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Belgian Polyposis Project
Hereditary Colorectal Cancer Project

Duodenale poliepen bij FAP

23 november 2019

TECHNOPOLIS



Prof. dr. Philip Roelandt
Dienst Maag-, Darm- en Leverziekten



Stichting
tegen Kanker

Stichting van openbaar nut

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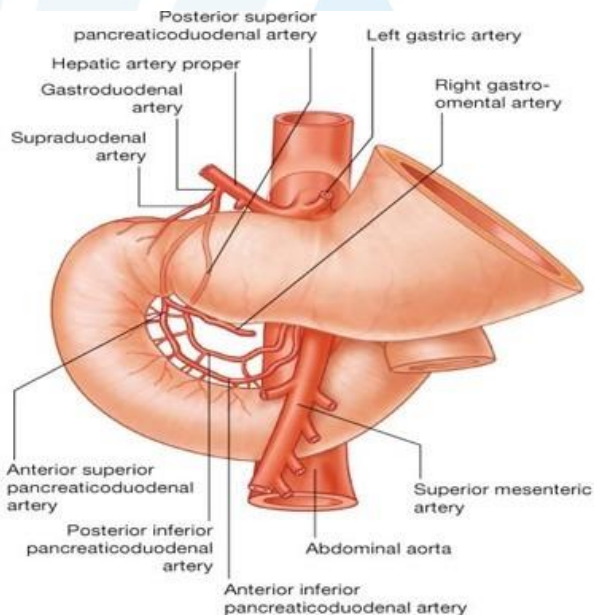
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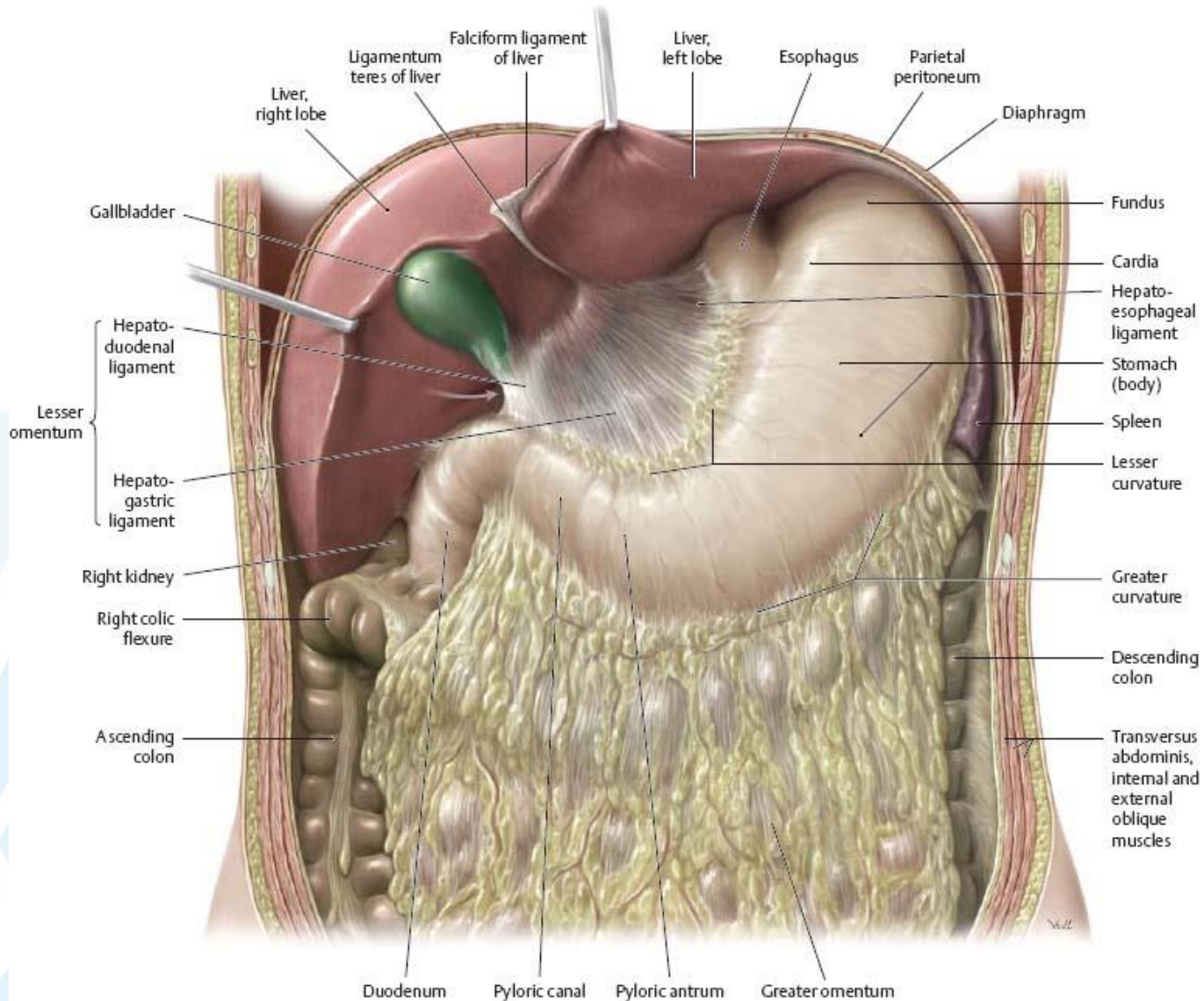
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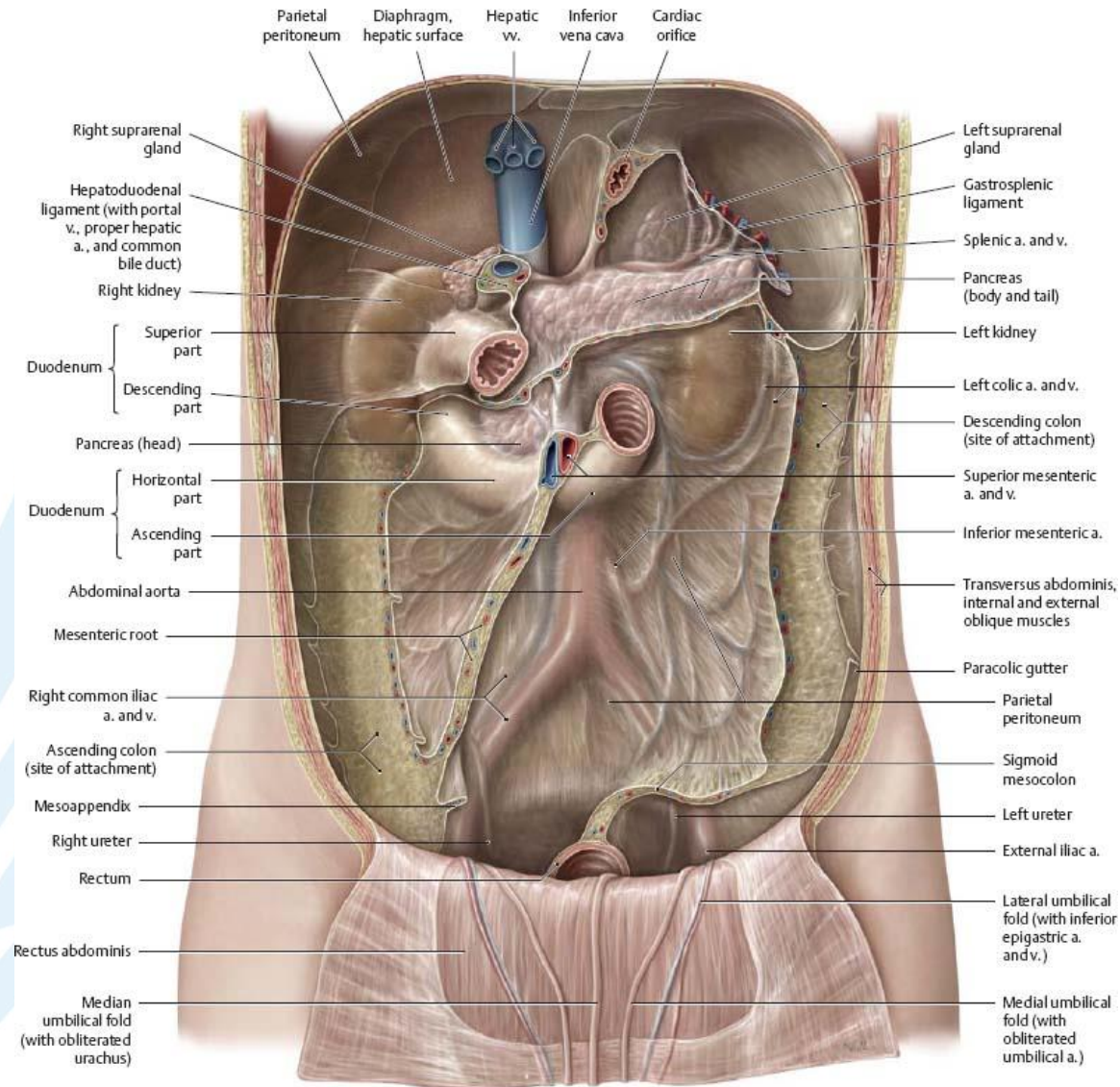
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Duodenum

