Coeliac Disease at ABCD

Peter Watson

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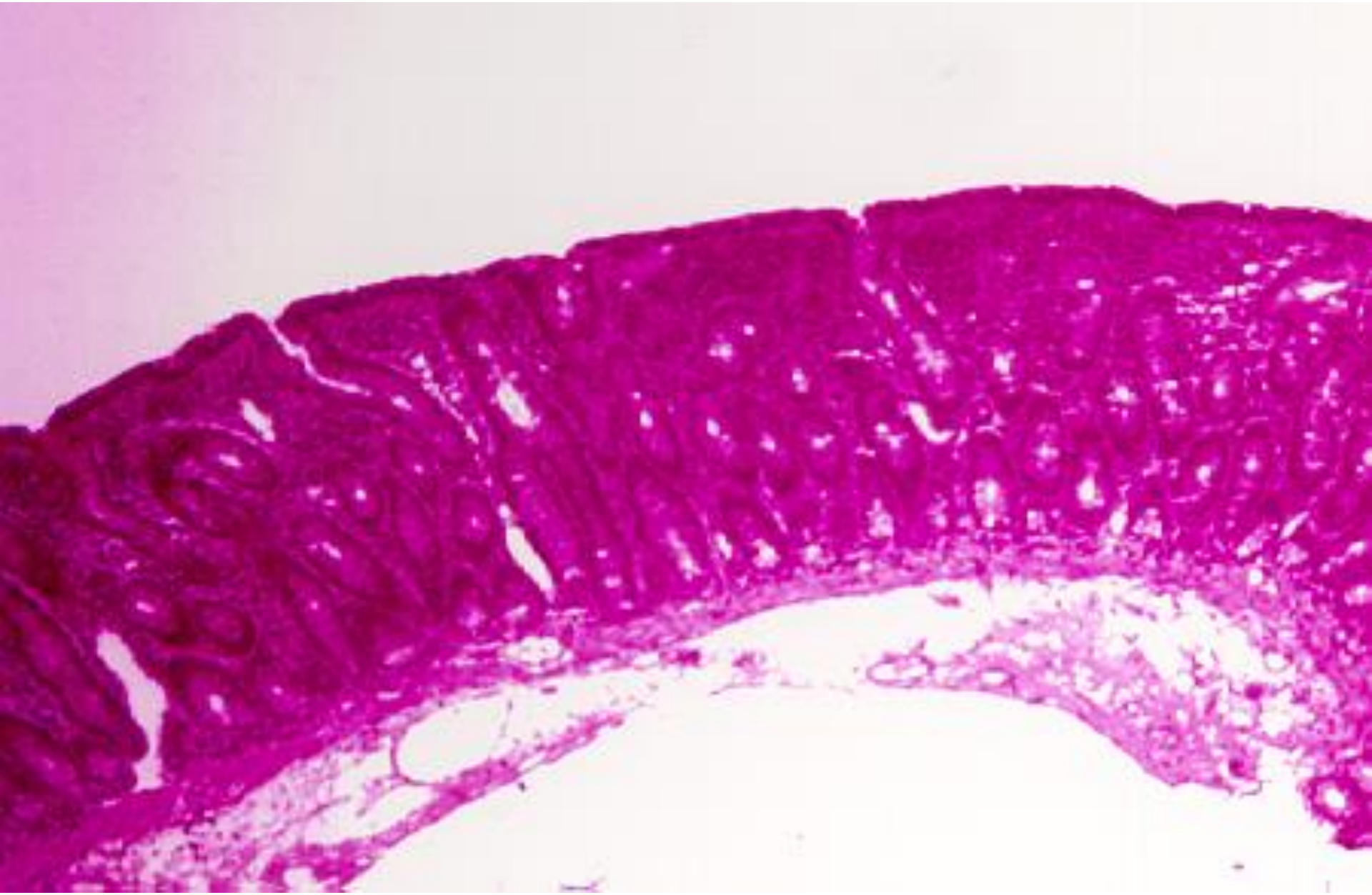
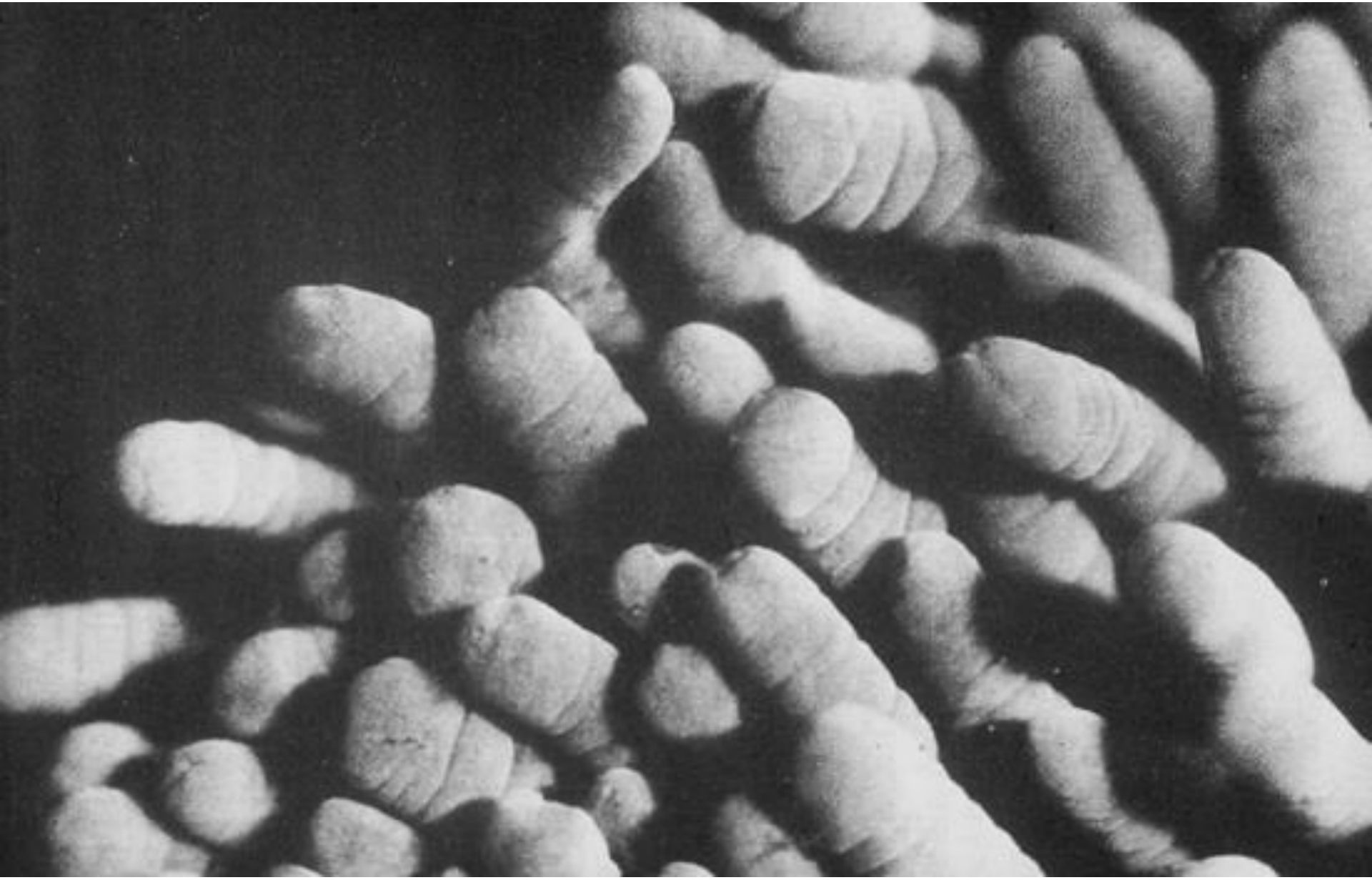
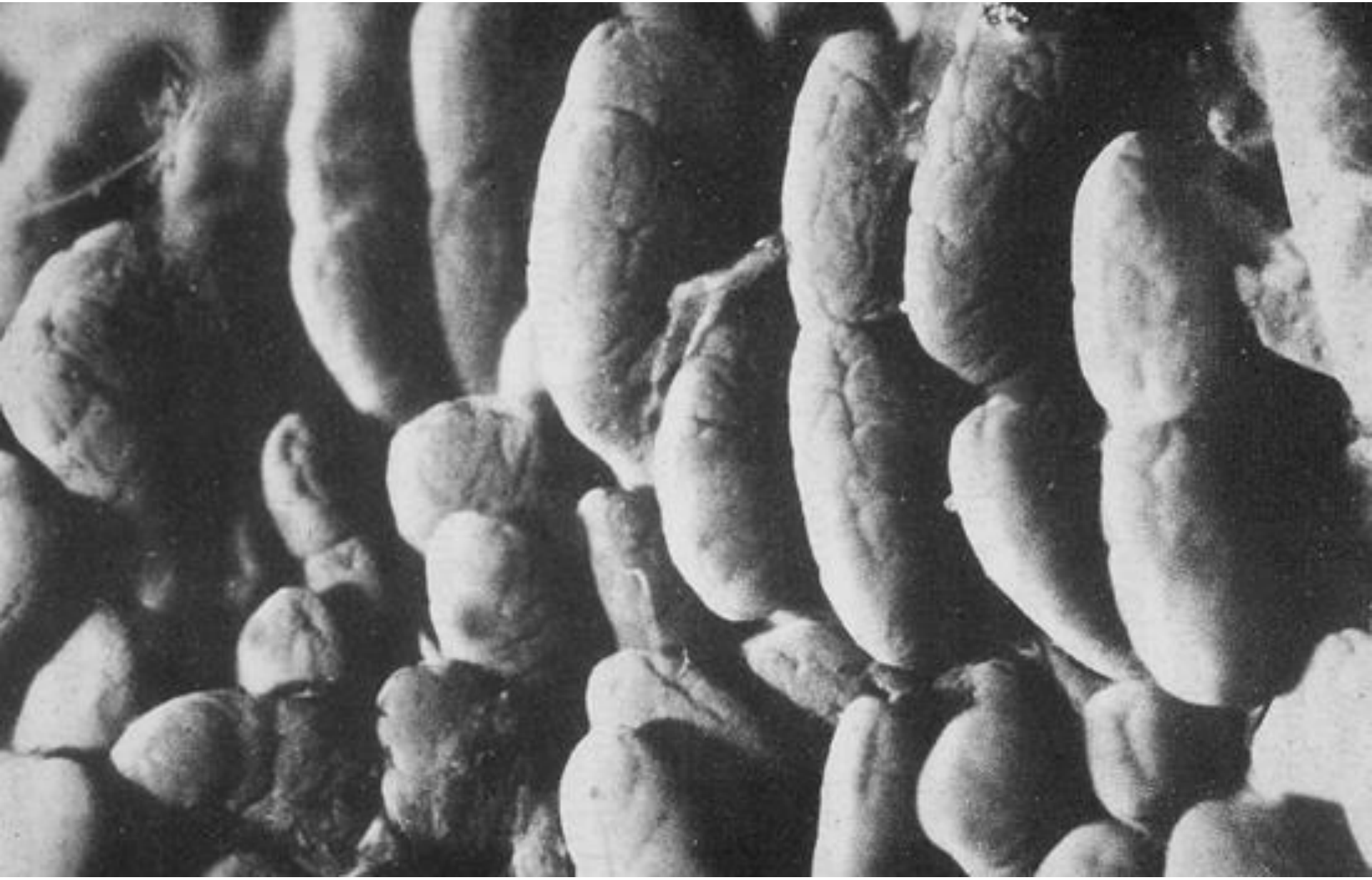
COELIAC DISEASE

