



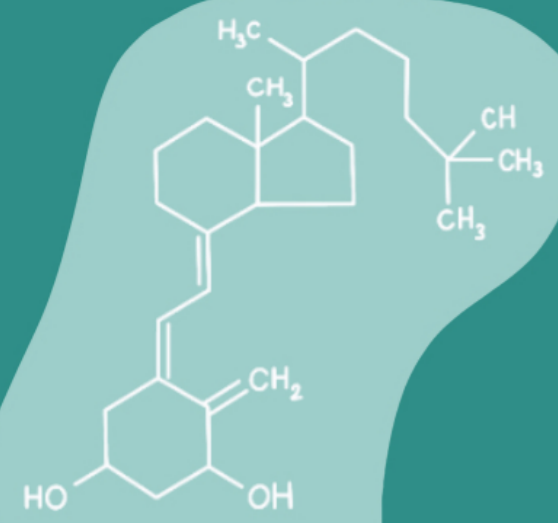
VITAMIN D & GUT HEALTH

PROFESSOR BERNARD CORFE

Webinar key messages
summarised for you.

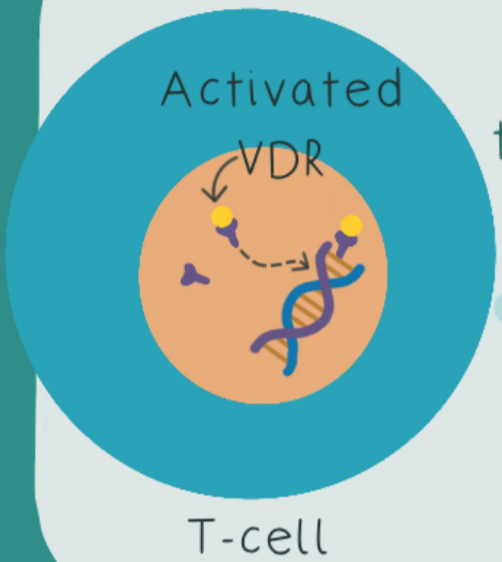


1



ROLE OF VITAMIN D IN THE GUT

THE VITAMIN D RECEPTOR



Active vitamin D ($1,25(OH)_2D_3$) is transported to target cells around the body where it binds to the vitamin D receptor (VDR) in order to activate it. Once activated by vitamin D, the VDR binds to specific sequences in DNA called response elements.

ROLE OF VDR IN THE GUT



There are very high levels of VDR found in the gastrointestinal (GI) tract, mainly the small intestine and the colon. Suggesting there is an important role for VDR and vitamin D in regulating gut function.

WHICH GENES ARE AFFECTED BY THIS PROCESS?

Research suggests there are several pathways related to immune and inflammatory responses that are up weighted by vitamin D binding to VDRs in cells.

In HCT116 cells (associated with colorectal cancer) an increase in vitamin D is associated with a significant increase in genes linked to cancer homeostasis.

WHAT DOES THIS MEAN?

These mechanisms suggest that vitamin D appears to have a potent role in regulating and changing the transcribed genetic environment of cells to offer some protective benefit.

THE MICROBIOME

Bacterial metabolites (e.g., short chain fatty acids such as butyrate) are key to gut health.



The metabolites produced by a healthy microbiome can alter the VDR and the function of vitamin D on the gut.

Animal research shows that if you eliminate VDR, there is also a change in the functional microbiota of the gut — resulting in the production of less beneficial metabolites.



VITAMIN D & CANCER



Work in this space was initiated by researchers Garland and Garland in 1980, who investigated the idea that vitamin D may play a role in colorectal cancer mortality. Their research found that in areas where there was higher sunlight exposure, colorectal cancer mortality rates were lower.

WHAT DOES THE RESEARCH SAY TODAY?

One meta-analysis looking at circulating vitamin D and risk or outcome of cancer found that vitamin D may offer some protection against colorectal cancer.

26% ↓ MORTALITY

16% ↓ RATE OF DISEASE PROGRESSION

There are important limitations to the research and acute inflammation in itself can reduce the levels of circulating vitamin D.

WHAT ABOUT SUPPLEMENTS?

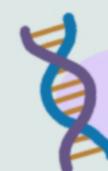
Research suggests that supplementation offers little to no benefit in the reduction of cancer risk, but may offer a protective affect on mortality.