- Twaalfvingerige darm

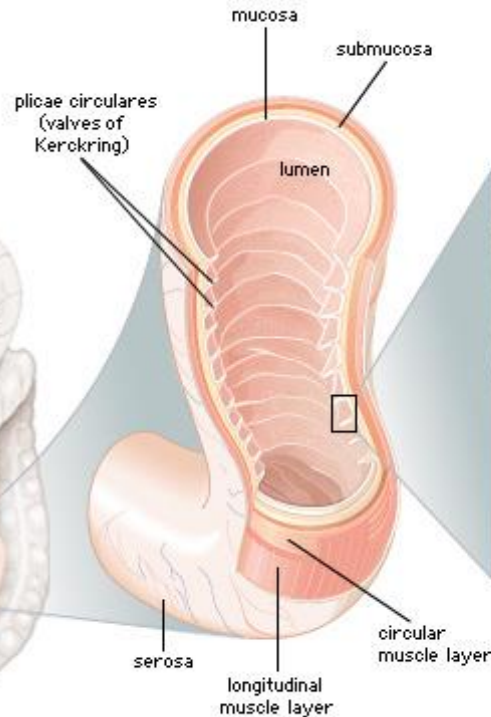
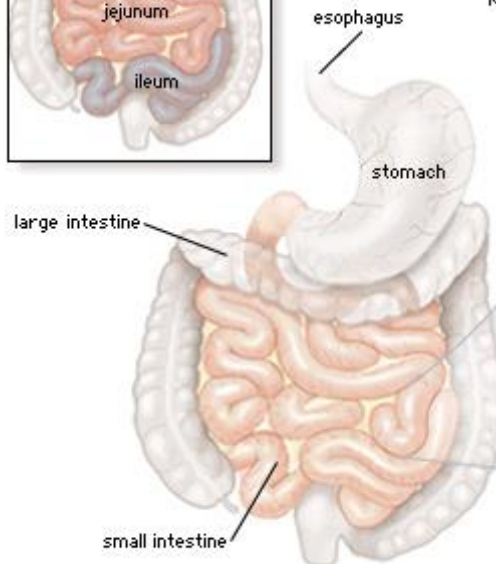
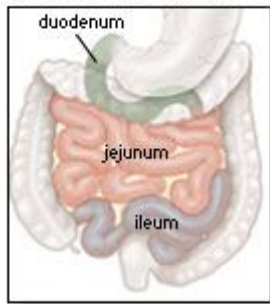