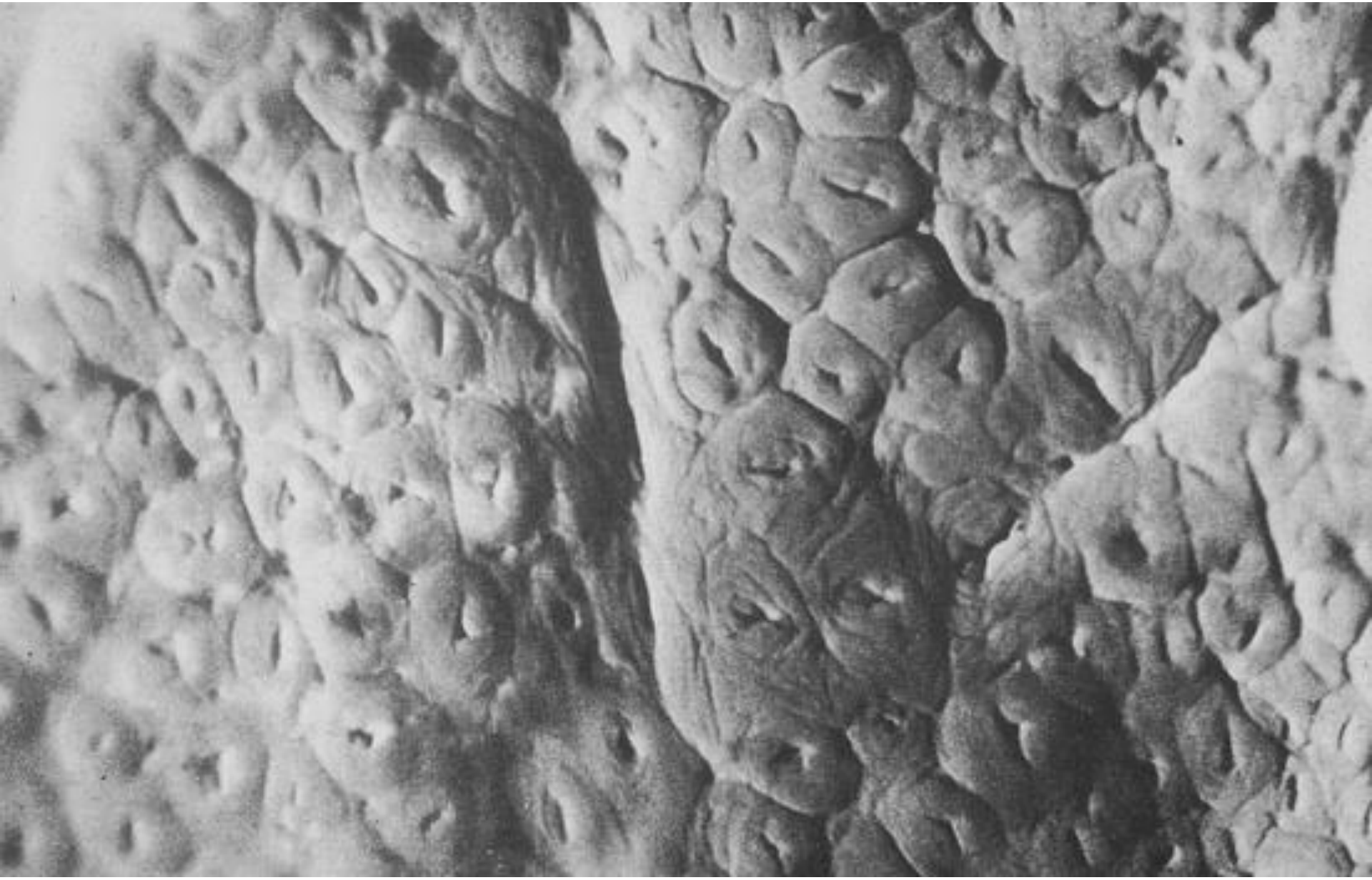
INVESTIGATION OF THE HARMFUL EFFECTS OF CERTAIN TYPES OF CEREAL ON PATIENTS SUFFERING FROM COELIAC DISEASE

