The Gut, Nutrition and Health in the Aged

John McLaughlin
Manchester University/
Hope Hospital, Salford UK

Salford Royal NHS
NHS Foundation Trust

Scene setting
Gut has 2 conflicting roles

- Digestion and absorption: get food and water in

  » Versus

- Barrier function: keep microbes and toxins out

Do these change with age?

Animals are designed for survival

- Maximal absorption of nutrients is essential
  - Biological and evolutionary pressure is of food scarcity
  - And not cooked/processed/biologically safe
  - So human gut is highly over-efficient
    - Age is not the *major* limitation in health

…Gut epithelium self-replaces every 4-7 days so no 'wear and tear' ageing

Not so for muscle/nerve/immune cells

Nutrition and age

- ***Reduced Intake***
- ↓ Absorption
- ↓ Utilisation

impaired nutrition

Consequences

eg resilience to disease/trauma/surgery, QoL AND organ specific issues (not covered today; malnutrition addressed by next speakers)

Nutrition and age

- Reduced Intake
- ↓ ***Absorption***
- ↓ Utilisation

impaired nutrition

WHAT DO WE KNOW?

We have a very inadequate, non-integrated understanding of how human GI function changes during the ageing process, or how functionality can be maintained or manipulated.

Essential dietary components

- Calories: energy intake must equal loss via work done and body heat generated to maintain a steady state
  - Otherwise tissue and weight loss <u>*OR*</u> obesity occur
- ~2000kcal/day for basic adult needs
- + extra depending on activity

  + illness/surgery, pregnancy

  ...Life stages also have a large impact

Essential dietary components

- Protein
- Fat
- Minerals
- Vitamins

…Do we really know precise needs?

Also *'bioactives'*

BUT REALLY…. most problems arise before anything needs absorption in the gut…

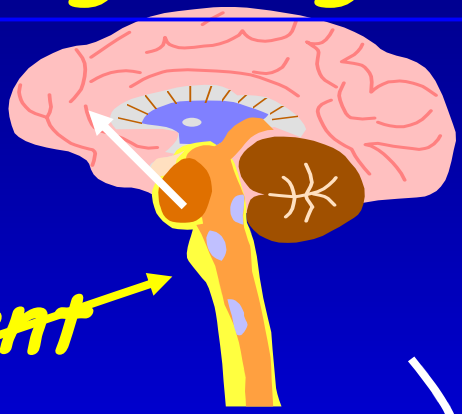
- *Poverty, reduced mobility, isolation, cognitive loss…*
- Dry mouth
  - drugs
- Dentition and dentures
- Weak chewing
- Sore mouth
- Lost taste/smell
- Anorexia/nausea
- Gut and other diseases…

Gut function *broadly* preserved with healthy ageing

- Limited impact on QoL and nutrition <u>if adequate feeding is maintained</u>
- GI diseases are however prevalent in the elderly

Satiety mirrored by delayed gastric emptying via vagal signalling

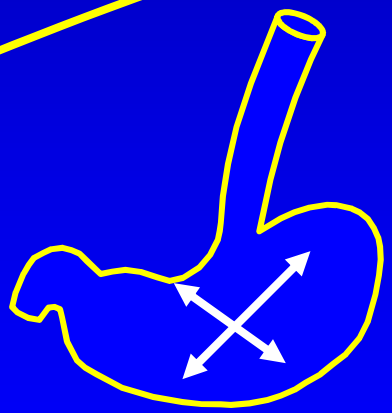
satiety



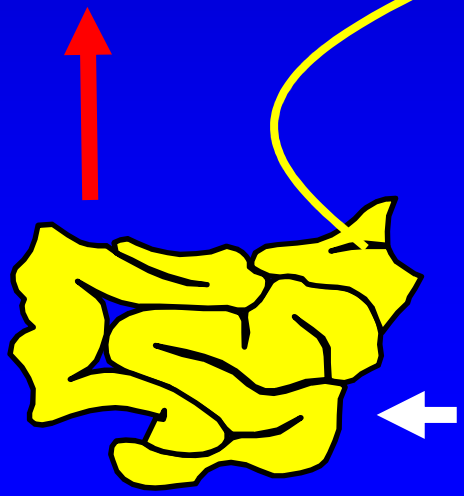
Gut hormones

vagal afferent

vagal efferent
(also oral and cephalic phases before eating)