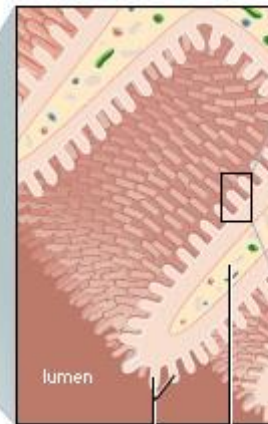


Duodenum – jejunum – ileum

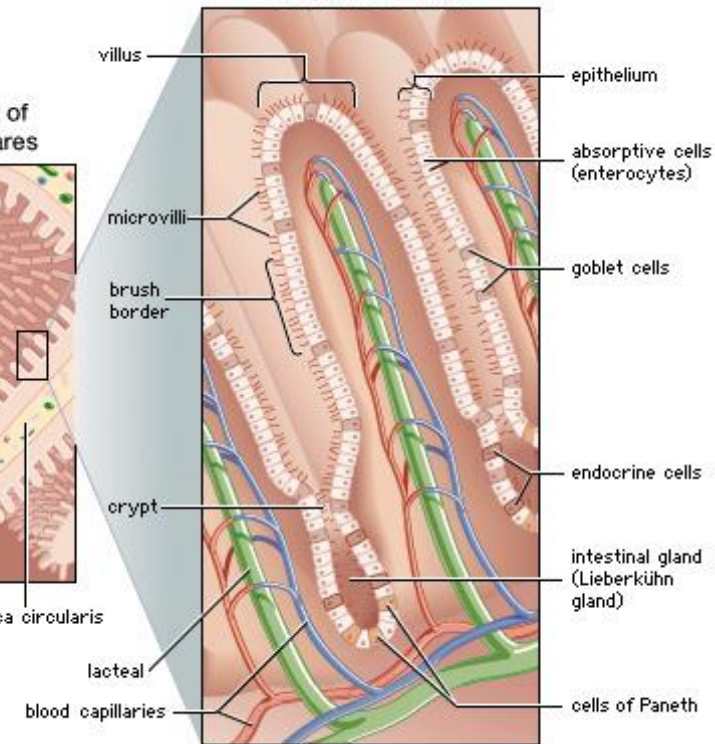
Regions of the small intestine



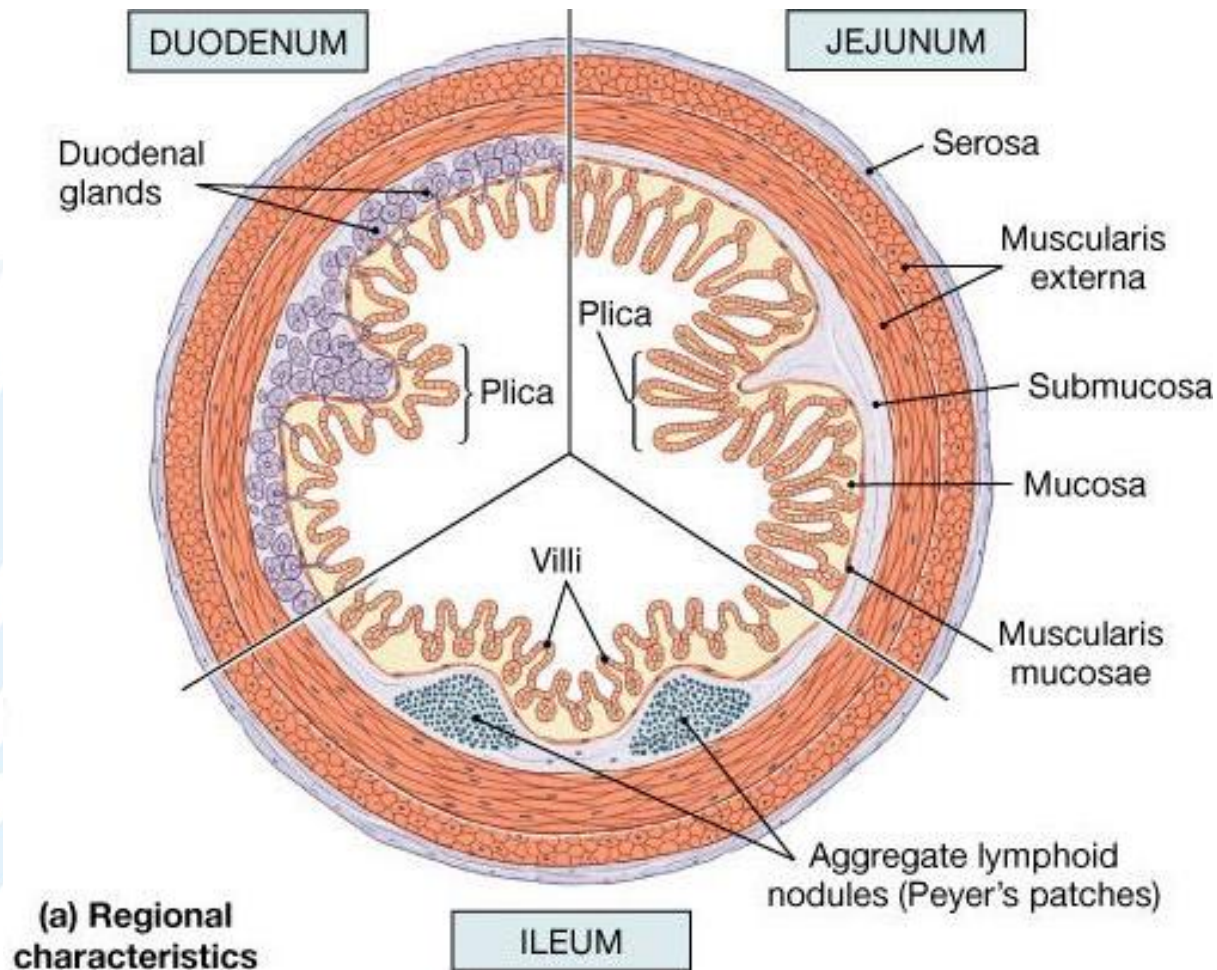
Enlargement of plicae circulares



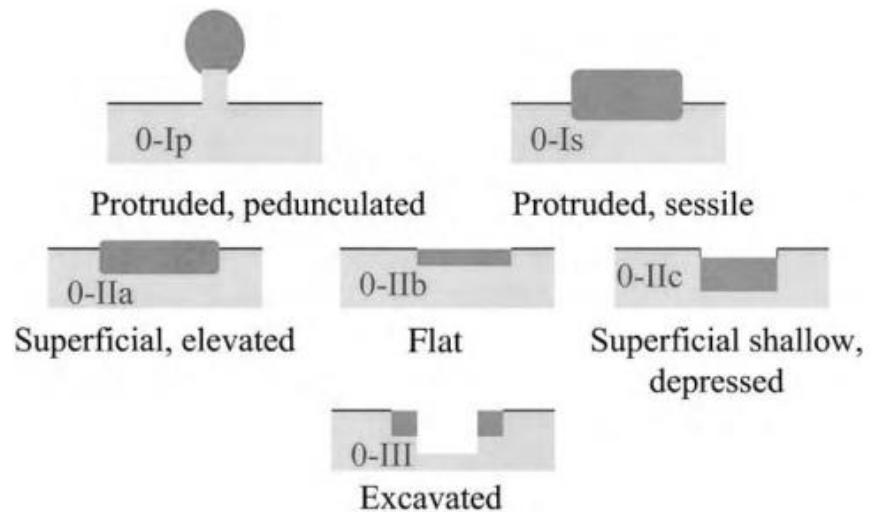
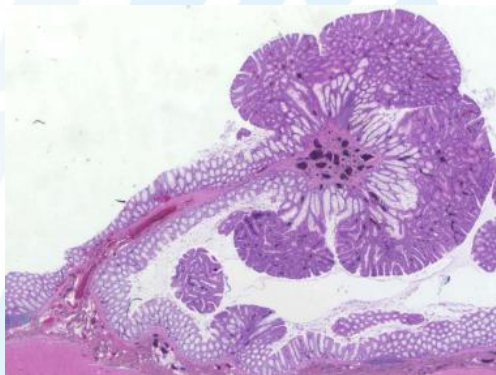
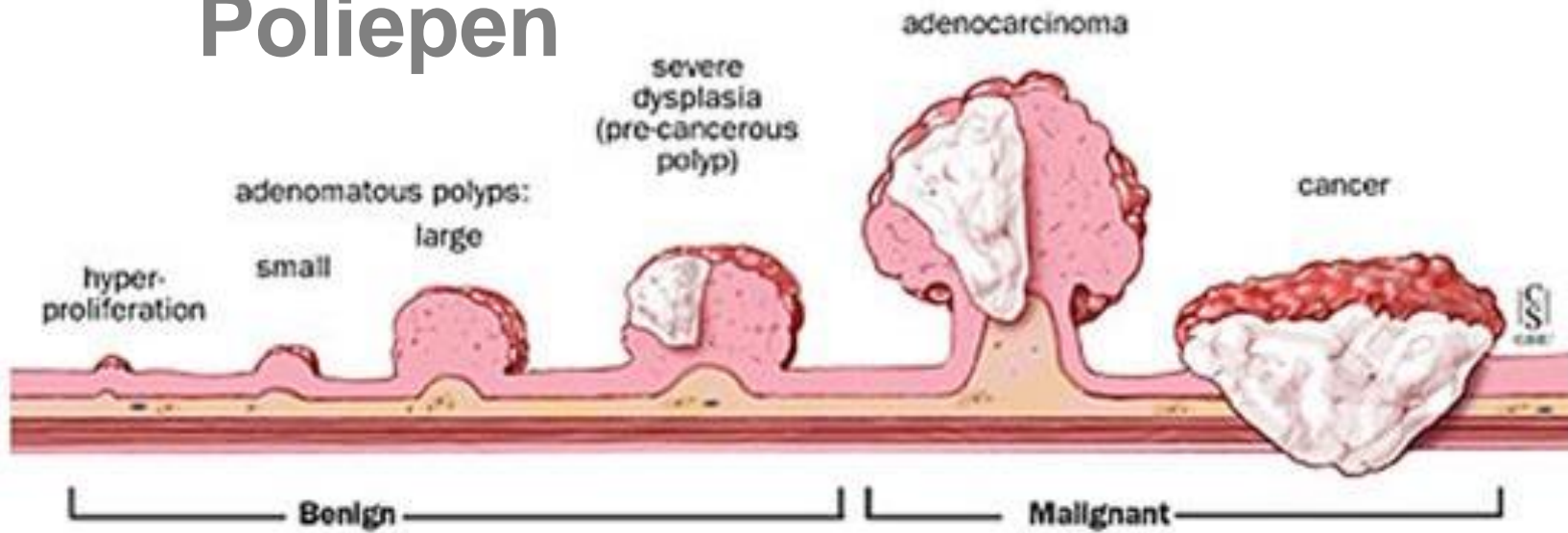
Structure of a villus



Duodenum – jejunum – ileum

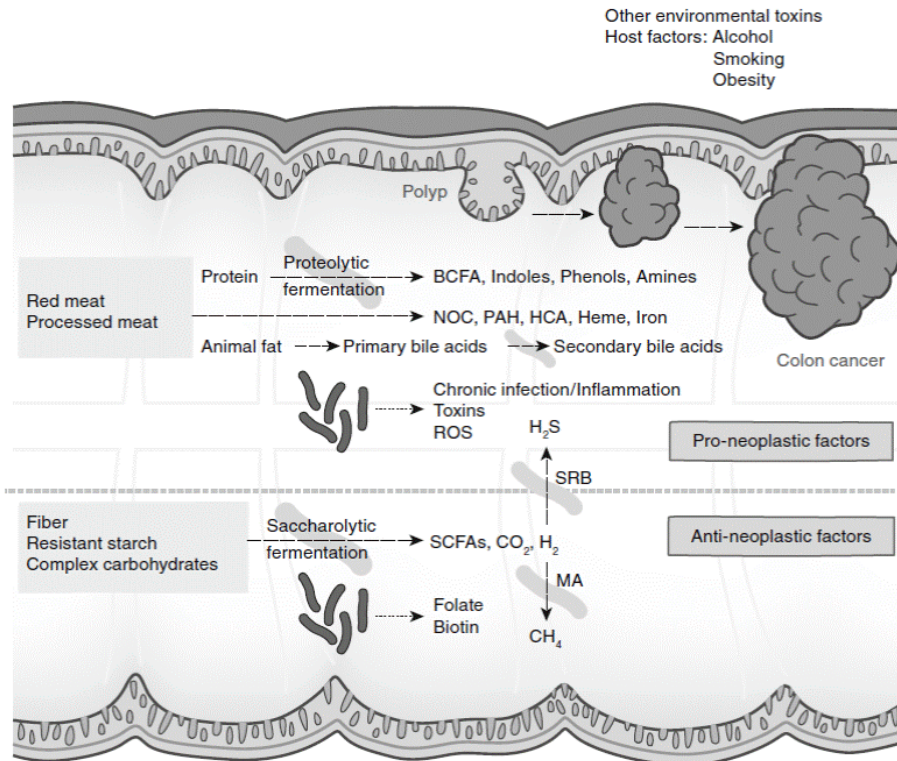


Poliepen



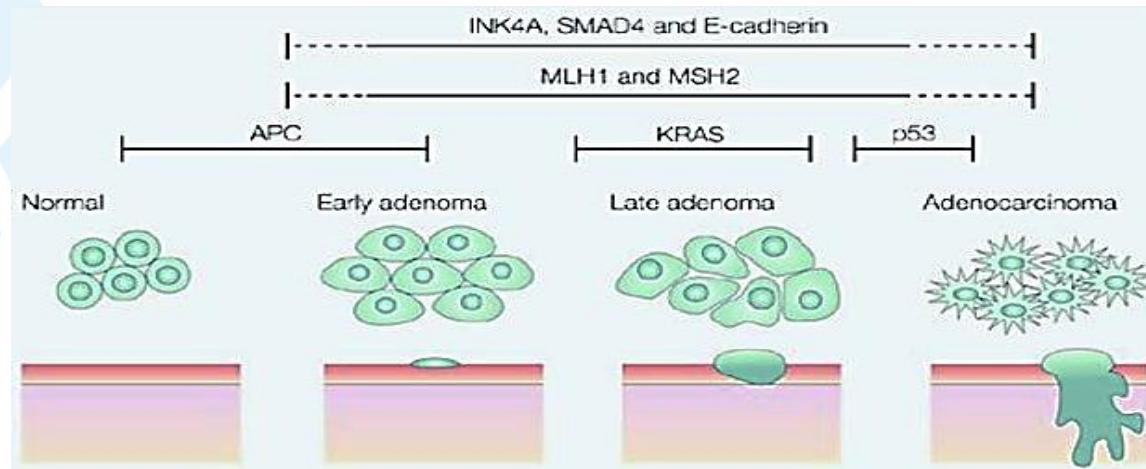
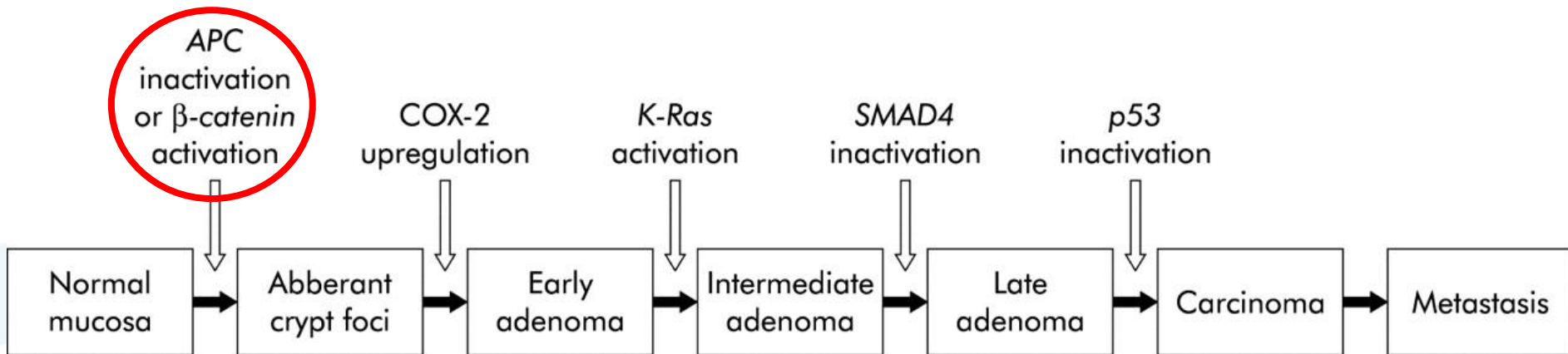
Colonpoliepen

Duodenale poliepen

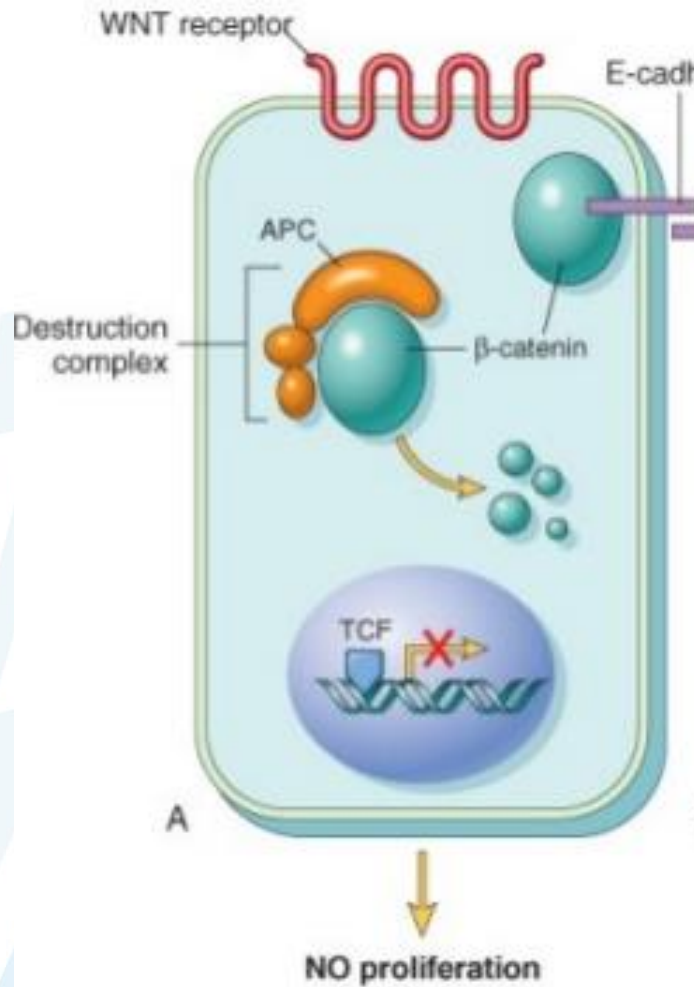


Van poliep tot kanker?