W.K. DICKE

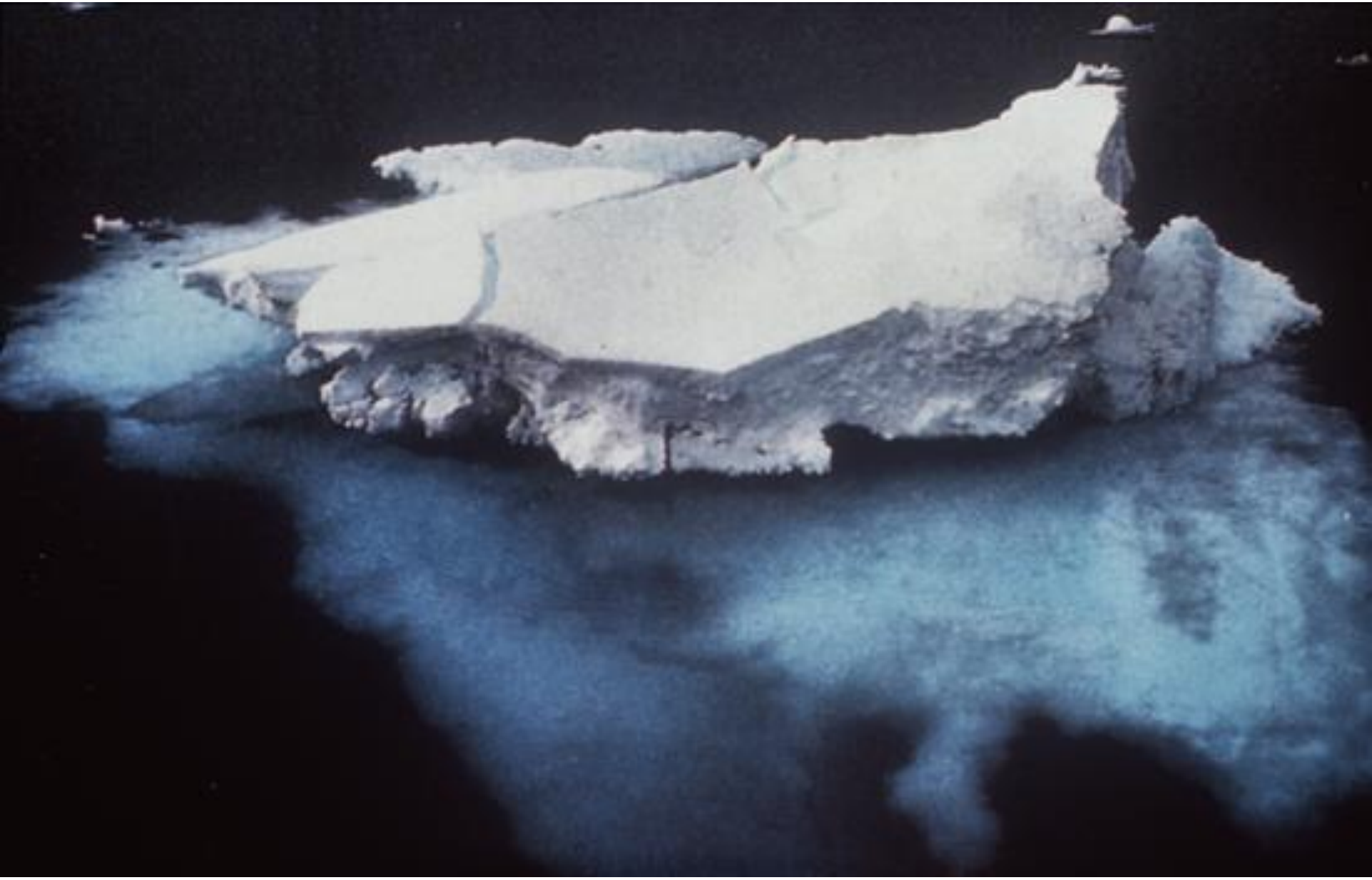








- Epidemiology
- Diagnosis
- Refractory coeliac disease
- New treatments




(a)
(b)

Epidemiology:

- In screening studies using antibody testing (EMA, tTG) followed by biopsy the prevalence of coeliac disease in virtually all communities studied is 1:300 – 1:100

Typical Coeliac Profile

- Commonest clinical feature anaemia
- Minor GI symptoms if any (IBS)
- Lethargy
- Adult, age 60 +

Recognised associations with coeliac disease

Family history
Insulin-dependent diabetes mellitus
Inflammatory bowel disease
Primary biliary cirrhosis
Primary sclerosing cholangitis
Epilepsy (with cerebral calcification)
IgA mesangial nephropathy
Autoimmune thyroid disease
IgA deficiency
Rheumatoid arthritis
Adverse preganancy related problems
Down’s syndrome
Dyspepsia

Coeliac Disease and Type 1 Diabetes

- Adults: 1:16 – 1: 76
- The majority of patients do not have gastrointestinal symptoms
- Children: 1:6 – 1:103
- In children they may initially be negative for antibodies and then subsequently become positive, hence if 1st screen -ve check again eg 1, 3 and 5 years post diagnosis.

