The normal gut flora
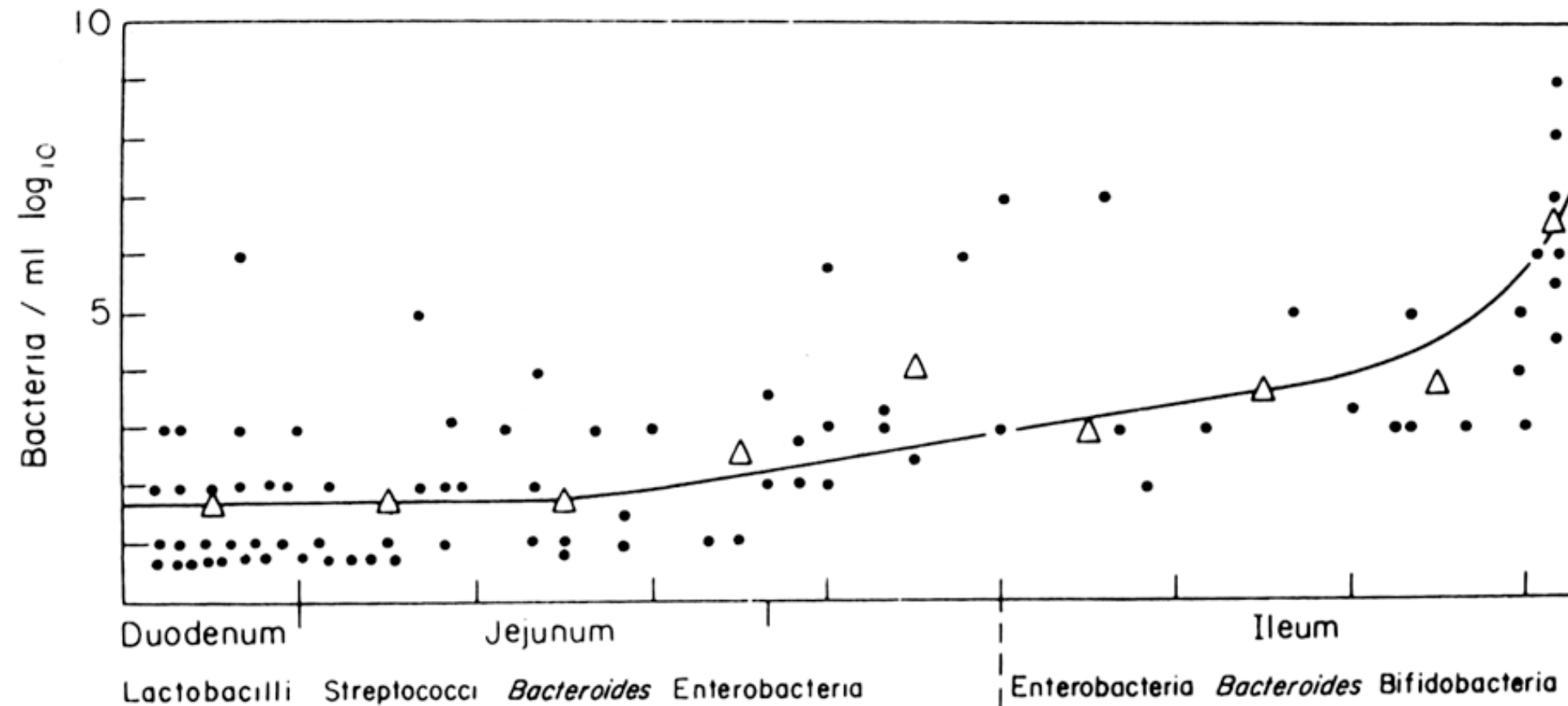

The upper gut has very low populations of bacteria due to a range of factors including gastric acidity, propulsive motility, and pancreatic enzymes.

The large intestine has a very stagnant motility with retropulsive contractions keeping the contents in the proximal colon for long periods. The pH of the colon is buffered by bicarbonate secretion. This allows a large and complex bacterial ecosystem to develop. Most of the contents of the colon are actually bacteria. There are approx. 10^{12} cfu/g which is 75% of the wet weight.