Van adenoom tot carcinoom?

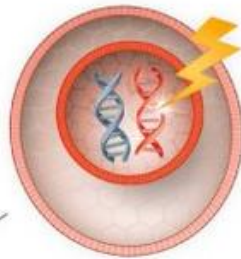


APC = tumor suppressor gene **FAP**



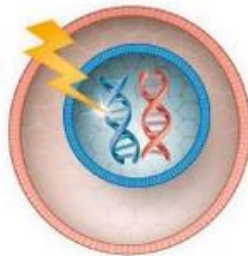
Poliepen en FAP

Mutation of a gene into an **oncogene**

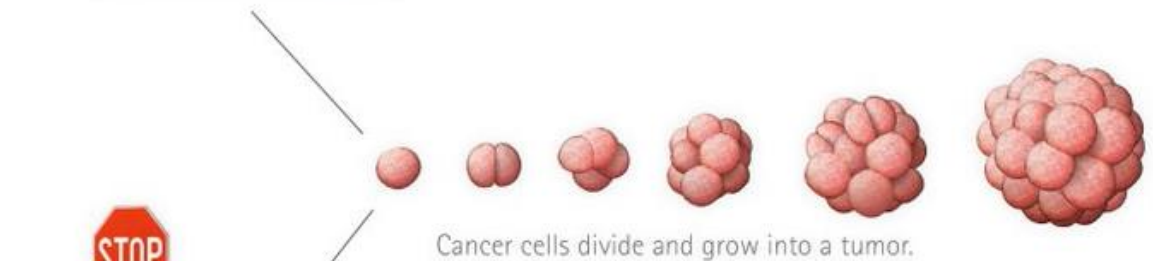


Healthy cell

Mutation in a **tumor suppressor gene**



Mutations in oncogenes are like a **jammed gas pedal** in a car: they increase the speed of cell division.



Cancer cells divide and grow into a tumor.

Mutations in tumor suppressor genes behave like **defective brakes**: the cells continue to divide uncontrollably.

FAP

Duodenale poliepen

- Zeldzaam (0.3-4.6%) in algemene bevolking

T

TABLE 3. Endoscopic Findings in Familial Adenomatous Polyposis Patients With Extra-ampullary Duodenal Lesions (47 Cases)

Parameters	Value
Histologic type (dysplastic lesion/cancer) (n)	46/1*
Single/multiple lesions (n)	7/40
Tumor size [median (range)] (mm)	8 (2-30)
Main lesion macroscopic type (n)†	
Protruded (0-I, 0-IIa)	33
Depressed (0-IIc)	12
Mixed (0-IIa + IIc)	2
Location of lesion (n)	
Bulb	1
Second portion	40
Bulb and second portion	6
Ampullary tumors (present/absent) (n)	17/30

Evolutie naar maligne letsel?

Table 3 Prevalence of duodenal cancer in polyposis registries reported in the literature

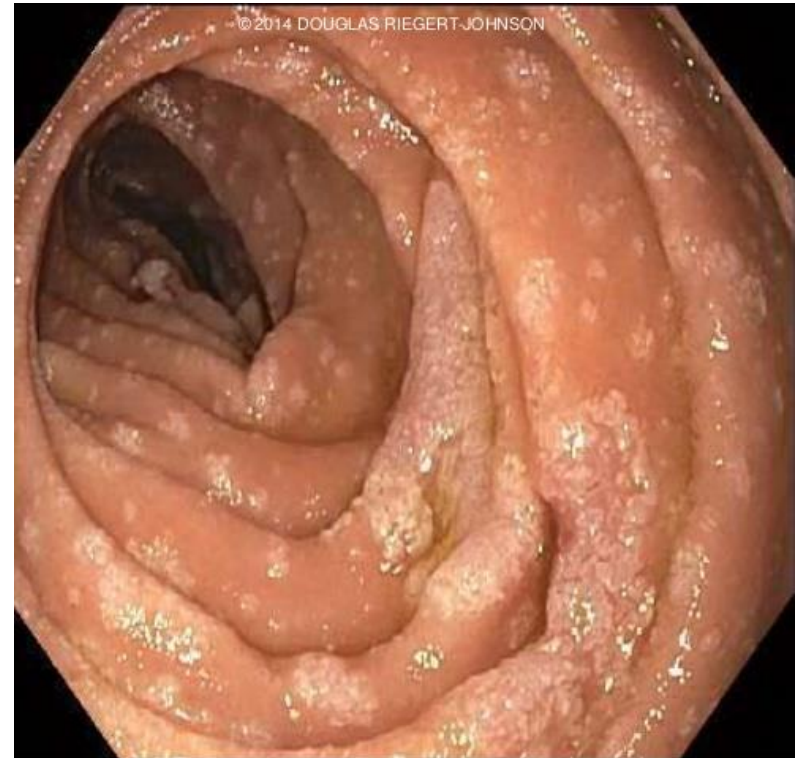
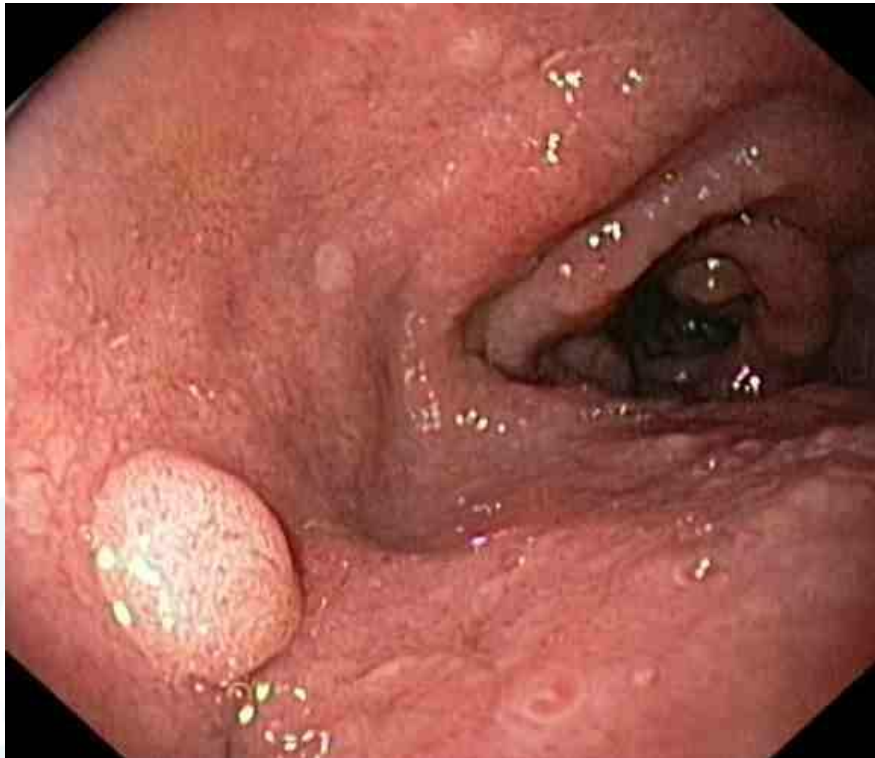
Author	Registry	FAP	Duodenal cancer, n (%)	Period
Jagelman 1988	10 registries	1,255	39 (3.1)	–
Nugent 1994	St Mark's Hospital Polyposis Registry	70	1 (1.4)	57 months
Kadmon 2001	Heidelberg Polyposis Register	231	4 (1.7)	Literature review
Groves 2002	St Mark's Hospital Polyposis Registry	114	6 (5.3)	10-year follow-up
Bullow 2004	Nordic countries and the Netherlands	368	6 (1.6)	1990–2001
Latchford 2009	St Mark's Hospital Polyposis Registry	1,052	20 (1.9)	1969–2005
Park 2011	National Cancer Center of Korea	148	1 (0.7)	1978–2006
Van Heumen 2012	Dutch polyposis registry	1,066	18 (1.7)	1975–2008
Yamaguchi 2016	Japanese multicenter	247	7 (2.8)	2000–2012
Present study	Brazilian single-center	145	5 (3.4)	1958–2016

FAP, familial adenomatous polyposis.