Holmes GKT et al Malignancy and coeliac disease-effect of a gluten free diet. Gut 1989;30:333-338

A gluten free diet is protective

Should We Actively Look For (Screen for) Asymptomatic/Minor Symptomatic Coeliac Disease (incl Diabetes)?

- Does it reduce future morbidity and mortality?
- How feasible is it?

To Screen or Not to Screen for CD (in Diabetes): mortality

- Mortality in CD slightly increased:1.31 (CI 1.13-1.5) 4732 patients with CD vs 23,620 controls (From GP data base West et al 2004); GI cancer risk 1.85 (1.22-2.81); lymphoproliferative disease 4.8 (2.71-8.5)
- European multi centre study 2006: 1446 NHL's vs 9676 controls, patients with NHL increased risk of CD (OR 2.6 (1.4-4.9)
- In N Ireland 13 T cell lymphomas of small bowel in 10 years=incidence of < 1 per million per year. With prevalence of CD of 1:100 risk of EATL circa 1:10000 per year (Johnston SD, Watson RGP 2000)

To Screen or Not to Screen for CD (in Diabetes): morbidity

- To avoid bone mineral loss
- Improved metabolic control (growth)
- Avoidance of future autoimmune diseases
- Unrecognised illness

- Not associated with fractures
- Not universally improved control
- Controversial

- Controversial
- Additional dietary restriction: patient compliance and QOL

Learning point:

- **Proactively look for coeliac disease when there are symptoms (incl anaemia, poor diabetic control, poor growth)**
- **Any benefit to asymptomatic patients is likely to be in the future and to be minimal and tenuous.**
- **For asymptomatic patients compliance with a GFD is likely to be poor**
- **Therefore (in my view) there is insufficient evidence to support screening in asymptomatic individuals (incl diabetes)**

Diagnosis of coeliac disease

Serology (EMA, tTG)	Biopsy	Symptoms	Rx
+	**+**	**+/-**	Treat
+	**-**	**+**	Review histo + serology, repeat histo, review/treat
+	**-**	**-**	Review
-	**+**	**+**	Treat
-	**+**	**-**	Review
-	**-**	**+**	Review

Pre-Infiltrative

Infiltrative

Hyperplastic

Flat destructive

Irreversible
hypoplastic/atrophic

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+	**-**	**-**	Review
-	**+**	**+**	Treat
-	**+**	**-**	Review
-	**-**	**+**	Review

Learning point:

- **Where investigations are not clear cut carefully evaluate possibilities, be willing to review patients and make the diagnosis at a future point in time in light of clinical progress and repetition of investigations.**

Persistence of symptoms

- (Inadvertent) gluten ingestion (most common)
- Wrong diagnosis
- Lactose or fructose intolerance
- Pancreatic insufficiency
- Bacterial overgrowth
- Microscopic/collagenous colitis
- IBS
- Refractory coeliac disease

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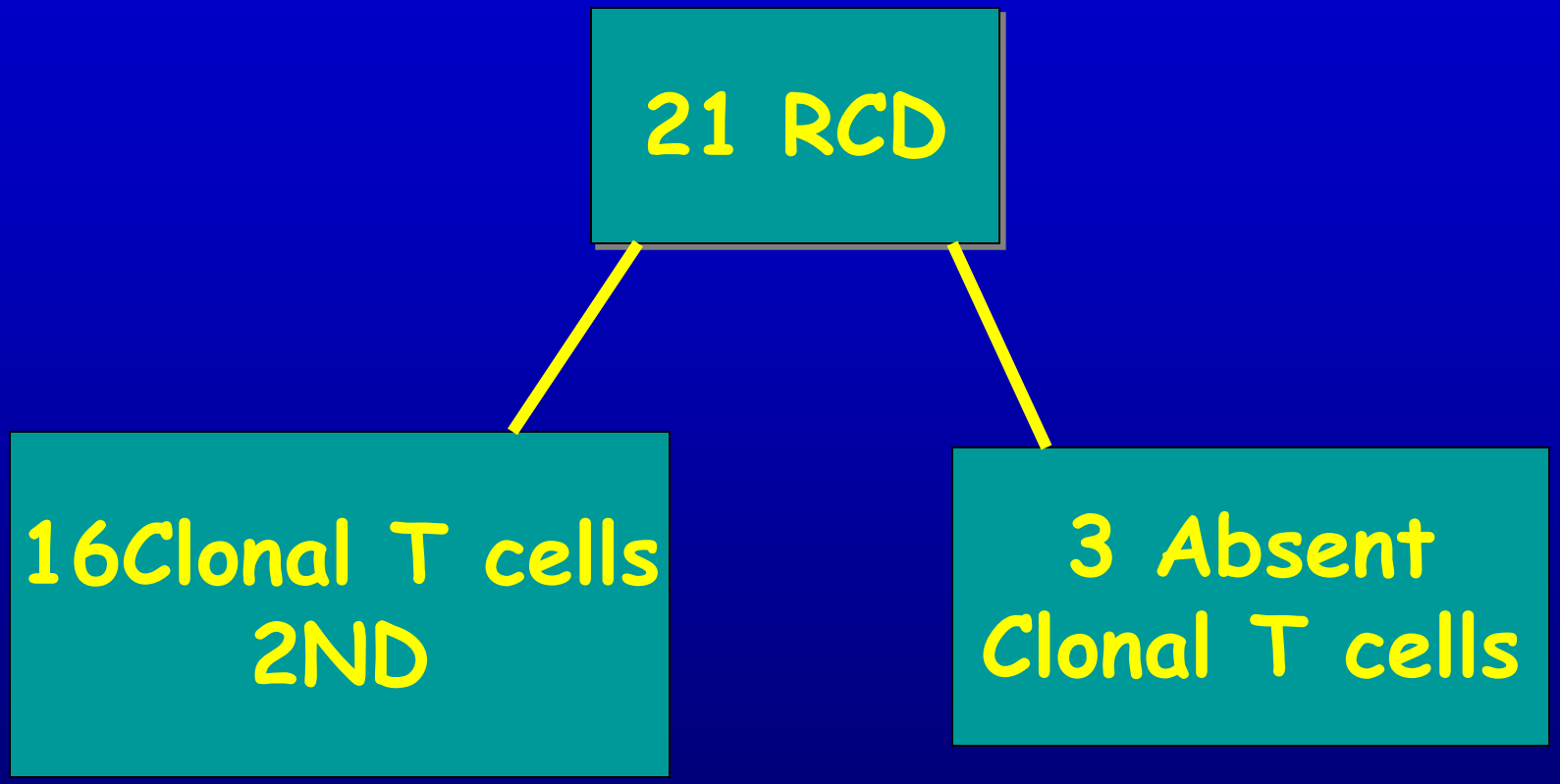
Cellier et al 2000