↓gastric emptying

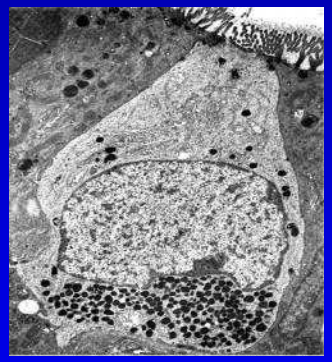


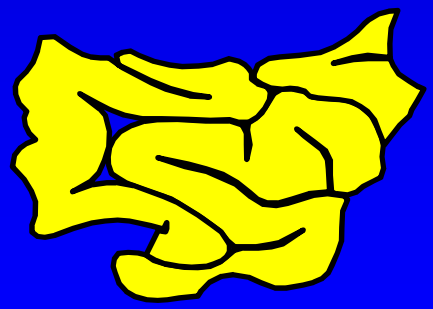
nutrients

Gastric emptying

- Increasingly slow with age
  - e.g. increased gut hormone responses with age
- May potentiate sensation of *satiety* post-prandially
  - Persistent gastric distension: 'fuller for longer'
  - Slower delivery of nutrients prolonging satiety signals
  - ? Altered neuropeptide signalling

How does the gut let the brain know what is in it?

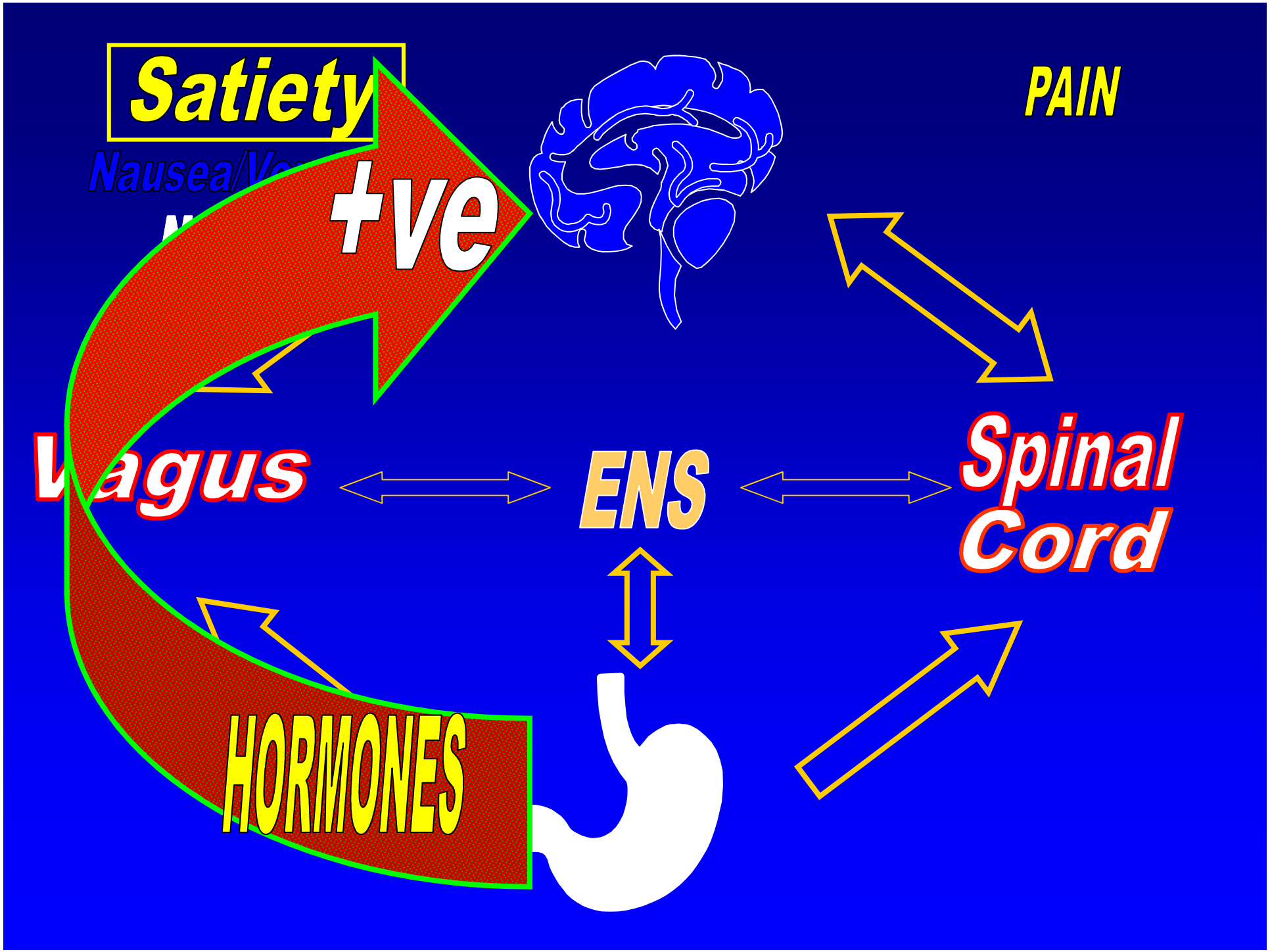




Signals directly to the brain by **the vagus nerves**

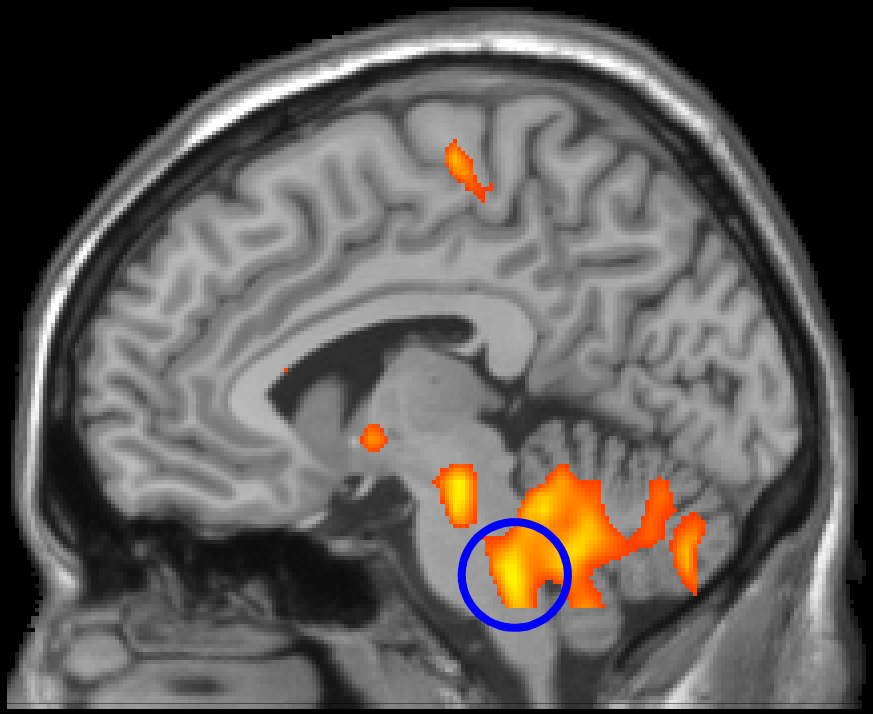
Gut hormones and anorexia of ageing?