Screening = endoscopie



Screening = endoscopie



Screening = endoscopie

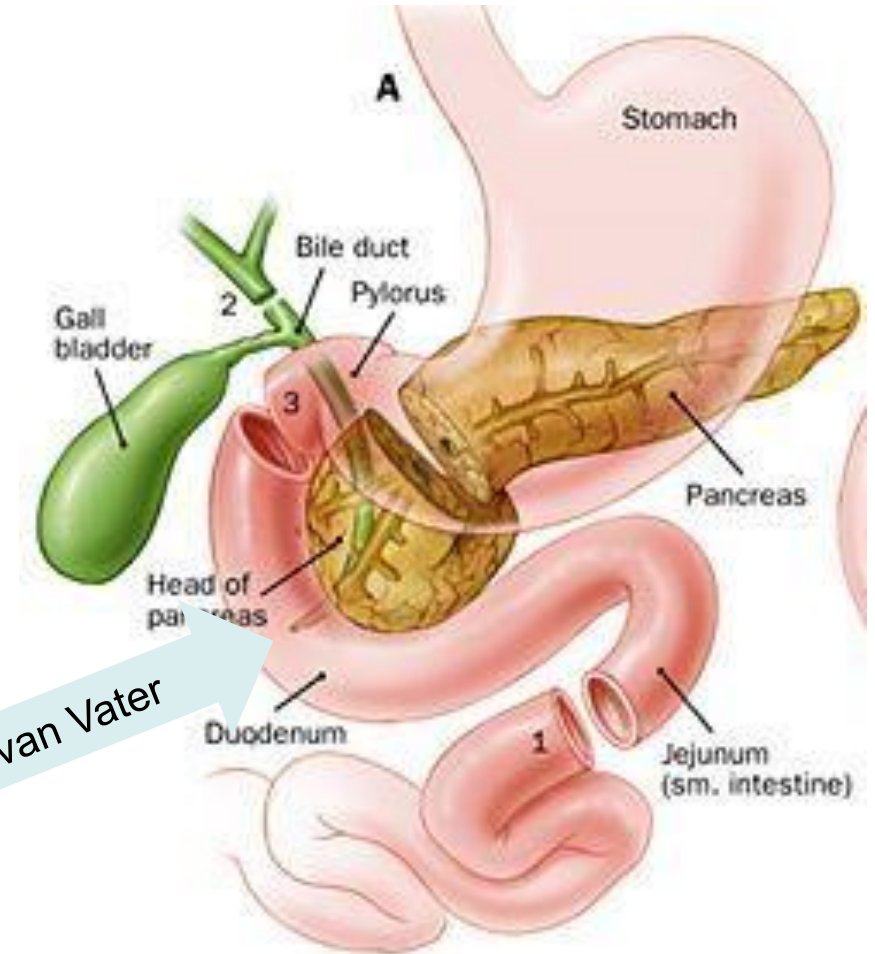
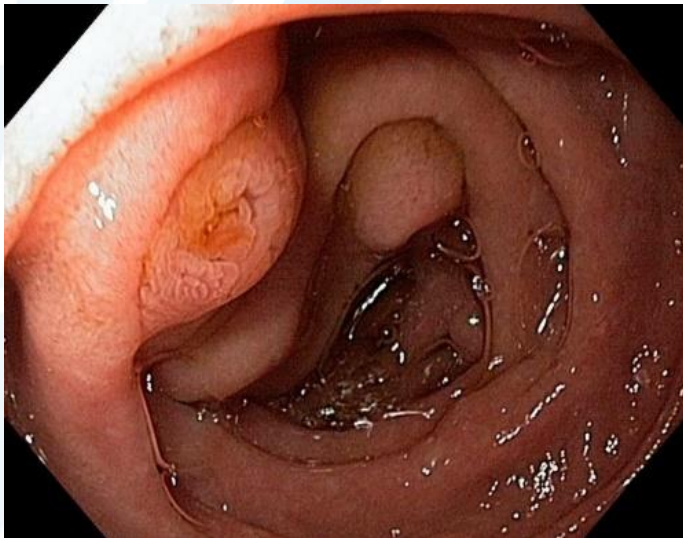
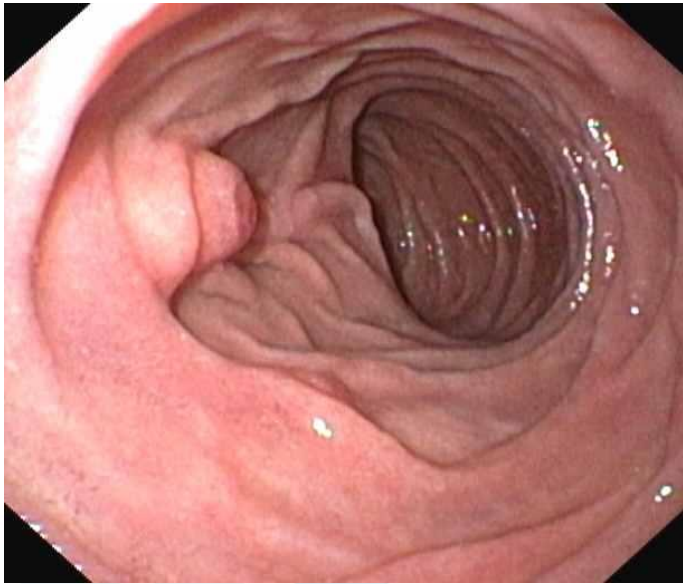
TABLE 2. Clinical Background of FAP Patients With Duodenal Lesions (47 Cases)

Parameters	Value
Age at the first EGD (mean \pm SD) (y)	38 \pm 13
Male/female (n)	35/12
FAP phenotype (profuse/classical) (n)	6/41
Median number of EGDs (range)	12 (1-40)
Endoscopy interval (n) (mo)	
6	11
12	33
\geq 18	1
Median observational period (range) (y)	10.0 (0-17)
Age at the time of diagnosis (mean \pm SD) (y)	
For duodenal lesions	40 \pm 14
For duodenal carcinoma or HGD	43 \pm 14

Spigelman classificatie

figuur 5.1 Classificatie van de ernst van duodenale polyposis bij FAP volgens Spigelman (1989).
Voor bepaling van het stadium wordt het aantal punten opgeteld





Papil van Vater

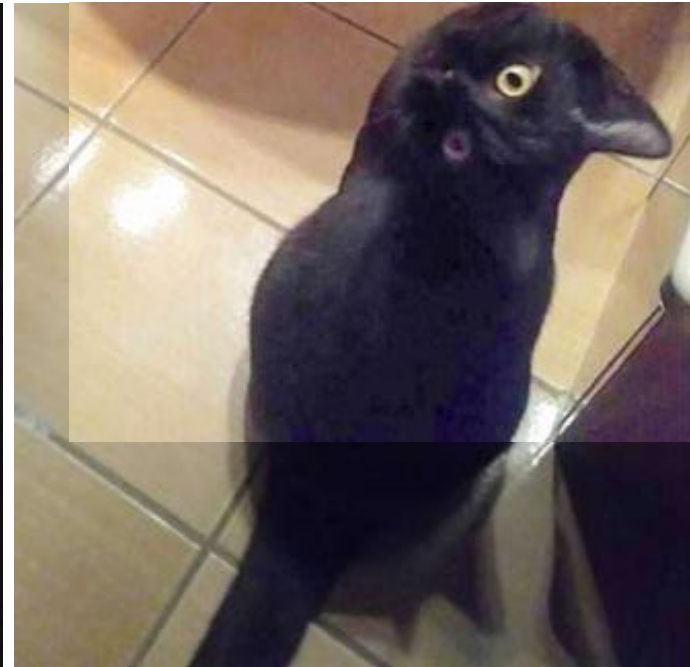
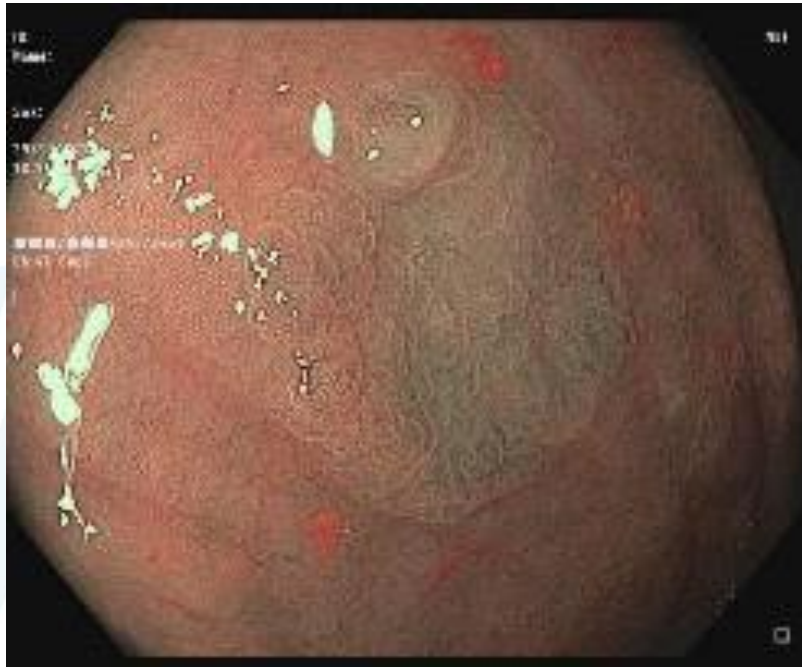
Screening papil = side view



Was man weiß, sieht man erst! (Johann Wolfgang von Goethe)



Was man weiß, sieht man erst! (Johann Wolfgang von Goethe)



Chromo-endoscopie?