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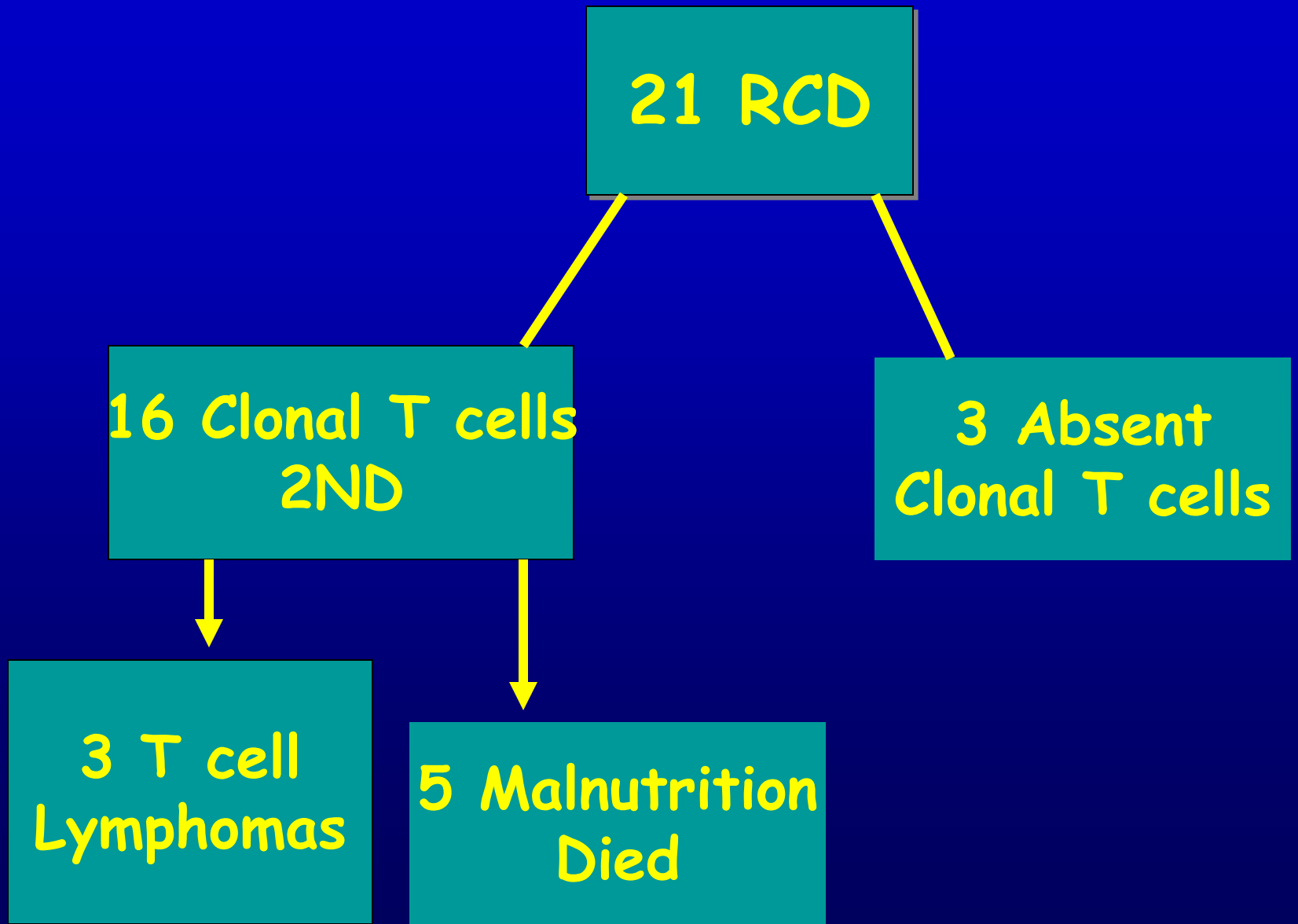

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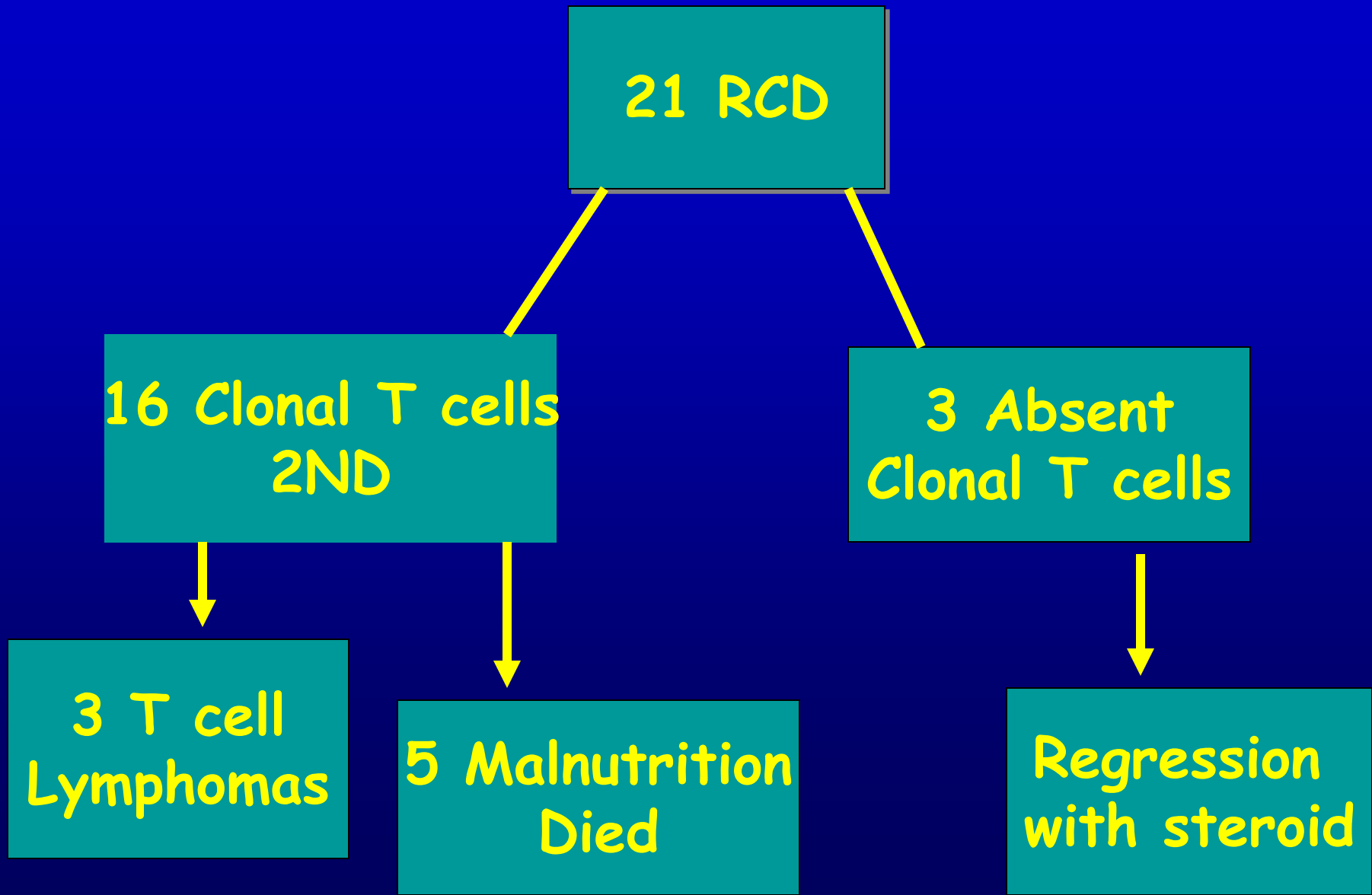
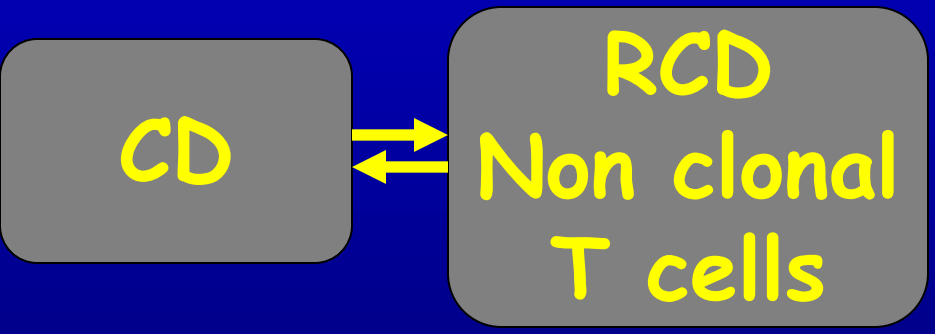