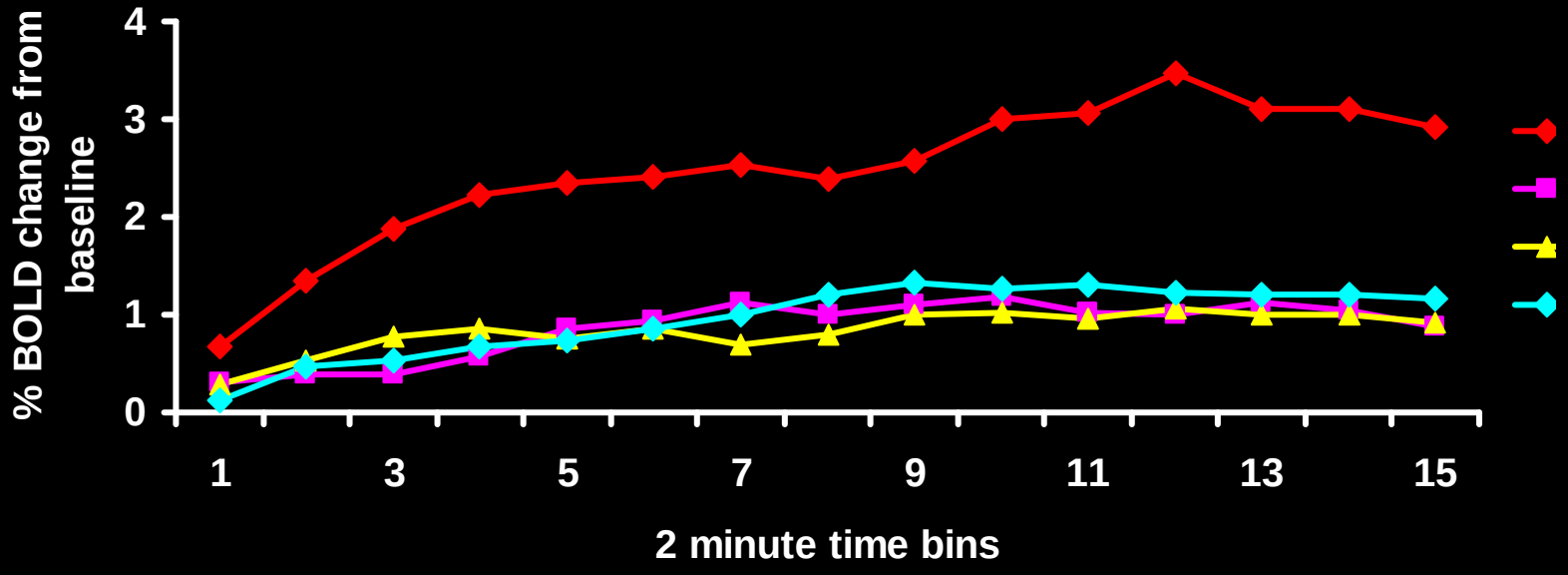
Elevated hormones (PYY) data desribed


Satiety
Nausea/Ve
+ve
PAIN
Vagus
ENS
Spinal Cord
HORMONES

Can we visualise gut-to-brain nutrient signalling in vivo?