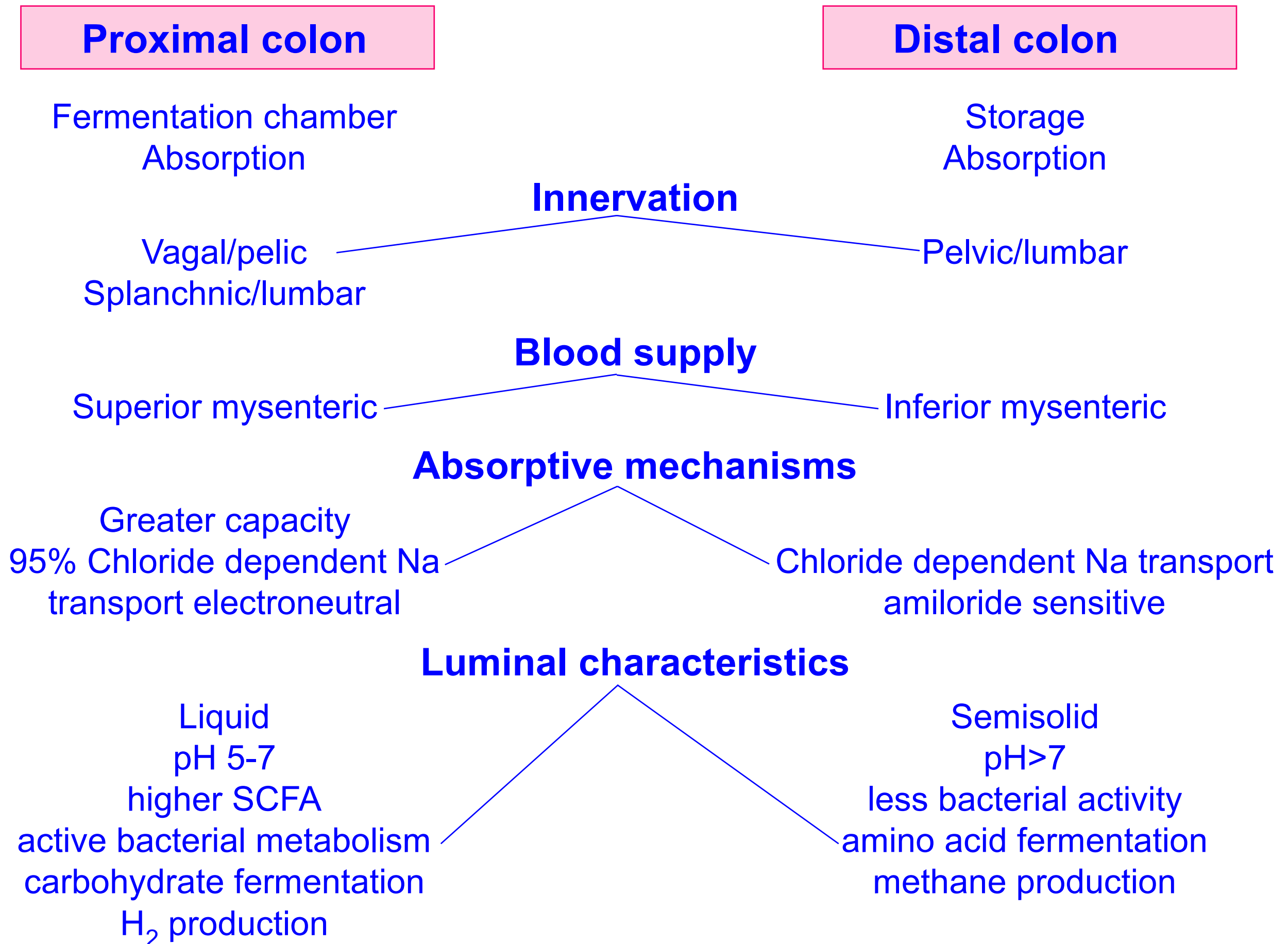There are up to 400 different species in the colon and the vast majority (99.9%) are strict anaerobes.

The normal faecal flora of healthy adult humans

Genus	Log$_{10}$ bacteria per gram faeces
Non-sporing anaerobes	
Bacteriodes spp.	10 - 11
Bifidobacterium spp.	10 - 11
Eubacterium spp.	9 - 11
Propionibacterium spp.	9 - 11
Veillonella spp.	5 - 8
Sporing anaerobes	
Clostridium spp.	5 - 9
Sporing aerobes	
Bacillus spp.	
Microaerophiles	
Lactobacillus spp.	7 - 9
Streptococcus spp.	7 - 9
Enterococci	5 - 7
Facultative organisms	
Coliforms	7 - 9
other *Enterobacteria*	5 - 9

The environment of the proximal colon differs from that of the distal colon in several ways (see below). This affects the bacterial metabolism. Most colonic disease occurs in the distal colon.

The gut associated immune system develops in infancy while the gut is being colonised by the commensal bacteria. It appears that a tolerance is established preventing an immune response to the colonic flora. The gut mucosal barrier is also very effective in preventing infection by the bacteria in the gut but if the mucosal barrier is breached or if faecal bacteria enter and open wound some gut bacteria, *bacteroides spp* for example are very pathogenic. Other gut bacteria such as Bifidobacteria and Lactobacilli are not pathogenic.