Progression of CD to RCD and EATL



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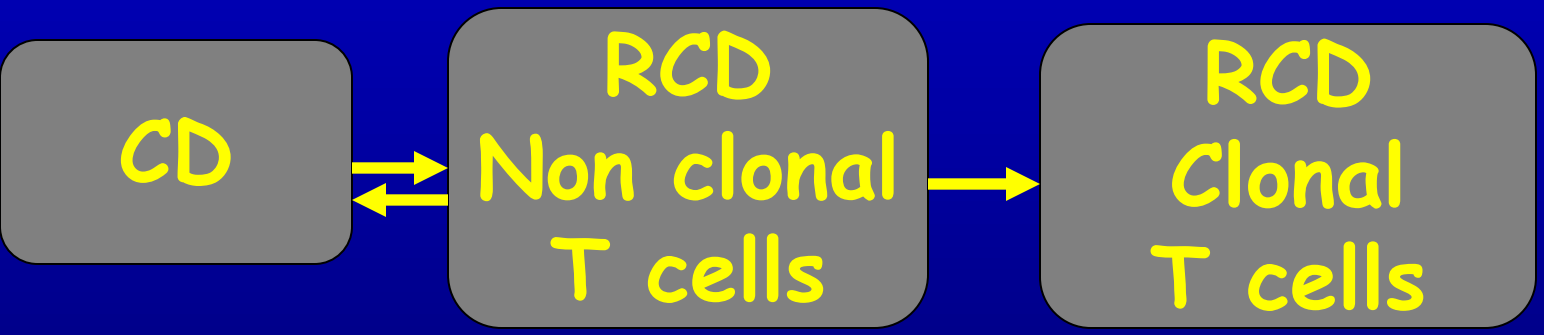

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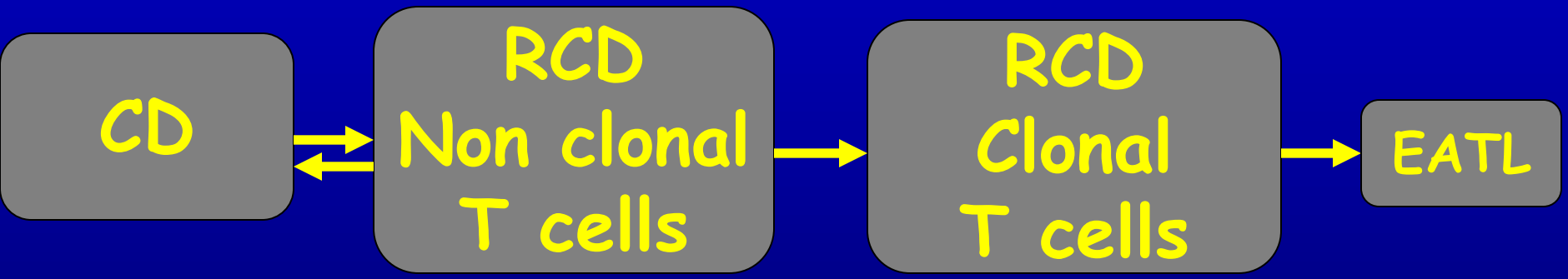

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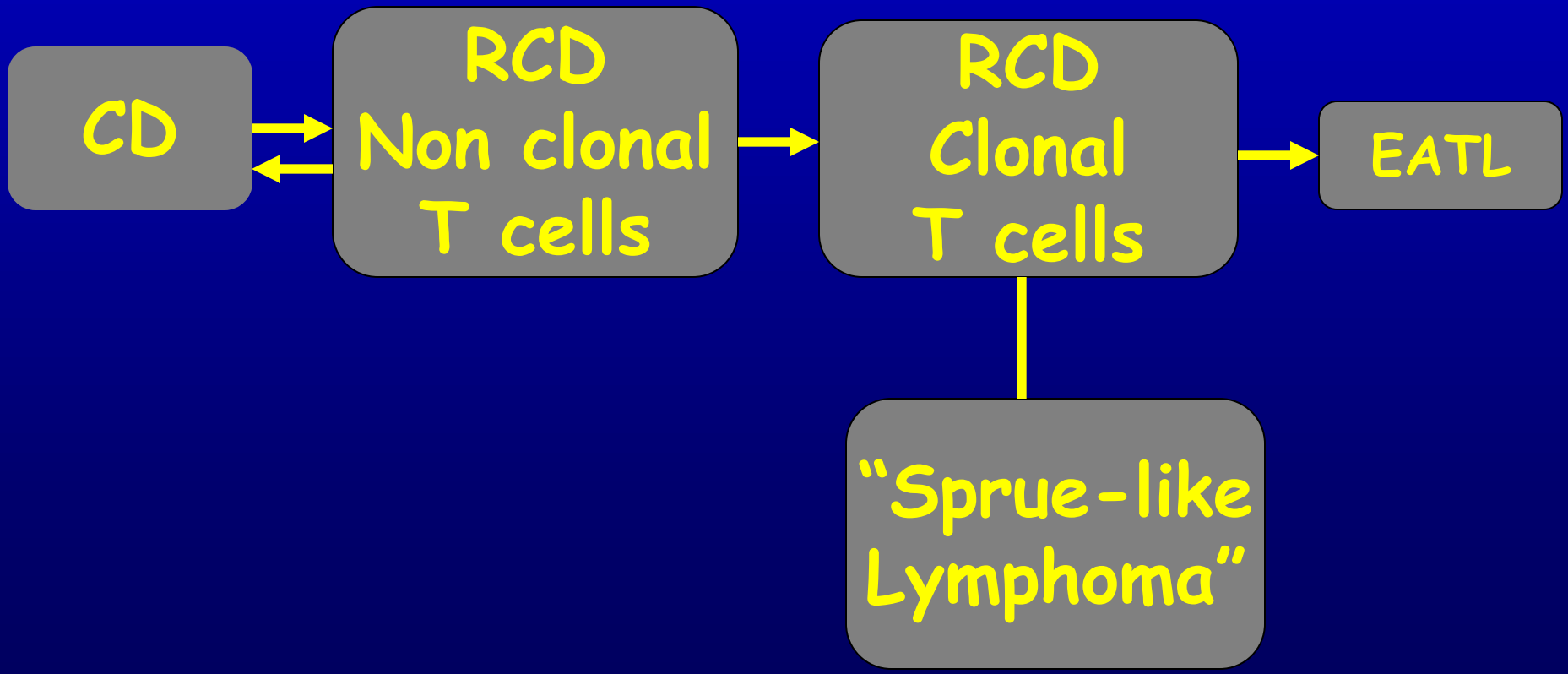