fMRI scan

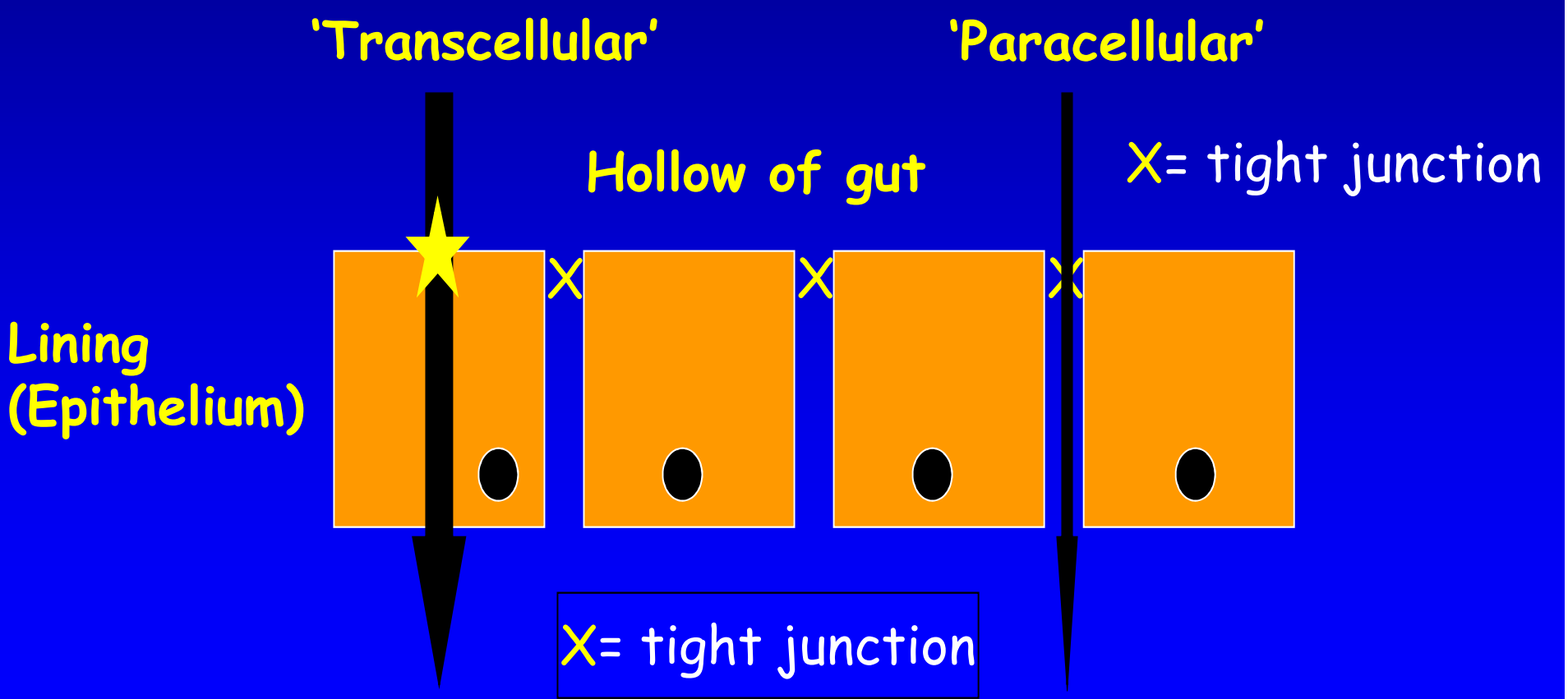



% BOLD change from baseline
0
1
2
3
4
1
3
5
7
9
11
13
15
2 minute time bins

Motility and age

- Gastric emptying slows
  - Drug delivery consequences
- Small bowel speed: largely preserved *unless* intercurrent disease
  - Diabetes, Drugs, Hypothyroidism…
- Colonic transit tends to slow
  - ↑ water absorption, ↑ constipation… consequent symptoms

Transport and absorption



Small bowel is lined by highly adapted cells

- Differentiation from crypt stem cells
  - Absorptive cells (~90%)
    - Transporters +++
    - TRANSPORT DEFECTS UNLIKELY TO CONTRIBUTE TO eg SARCOPAENIA
    - *Calcium/zinc absorption maybe age limited*
  - Secretory cells also (~10%)
    - Endocrine (hormones as above)
    - Goblet cells (mucus: reduced in age)
    - Paneth cells (defence: age effects unclear)

Ageing has little impact on small bowel nutrient transport

- Villus/crypt architecture preserved
- *And* little evidence for absorptive/digestive organs 'simply' failing with age:
  - Small intestine has reserve capacity++
  - Absorption time probably prolonged
  - ***eg 72 hour faecal fat excretion not affected by age***

And if fat can be absorbed, anything can…!

Gut diseases cause malabsorption in the elderly, not age

- Loss or damage
  - Bacterial overgrowth
  - Flat lining of any cause:
    - e.g. coeliac
  - Ischaemia
  - Crohn's
  - Drugs
  - Pancreas and liver diseases

Ageing and the gut

- Adaptation after injury is however impaired
  - Surgery
  - Infection/inflammation
  - Radiotherapy
- Resilience vs vulnerability

Colonic microflora

- There are ~10^{10} bacteria in the gut
- There are ~ 10^{9} cells in the body
- Therefore…you are 90% bacteria..
- A delicate balance exists
- Parasites also

Microbiome

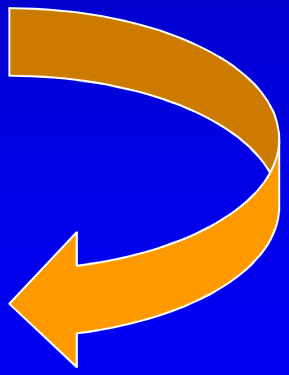
- Diversity++
  - Colonised at birth
  - Stability? Seems mainly yes.
- Loss of *diversity* observed *eg* in Inflammatory Bowel Disease

Microbiome: ageing effects?

- Limited and conflicting data
- No global or consistent change
- Increased pathobiont numbers
  - eg *Staphylococci, Enterococci*
- Reduced numbers/diversity of *Bifidobacteria sp*
  - *'Health promoting'*
- Magnified by antibiotic use
  - *C. difficile*
- Prebiotics/probiotics?

