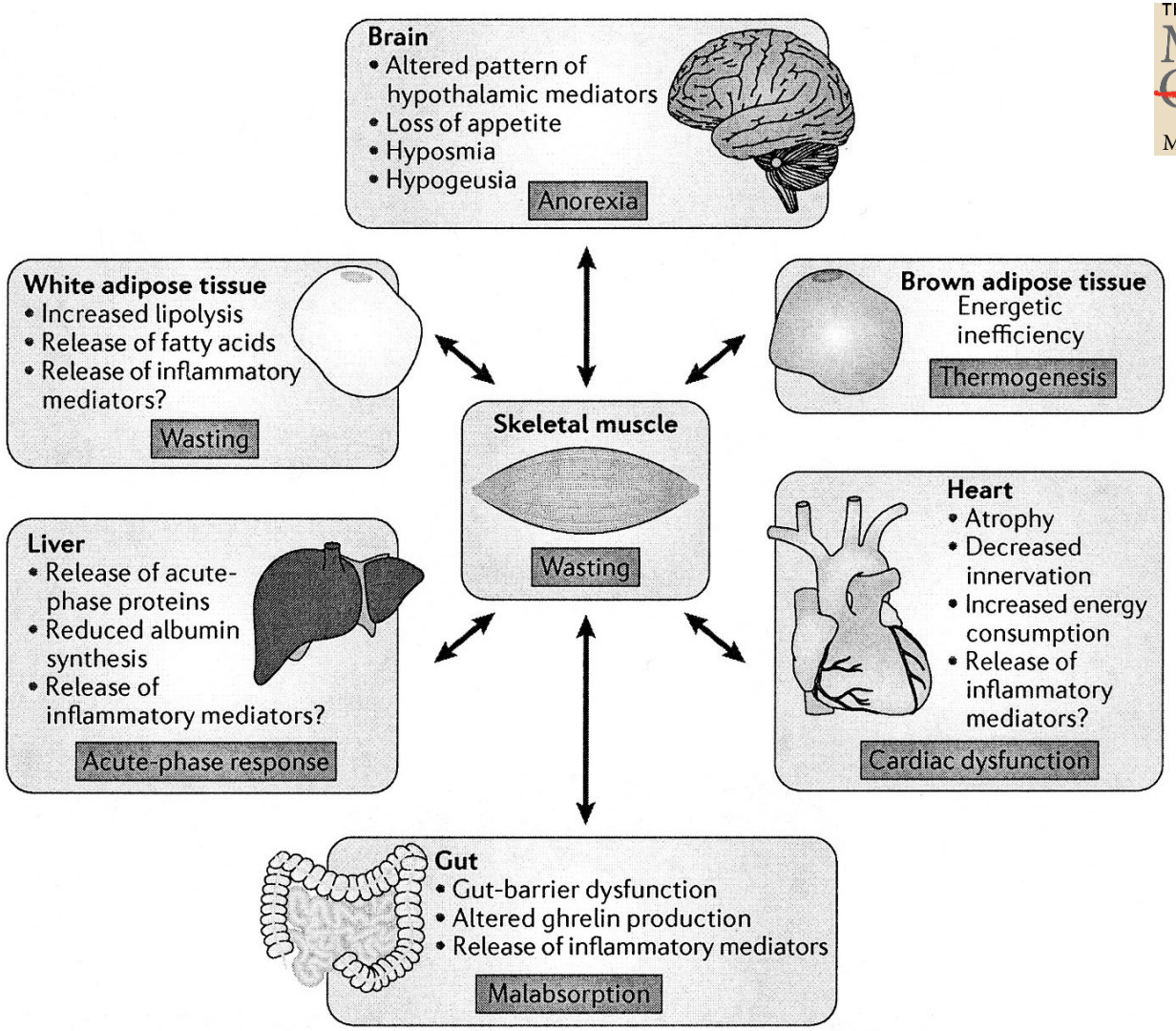

Figure 4 | **Cachexia as a multi-organ syndrome.** In addition to skeletal muscle and adipose tissue, other organs are affected by the cachectic process. In fact, the wasting that takes place in muscle could well be dependent on alterations in other organs or tissues, such as white adipose tissue (see the main text). Abnormalities in heart function, alterations in liver protein synthesis, changes in hypothalamic mediators and activation of brown adipose tissue are also involved in the cachectic syndrome.