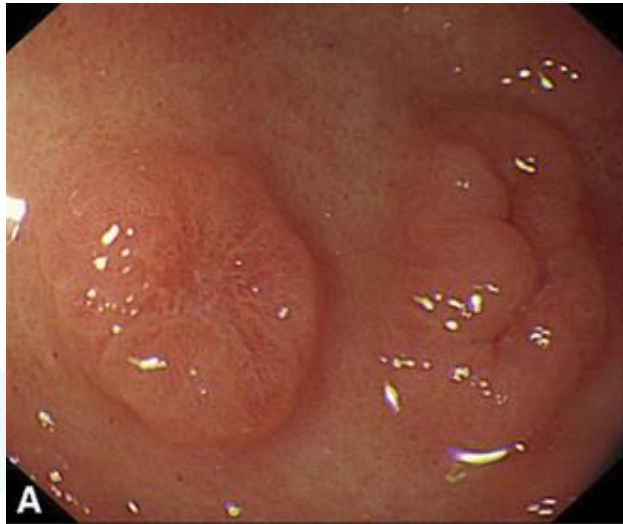


TABLE 3. Duodenal adenoma characteristics in patients with FAP (n = 19)

Gastroduodenoscopy findings	Pre-staining	Post-staining	P value
Number of duodenal adenomas, median (total)	4 (150)	14 (442)	.002516*
Largest size (mm), median (range)	6 (2-23)	6 (2-30)	.1814
Spigelman stage, median (range)	II (0-IV)	II (0-IV)	.03125*

Richtlijnen screening 2019

- Eerste gastroscopie 25-30 jaar
- Follow-up volgens Spigelman

Spigelman

0 & I

II

III

IV

Interval

5 jaar

3 jaar

1 jaar + sideview

overweeg behandeling
anders ½ jaar + side view

- Ook voor aFAP en MAP

Behandeling = resectie

- Succes ~ grootte en aantal
- Na 5 jaar tot 25% recidief
- Als $> 1/3$ omtrek indicatie voor heelkunde
- Relatief grote kans op complicaties
 - Bloeding 3.2% bij letsels < 3 cm, tot 26.3% bij letsels > 3 cm
 - Perforatierisico duodenum $>$ colon

Technieken

Procedure	Appropriate lesion size	Used for non-ampullary lesions	Used for papillectomy	Piecemeal resection possible	Can be done using a duodenoscope	Degree of difficulty
Snare polypectomy (<i>en bloc</i>)	≤ 10 mm	Y	Y	N	Y	+
Cap-assisted EMR (requires submucosal lifting)	≤ 18 mm	Y	N	Y	N	+++
Cap-band-assisted EMR	≤ 11 mm	Y	N	Y	N	++
Conventional EMR (with submucosal injection)	Any size	Y	Y	Y	Y	+++
Underwater EMR	Any size	Y	Y	Y	Y (forward-viewing scope with a cap is preferred)	+++
ESD	Any size	Y	N	N/A (goal of ESD is <i>en bloc</i> resection)	N	++++