Characteristics of the proximal and distal colon

Proximal colon	Distal colon

Fermentation chamber
Absorption

Storage
Absorption

Innervation

Vagal/pelic
Splanchnic/lumbar

Pelvic/lumbar

Blood supply

Superior mysenteric

Inferior mysenteric

Absorptive mechanisms

Greater capacity
95% Chloride dependent Na
transport electroneutral

Chloride dependent Na transport
amiloride sensitive

Luminal characteristics

Liquid
pH 5-7
higher SCFA
active bacterial metabolism
carbohydrate fermentation
H_2 production

Semisolid
pH>7
less bacterial activity
amino acid fermentation
methane production

The factors controlling the composition of the gut bacterial flora

Physicochemical factors

pH
Oxidation-reduction potential
Oxygen tension
Nutrient supply

Host-bacteria interactions

Saliva
Bile
Gastric secretions
Pancreatic secretion
Immune systems

Microbe-microbe interactions

Bacteriophages
Bacteriocines
Toxic metabolites

Potential Harmful Metabolic Activity of the Colonic Flora

Range of biochemical transformation by intestinal bacteria

Hydrolysis

Glucuronides
Esters
Amides

Aromatization

Ethereal sulphates
Sulphamates
Glycosides

Reduction

Carbon-carbon double bonds
Nitro-acid A20 bonds
N-oxides, N-hydroxy compounds
Carboxyl groups
Alcohol, phenols
Arsonic acid

Degraduation

Decarboxylation
Dealkylation
Deamination
Dehalogeneration

Synthesis

Esterification
Acetylation
Formation of nitrosamines

Potential harmful products

Carcinogens and Toxins   The bacteria release the toxins and carcinogens from glucuronides and gycosides e.g. Dimethyl hydrazine a potent carcinogen

Azo dyes   Azoreductase releases toxic dyes and other toxins

Phenols and paracresols   Products of protein catabolism may injure mucosa and influence brain

H_2S   Toxic to colonic cells

Hydroxy fatty acids   1) Toxic to mucosa
2) Cathartic

Secondary bile acids   1) Possible co-carcinogen
2) Increase risk of gallstones

The colonic flora has a wide range of metabolic activities, which could be harmful in the colon. However the exact role of these activities in colitis, colon cancer and other diseases are not proven.

Factors affecting the harmful bacterial activity

- The activity of some of the enzymes can be reduced at the low pH caused by carbohydrate fermentation.

- However if bacterial cells increase in number the enzymes will also increase.

The balance is important

- Increased insoluble fibre will speed transit through colon and reduce exposure time to the toxins and carcinogens.

- Decreased protein in the colon and increased production of bacterial cells will reduce production of ammonia, phenols and paracresols and H_2S.

Beneficial actions of colonic flora

60g Carbohydrate per day
(fibre, starch, oligosaccharides)

↓

Colonic bacteria

↓

Acetic, propionic, butyric acids
+
CO_2, H_2, CH_4

Low pH
4.5 - 7.0

The colonic microflora enables the colon to salvage energy and nutrients, which escape absorption in the small intestine.

About 60g of carbohydrate is fermented by the bacteria each day to short chain fatty acids (SCFA) which are rapidly absorbed.

The SCFA produced include acetic acid, propionic acid and butyric acid. These acids have important actions in the colon and in the body as a whole.

Benefits of SCFA

Acetic acid is an energy source for the body and is a substrate for fat synthesis in the liver.

Propionic acid is also an energy source for the liver, is gluconeogenic (i.e. can be used to make glucose) and may reduce cholesterol synthesis.

Butyric acid is the major fuel for colonic cells and has been shown to stimulate differentiation and programmed cell death of cancer cells.

SCFA enemas have been used effectively in the treatment of ulcerative colitis.

SCFA produced in the colon increase cell proliferation throughout the whole gut.

SCFA are also very important because they promote water absorption and prevent osmotic diarrhoea.

SCFA inhibit the growth of pathogenic bacteria.

What happens if you reduce colonic bacterial activity?