Learning point:

- Persistence of symptoms and lack of response is most commonly due to continued gluten ingestion
- If mucosa apparently recovered look for additional problems eg microscopic colitis
- Refractory coeliac disease in some cases may be a diffuse lymphoma and has a poor prognosis

α-Gliadin:

MVRVPVPQLQPQNPSQQQPQEQVPLVQQQQFPGQQQPFPPQ

QPYPQPQPFPSQQPYLQLQPFPQPQLPYPQPQLPYPQPQLPY

PQPQPFRPQQPYPQSQPQYSQPQQPISQQQQQQQQQQQQK

QQQQQQQQILQQILQQQLIPCRDVVLQQHSIAYGSSQVLQQST

YQLVQQLCCQQLWQIPEQSRCQAIHNVVHAIILHQQQQQQQQQ

QQQPLSQVSFQQPQQQYPSGQGSFQPSQQNPQAQGSVQPQ

QLPQFEEIRNLALETLPAMCNVYIPPYCTIAPVGIFGTNYR

α-Gliadin: proline content

MVRV**P**V**P**QLQ**P**QN**P**SQQQ**P**QEQV**P**LVQQQQF**P**GQQQ**P**F**PP**Q

Q**P**Y**P**Q**P**Q**P**F**P**SQQ**P**YLQLQ**P**F**P**Q**P**QL**P**Y**P**Q**P**QL**P**Y**P**Q**P**QL**P**Y

PQ**P**Q**P**FR**P**QQ**P**Y**P**QSQ**P**QYSQ**P**QQ**P**ISQQQQQQQQQQQQK

QQQQQQQQILQQILQQQLI**P**CRDVVLQQHSIAYGSSQVLQQST

YQLVQQLCCQQLWQI**P**EQSRCQAIHNVVHAIILHQQQQQQQQQ

QQQ**P**LSQVSFQQ**P**QQQY**P**SGQGSFQ**P**SQQN**P**QAQGSVQ**P**Q

QL**P**QFEEIRNLALETL**P**AMCNVYI**PP**YCTIA**P**VGIFGTNYR

α-Gliadin: immunogenic epitopes

MVRV**P**V**P**QLQ**P**QN**P**SQQQ**P**QEQV**P**LVQQQQF**P**GQQQ**P**F**PP**Q

Q**P**Y**P**Q**P**Q**P**F**P**SQQ**P**YLQLQ**P**F**P**Q**P**QL**P**Y**P**QPQL**P**Y**P**QPQL**P**Y

PQ**P**Q**P**FR**P**QQ**P**Y**P**QSQ**P**QYSQ**P**QQ**P**ISQQQQQQQQQQQQK

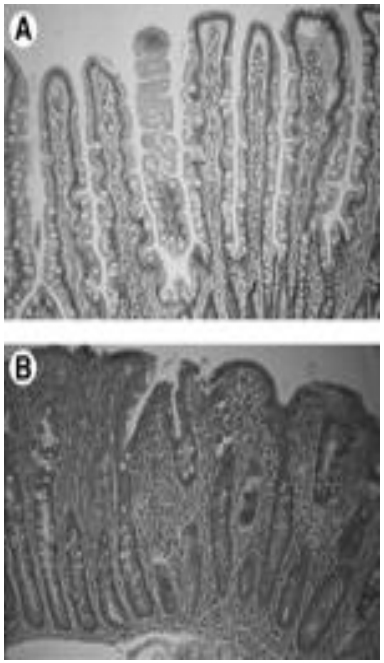
QQQQQQQQILQQILQQQLI**P**CRDVVLQQHSIAYGSSQVLQQST

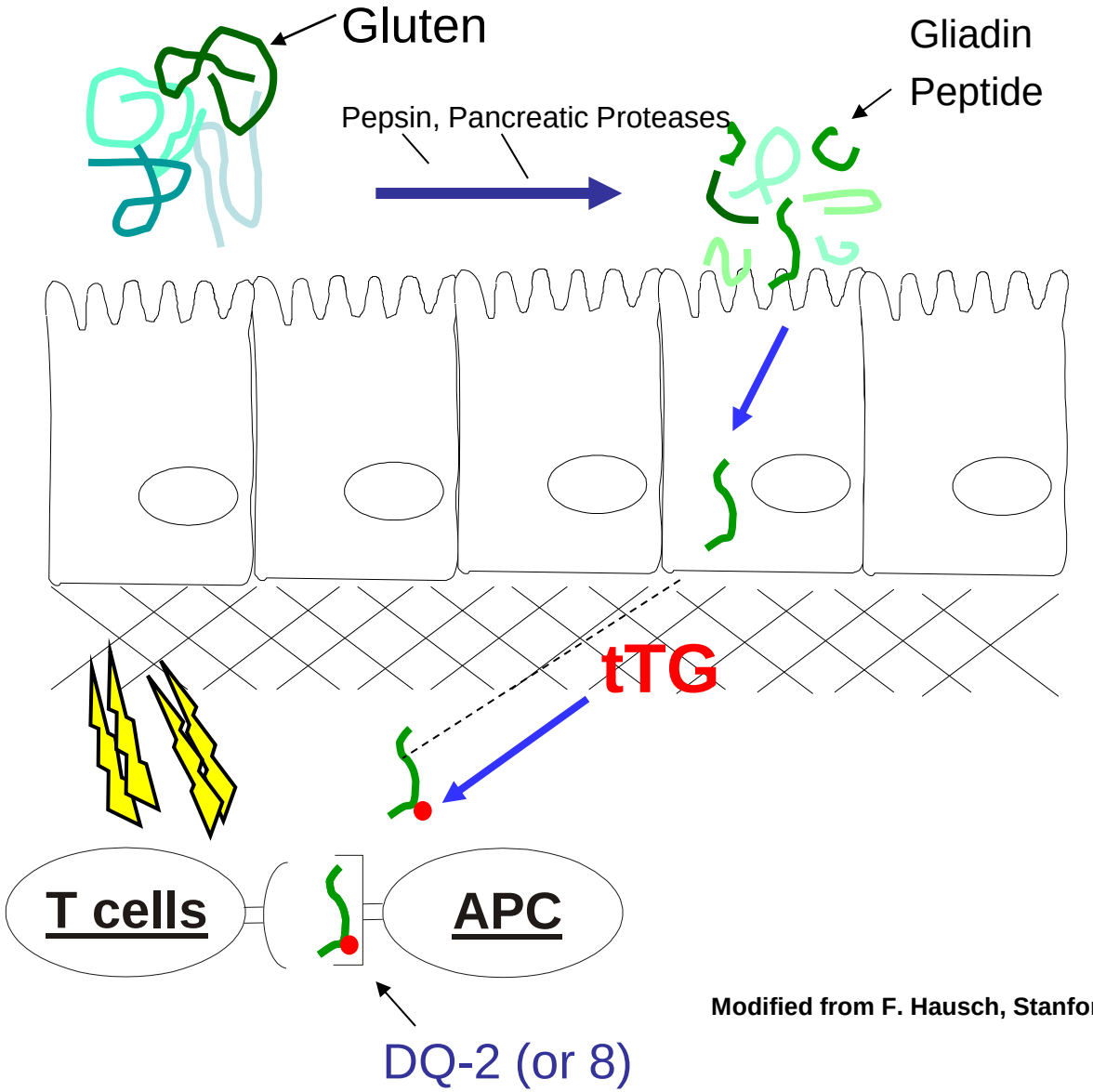
YQLVQQLCCQQLWQI**P**EQSRCQAIHNVVHAIILHQQQQQQQQQ