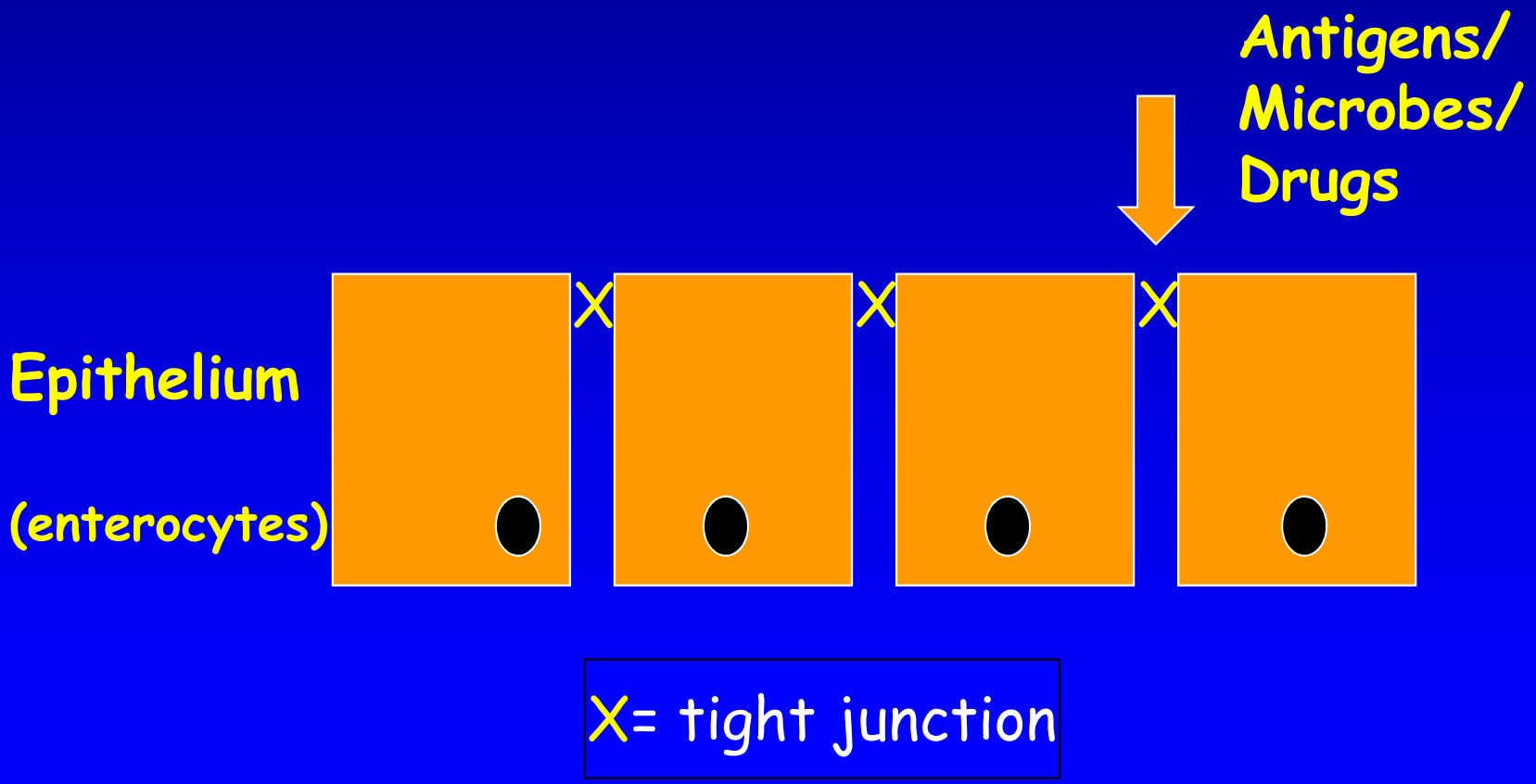
Immunosenescence

- Age related reduction in
  - gut-associated immune cells
  - intestinal antigen-specific IgA antibody secretion