Argilés, J – Nature Reviews 2014

Anorexia / Cachexia: Metabolic Alterations

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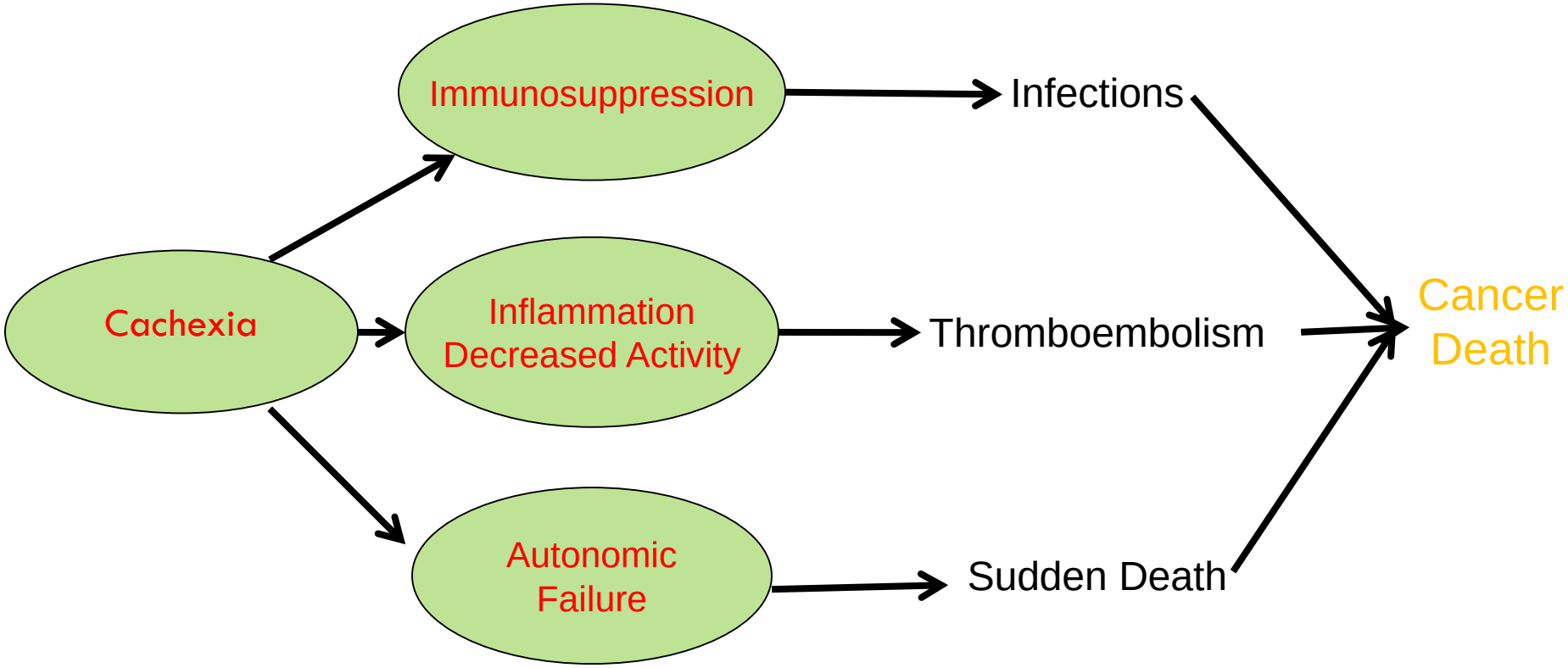
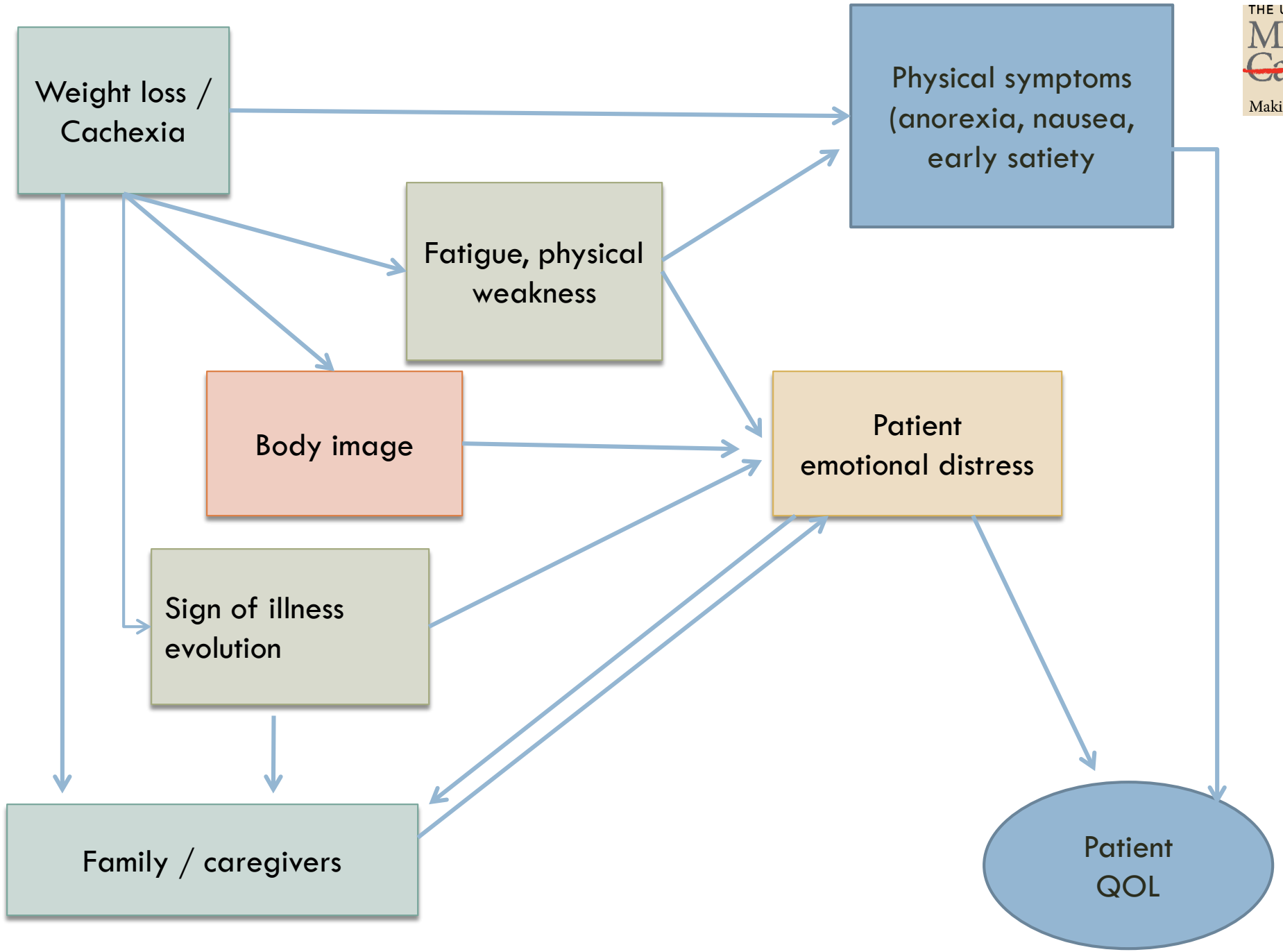
	Cachexia	Starvation
Energy expenditure	⇑	⇓
Proteinsynthesis		
• overall	⇑	⇓
• muscle proteins	⇓	⇓
• acute phase proteins	⇑	⇔
Proteolysis		
• muscle proteins	⇑⇑	⇑
Lipogenesis	⇓	⇓
Lipolysis	⇑	⇑⇑
Glucose turnover	⇑	⇓
Ketone bodies	⇓	⇑