QQQ**P**LSQVSFQQ**P**QQQY**P**SGQGSFQ**P**SQQN**P**QAQGSVQ**P**Q

QL**P**QFEEIRNLALETL**P**AMCNVYI**PP**YCTIA**P**VGIFGTNYR

The Intestine and Gluten in Celiac Sprue





Modified from F. Hausch, Stanford Univ.

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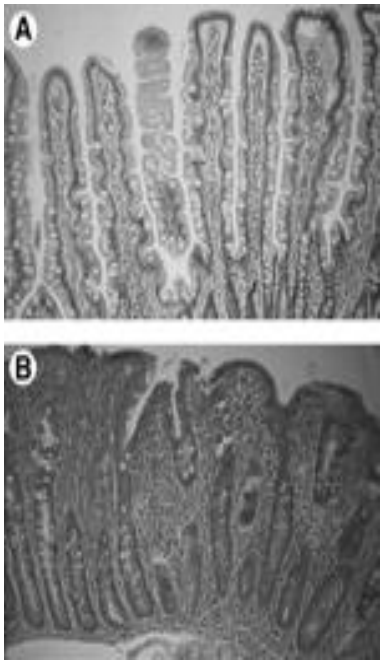

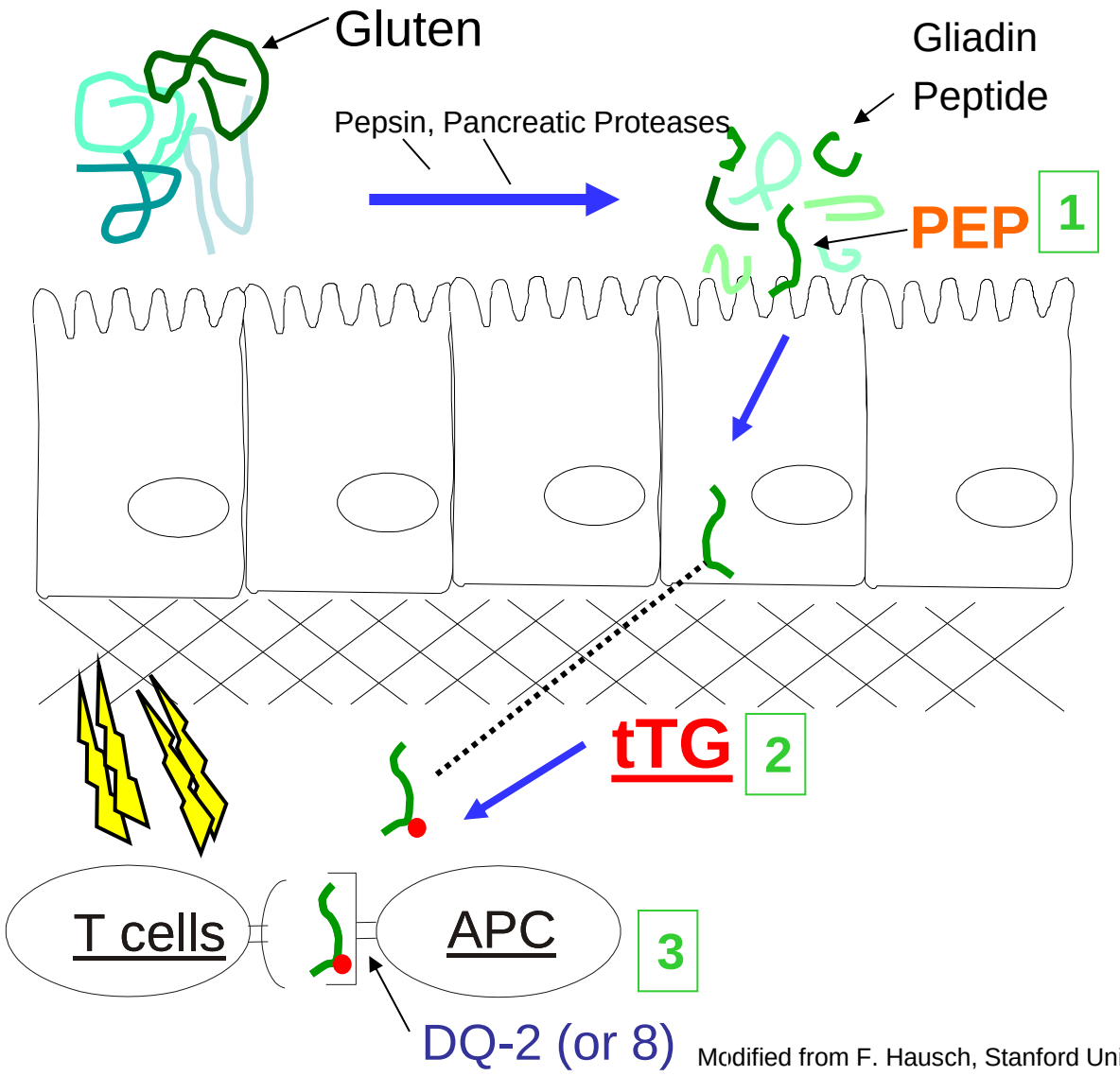

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Learning point:

- **The mainstay of treatment is a gluten free diet but with a better understanding of pathogenesis it should be possible in future to offer other therapeutic options**