Ingestion of broad spectrum antibiotics can inhibit the growth and metabolism of the normal colonic flora and result in an increased risk of diarrhoea.
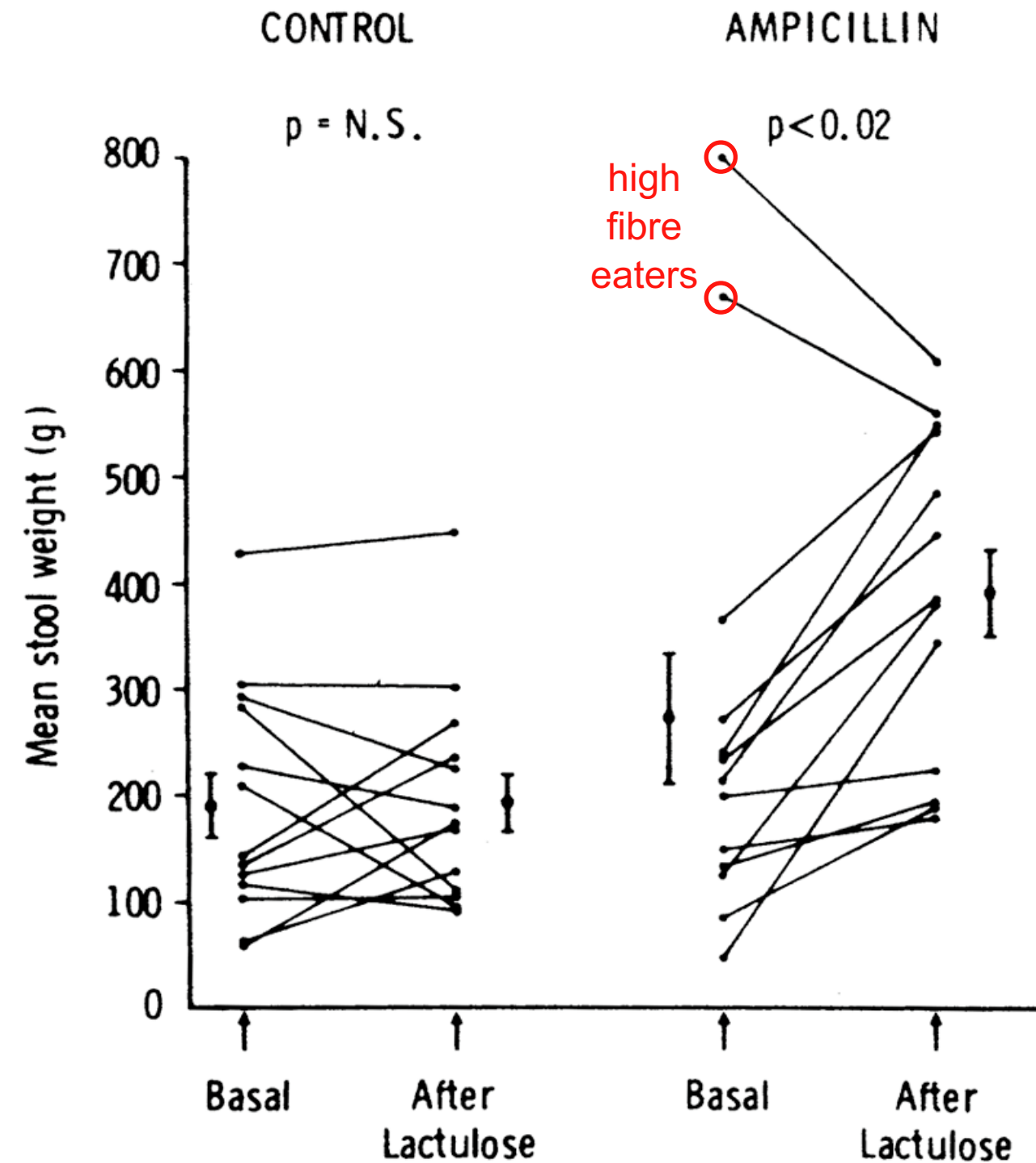
In an experiment to demonstrate this, subjects ate lactulose, a non-absorbable sugar.

Normally small doses of lactulose are well tolerated as it is fermented to SCFA, which are rapidly absorbed.

On a second occasion subjects ate the same dose of lactulose after taking ampicillin. This time they had a much bigger increase in stool output and frequency.

It interesting to note that two subjects with a high fibre diet (such as in vegetarianism) actually got diarrhoea before they took the second dose of lactulose.

Effect of ampicillin on stool output and transit time before and after administration of 20g of lactulose

	Control period	During ampicillin	p
Before lactulose	190 ± 31	273 ± 62	NS
Stool weight	1.4 ± 0.3	1.4 ± 0.3	NS
Stool frequency (day^{-1})	6	54	<0.0001
Stool consistency (% stools uniformed)			
After lactulose			
Stool weight	195 ± 29	391 ± 43*	<0.001
Stool frequency (day^{-1})	1.5 ± 0.1	2.3 ± 0.4*	<0.05
Stool consistency (% stools uniformed)	20	70	<0.001
Whole gut transit time (h)	33.4 ± 6.4	30.3 ± 3.7	NS

NS - not significant. Results expressed as mean $\pm$ SEM. *Significantly different values before ingestion of lactulose (p<0.02).