HOW DOES COLORECTAL CANCER OCCUR?

Colorectal cancer is the 4th most common cancer and the 2nd most common cause of cancer death.

The development of colorectal cancer is a long-term process which has strong links to diet and lifestyle.



Loss of a gene called APC.

Cells less prone to die and more prone to stick down.

Cells start to proliferate and take over.



As they are less prone to die, they accumulate mutations more readily which over time progresses to hyperplasia, dysplasia, and eventually invasive cancer.

TAKE HOME MESSAGE: The evidence on vitamin D reducing the risk of developing colorectal cancer is still inconclusive, however there is strong evidence to suggest it may play a role in reducing the risk of mortality or the development of more aggressive cancers.

VITAMIN D & IBD -

CROHN'S & ULCERATIVE COLITIS



WHAT IS IBD?

- ✓ Affects around 2.2 million people in Europe
- ✓ Onset typically in childhood or adolescence
- ✓ Chronic relapsing condition. It will typically flare up, then go into remission before flaring up again.
- ✓ Caused by a combination of genetics, environmental exposures and the microbiome

CROHN'S DISEASE: Inflammation across the entire thickness of the bowel wall, which can occur at any point along the GI tract making it a very challenging condition to treat.

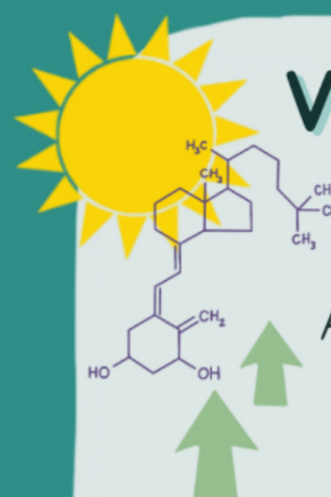
ULCERATIVE COLITIS: Inflammation at the mucosal level only. Associated with breakdown of the protective barrier of the gut wall, primarily in the colon.

TAKE HOME MESSAGE: We may never know about whether vitamin D reduces the risk of IBD onset, but there are potential benefits on the management of symptoms.

There is also a high prevalence of people with poor vitamin D status in IBD clinics, which in itself merits assessment and remedy.

4

VITAMIN D & THE ONSET OF IBD



A large study noted that patients with higher plasma vitamin D had a reduced risk of occurrence of Crohn's disease.

However, age of recruitment was 40-73 years, much later than the typical age of onset.

A smaller study found a higher-than-expected level of vitamin D deficiency in IBD patients, especially in those with Crohn's disease. Lower levels of vitamin D were also associated with increased disease activity.

VITAMIN D & IBD RELAPSE

A study showed that patients with lower circulating vitamin D had a higher risk of surgery or hospitalisation.

Another study found that vitamin D deficiency was associated with a greater relapse rate.



VITAMIN D & IBS

WHAT IS IBS?

Irritable Bowel Syndrome (IBS) is a bowel condition with **no obvious pathology**, and no obvious cure.

Patients with IBS typically suffer with sustained problems with bowel movements such as diarrhoea, constipation, or a mixture of the two which does not resolve.

IBS IS THE MOST PREVALENT GI CONDITION, WITH BETWEEN 5-12% OF THE POPULATION IN WESTERN COUNTRIES.

IT'S NOT JUST IBS

A **positive shift** in the narrative surrounding IBS among medical practitioners means patients no longer hear the dismissive celebration that it is **'just IBS'** when receiving a diagnosis.

CAN VITAMIN D RELIEVE IBS SYMPTOMS?

Evidence on vitamin D and IBS is **very limited**.

A case study looking at an individual with IBS who had relieved their symptoms by self-supplementing with vitamin D, led to an exploratory RCT pilot study before a full trial was conducted. This well-designed research found **no difference** on IBS symptoms.

Other studies in this area have found a **significant effect** of vitamin D supplementation on IBS symptoms, but limitations to these study designs suggest the **jury is still out**.

TAKE HOME MESSAGE: The **jury is still out** on whether vitamin D can reduce IBS symptoms.

What we do know is that research has consistently shown a very high prevalence of low vitamin D status in IBS patients, therefore vitamin D supplementation within this group is **still beneficial**.