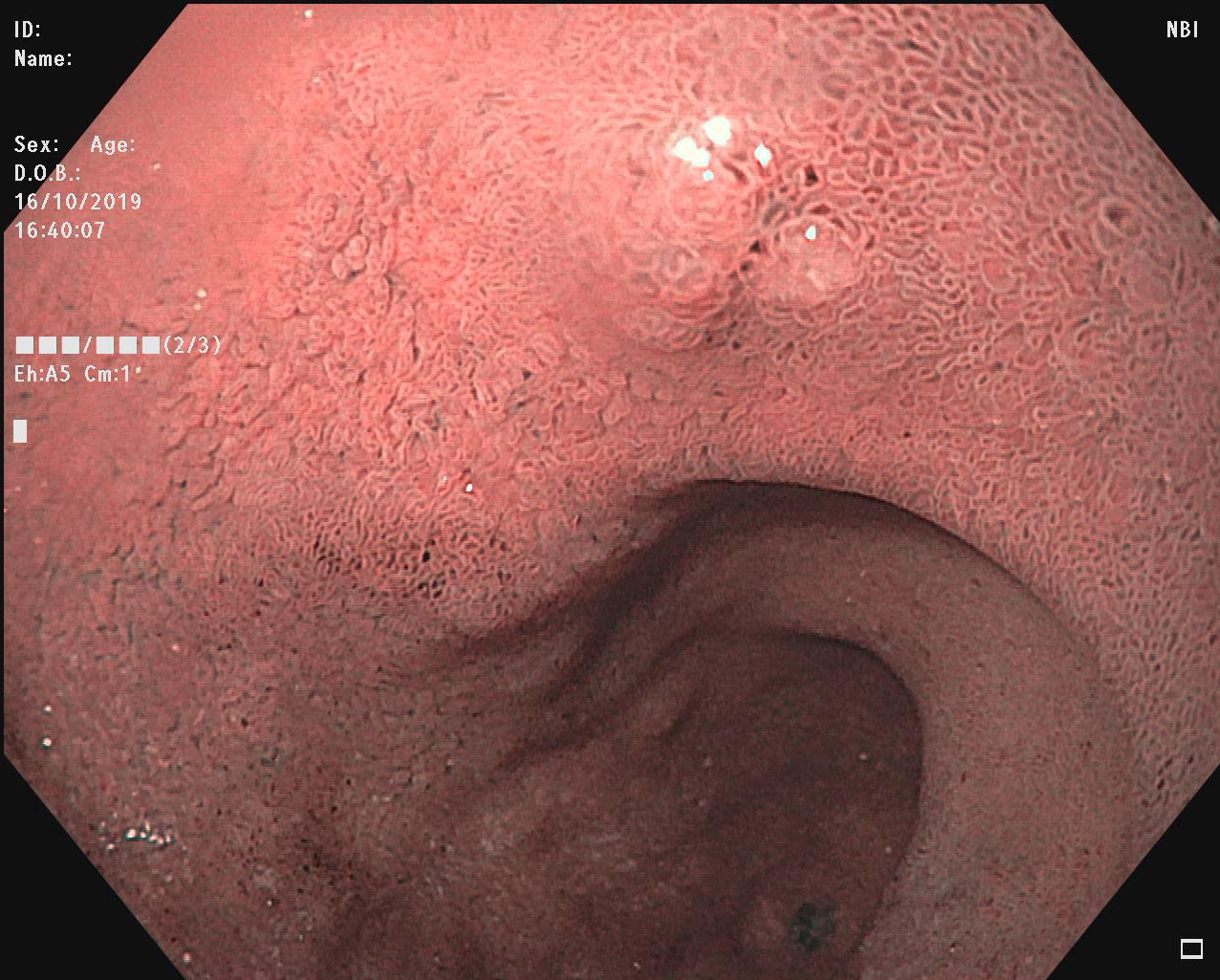
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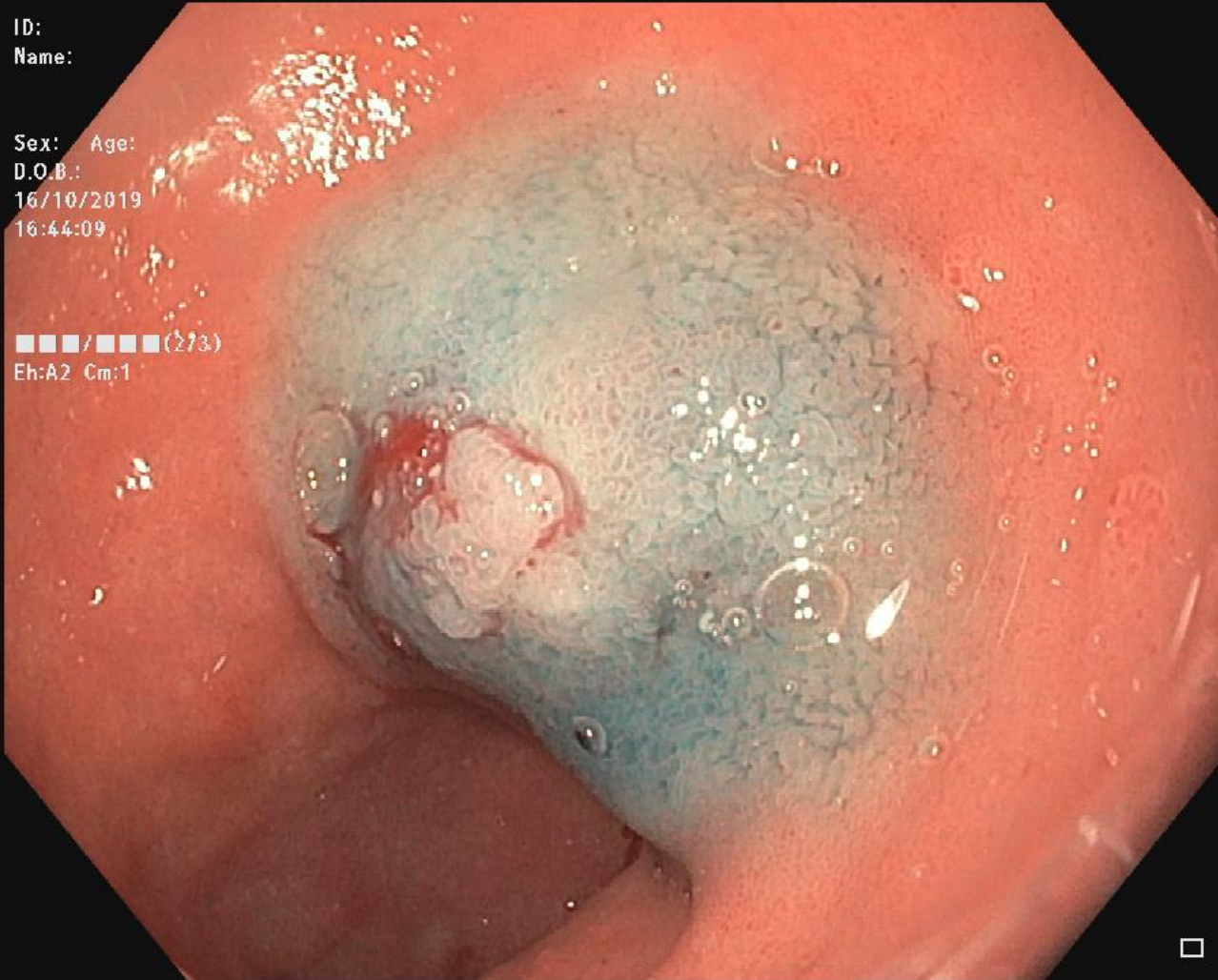
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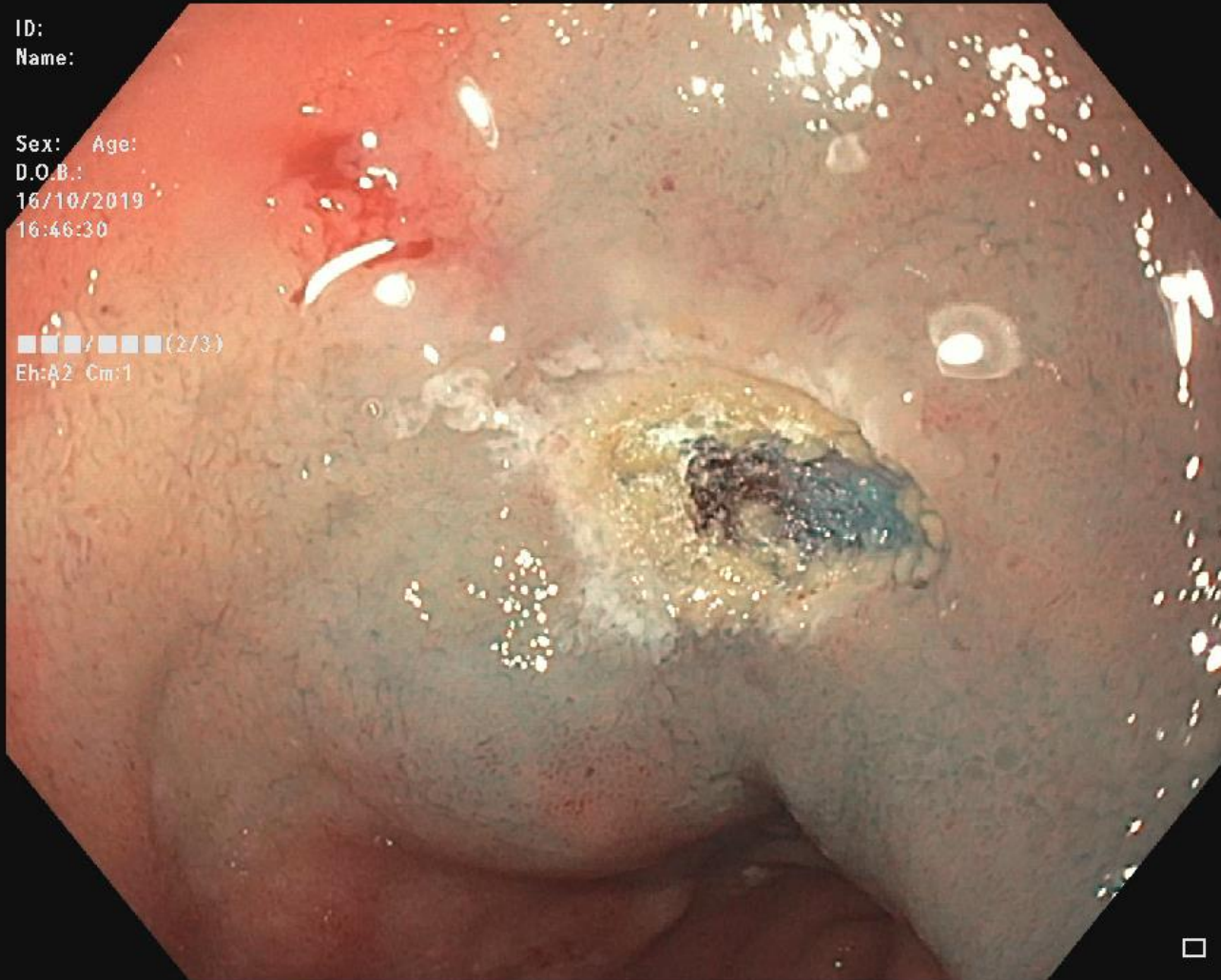
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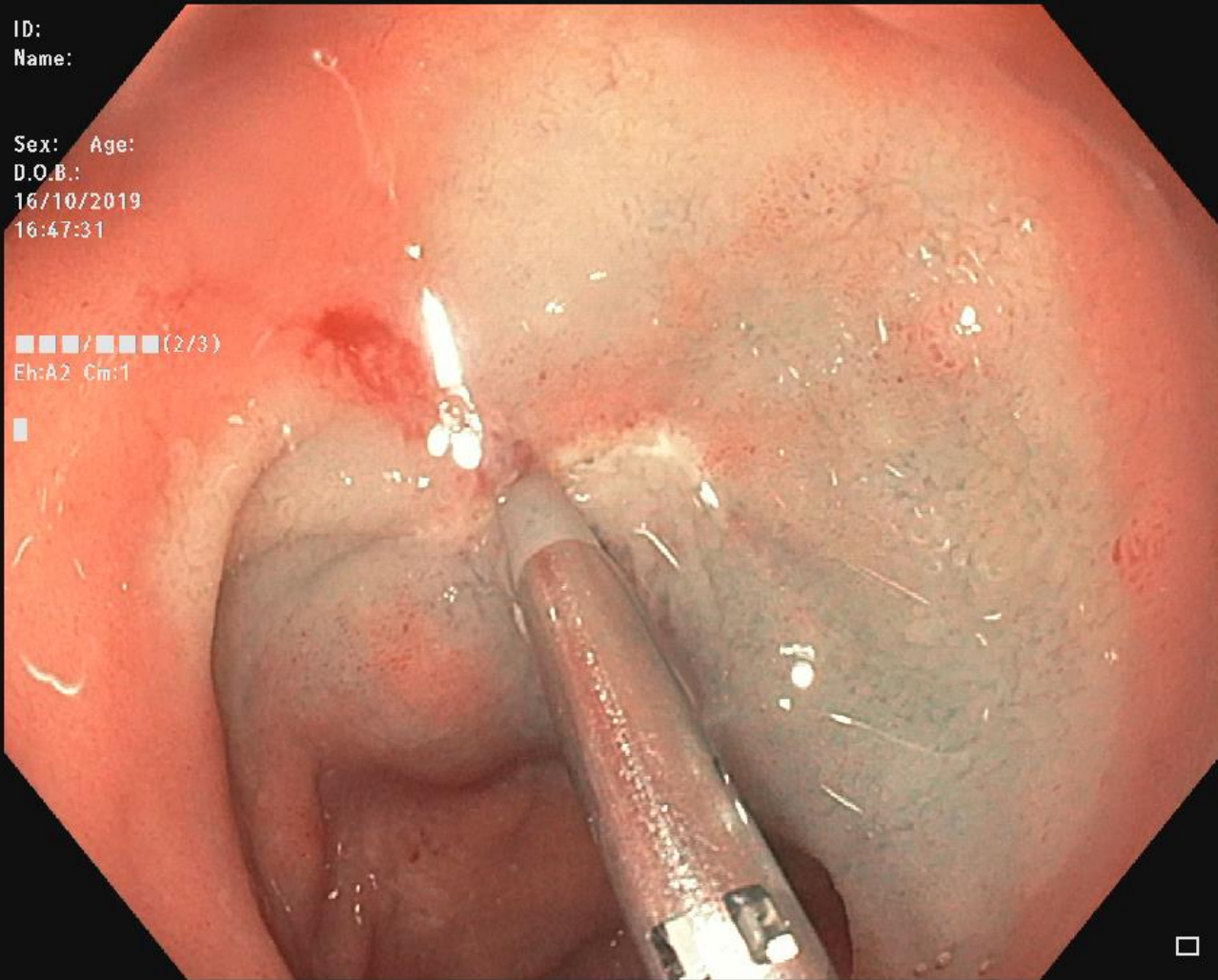
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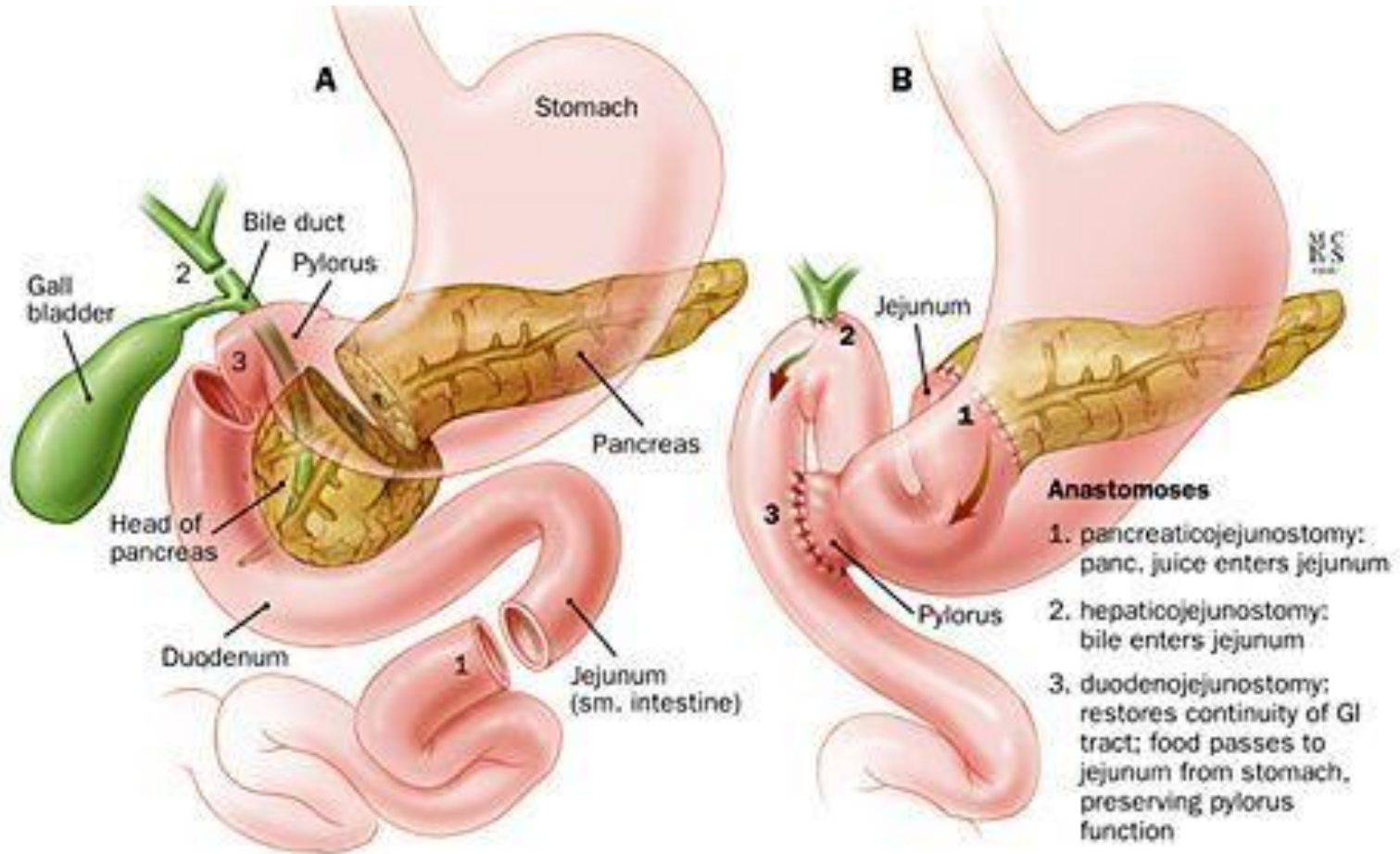