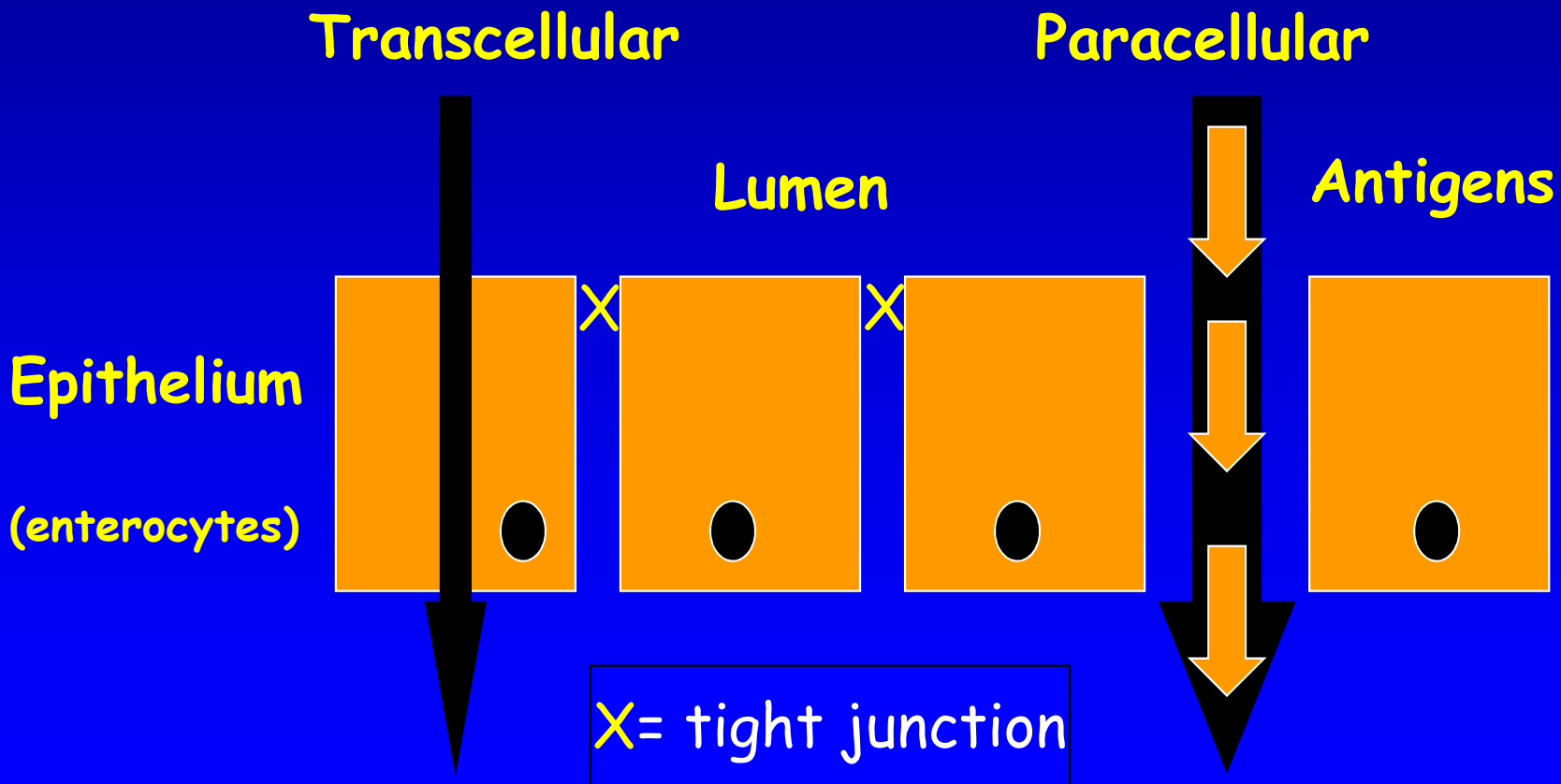


↑ GI infections
Morbidity and mortality
Nutritional impact- other systems?

Immune Barrier



Paracellular pathway is leaky in inflammation/malnutrition



'Inflamm-ageing'

May drive age related pathology eg sarcopaenia, neurodegeneration, postop sepsis?

Gut microbiome/immunity/ leakiness could be key factors

Future directions

The current research challenge is to understand how the function of the human gut changes with age, and the wider consequences for nutrition, health and resilience.

The design of future interventions can be informed by better understanding of the drivers, and consequences, of gut ageing.

Aims and Objectives of Our Proposal

(1) To generate a comprehensive account of how ageing affects the adult human gut, and how this interacts with nutritional state and diet;

(2) To identify new biomarkers and outcome measures of healthy gut ageing,

(3) To deliver interventions to assess the extent to which health-related functions of the gut can be preserved during human ageing.

(4) To develop openly data and tools for the wider ageing research community.

Thank you

- john.mclaughlin@manchester.ac.uk