Cachexia


Immunosuppression
Infections
Cachexia
Inflammation
Decreased Activity
Thromboembolism
Cancer
Death
Autonomic
Failure
Sudden Death



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Management of Anorexia-Cachexia

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Single modality/agent unlikely to be successful

- Treat causes of secondary cachexia
- Appetite stimulants
- Appropriate nutrition
- Identify and treat deficiencies
  - Testosterone , Thyroid, Vitamin D, B-12, folate
- Empiric treatment with multivitamin and omega-3 fish oil
- Exercise
- Anti-catabolic/Anti-metabolic agents/*Anabolic agents*

Treatment of secondary cachexia

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Symptoms	Examples of Interventions
Early satiety	**Metoclopramide, small frequent meals**
Nausea	Metoclopramide
Dysphagia	Swallow evaluation as appropriate; Antifungal, antiviral agents
Mucositis	Opioids, antifungal, antiviral
Constipation	Laxatives
Delirium	Identify cause, haloperidol, atypical agents (olanzapine)
Depression	Counseling, anti-depressants

Appetite Stimulants

- Progestational agents - megestrol acetate
- Corticosteroids –dexamethasone, prednisone
- Dronabinol
- Ghrelin or ghrelin mimetics

  - **None of the above prevent muscle loss**
  - **No improvement in survival**

Cannabinoids

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- Delta-9-tetrahydrocannabinol (THC): Dronabinol

- Indications for dronabinol (FDA approved):
  - **AIDS related anorexia**
  - **Chemotherapy-induced Nausea**

- AIDs patient study (n=139) : oral dronabinol vs. placebo *
  - significant improvement: ***Appetite, mood and Nausea***
  - **no body weight gain**

Side effects: **Somnolence, dizziness confusion, perceptual disturbance**

**Beal. JPSM 1995*

Other Agents

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- Psychotropics: Mirtazapine and Olanzapine:

  Via beneficial receptor antagonistic activities
  - Appetite (5-HT2, H-1)
  - Nausea (5-HT3)
  - Insomnia (H-1, 5-HT2)
- Mirtazapine useful if depressed mood or insomnia, nausea also present
- Olanzapine useful if presence of delirium or insomnia, nausea ; Well designed randomized controlled trials awaited
- Investigational agent: Oral Anamorelin (Ghrelin agonist) 100mg (Temel JS et al 2016; Takayama K et al 2016) has been found to improve lean body mass, QOL anorexia (FAACT) and fatigue (FACIT-F)scores scores. No improvement in function (Hand grip strength test)

Nonpharmacological-interventions

- **Compassionate communication**
  - reframe "starving to death" to the more complex one of irreversible (usually) metabolic abnormalities.
- **Nutritional counseling**
  - Remove dietary restrictions
  - Small and frequent meals
  - 25 to 30 calories/kg per day 1.5 to 2.0 g of protein/kg per day
- **Exercise:** aerobics and resistance training
- **Parenteral Nutrition**