Heelkunde: lokaal

Table 5 Local surgical treatment (duodenotomy with polypectomy and/or ampullectomy) for duodenal neoplastic lesions

Author	Treatment	Follow up	Patients	Outcome	Postoperative
Soravia ⁵²	Duodenotomy with polypectomy (1) or ampullectomy (4)	4–34 months (mean 18)	5 FAP	Recurrence in 4 patients. 1 patient died of cancer	1 transient duodenal fistula
Morpurgo ⁴⁴	Transduodenal ampullectomy (1) or polyp excision (1)	6–24 months (mean 19)	2 FAP	Recurrence in 1 patient	1 severe pancreatitis
Alarcon ⁴⁶	Local resection	8–33 months (mean 20.2)	5 FAP	Recurrence in 4 patients. 1 had progressive metastatic adenocarcinoma	NS
Heiskanen ⁵	Duodenotomy	0.4–15.1 years (median 6.8)	15 FAP	No significant difference in Spigelman stage preoperative and at latest endoscopy	No postoperative complications
Penna ⁵⁶	Duodenotomy with polypectomy	5–36 months (mean 13.3)	12 FAP	Recurrence in 12 patients	NS
Penna ⁵⁷	Duodenotomy with polypectomy	36–72 months (mean 53)	6 FAP	Recurrence in 6 patients	1 cholecystectomy for cholecystitis, 2 duodenal fistulas
de Vos tot Nederveen ⁵⁸	Duodenotomy with ampullectomy	4–13 months (mean 11)	8 FAP	Recurrence in 6 patients	1 minor morbidity*
de Vos tot Nederveen ⁵⁸	Duodenotomy with polypectomy	5–103 months (mean 29)	22 FAP	Recurrence in 17 patients. 1 death from metastatic disease	1 minor morbidity*
Ruo ⁵⁹	Duodenotomy with ampullectomy	35 months	1 FAP	Gastric cancer arising from a polyp at 35 months	No postoperative complications
Farnell ⁶⁰	Transduodenal local excision	10 years	53 sporadic and FAP patients	Recurrence rate of 32% at 5 years and 43% at 10 years of follow up	3 pancreatitis, 3 leaks, 2 delayed gastric emptying, 2 ileus, 1 fluid overload

Heelkunde: Whipple operatie

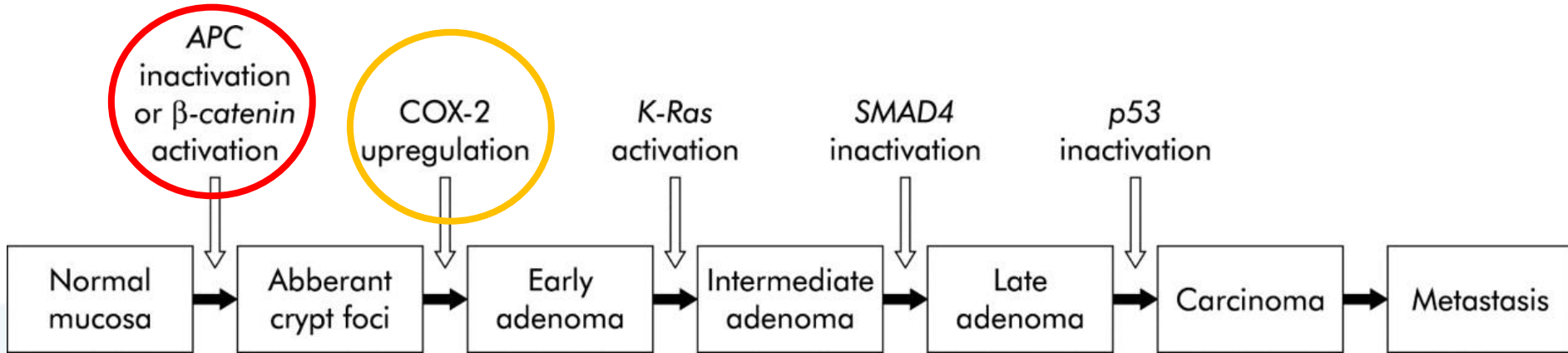


Heelkunde: Whipple operatie

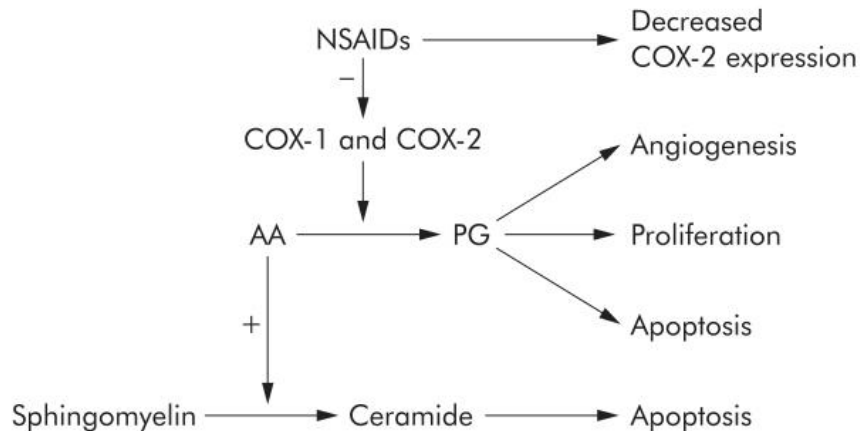
Table 6 Pancreaticoduodenectomy and pylorus or pancreas preserving duodenectomy for duodenal neoplastic lesions

Author	Treatment	Follow up	Patients	Outcome	Postoperative
Soravia ⁵² Morpurgo ⁴⁴	Pancreaticoduodenectomy Pancreaticoduodenectomy	NS NS	1 FAP 4 FAP	Unknown No recurrence reported	NS Increased number of bowel movements. One patient required pouch excision and end ileostomy to control diarrhoea. 3 patients experienced weight loss, 1 patients had episodes of pancreatitis
Alarcon ⁴⁶	Pancreas sparing duodenectomy	40–50 months (mean 45.7)	3 FAP	No recurrence. Two of three patients had a small tubular adenoma in the duodenal bulb.	NS
Penna ⁵⁷	Pancreaticoduodenectomy	9–108 months (mean 42) 1–9 years	7 FAP severe duodenal polyposis 5 FAP duodenal cancer	No recurrence in patients treated for severe duodenal polyposis. Only 1 patients with duodenal cancer survived >4 years	1 pancreatic fistula, 1 upper GI haemorrhage Resection not possible in 2 because of peritoneal carcinomatosis or distal lymph node involvement
de Vos tot Nederveen ⁵⁸	Pancreaticoduodenectomy	7–96 months (mean 47)	23 FAP	Recurrence in 3, 6 died of metastatic disease	5 minor morbidity*, 12 major morbidity†, 1 patient died of postoperative complications
de Vos tot Nederveen ⁵⁸	Pancreas sparing duodenectomy	2–15 months (mean 11)	6 FAP	No recurrence	1 minor morbidity*, 3 major morbidity†
de Vos tot Nederveen ⁵⁸	Pylorus preserving duodenectomy	7–93 months (mean 45)	12 FAP	Recurrence in 3 of 9, 3 died of metastatic disease	1 minor morbidity*, 4 major morbidity†
Ruo ⁵⁹	(Pylorus preserving) pancreaticoduodenectomy	37–162 months (mean 70.5)	7 FAP	1 patient developed jejunal adenomas 12 years after operation	1 patient developed pancreatic ascites
Chung ⁶¹	Pancreas sparing duodenectomy	0.5–3 years (mean 2.1)	4 FAP	No recurrence	1 gastric retention, 1 pancreatic fistula
Kalady ⁶²	Pancreas sparing duodenectomy	10 years	3 FAP	1 had polyp recurrence in jejunum at 5 years of follow up	1 postoperative wound infection, 1 biliary leak
Balladur ⁶³	(Pylorus preserving) pancreaticoduodenectomy	24 and 28 months	2 FAP	No recurrence	NS
Farnell ⁶⁰	(Pancreas sparing) pancreaticoduodenectomy	0.3–16 years (mean 5.6)	25 FAP and sporadic	No recurrences	10 leaks, 4 delayed gastric emptying, 1 delirium tremens, 3 abscesses. 1 patient died from bleeding and sepsis related to hepaticojejunostomy leak. Morbidity was higher after pancreas sparing duodenotomy.

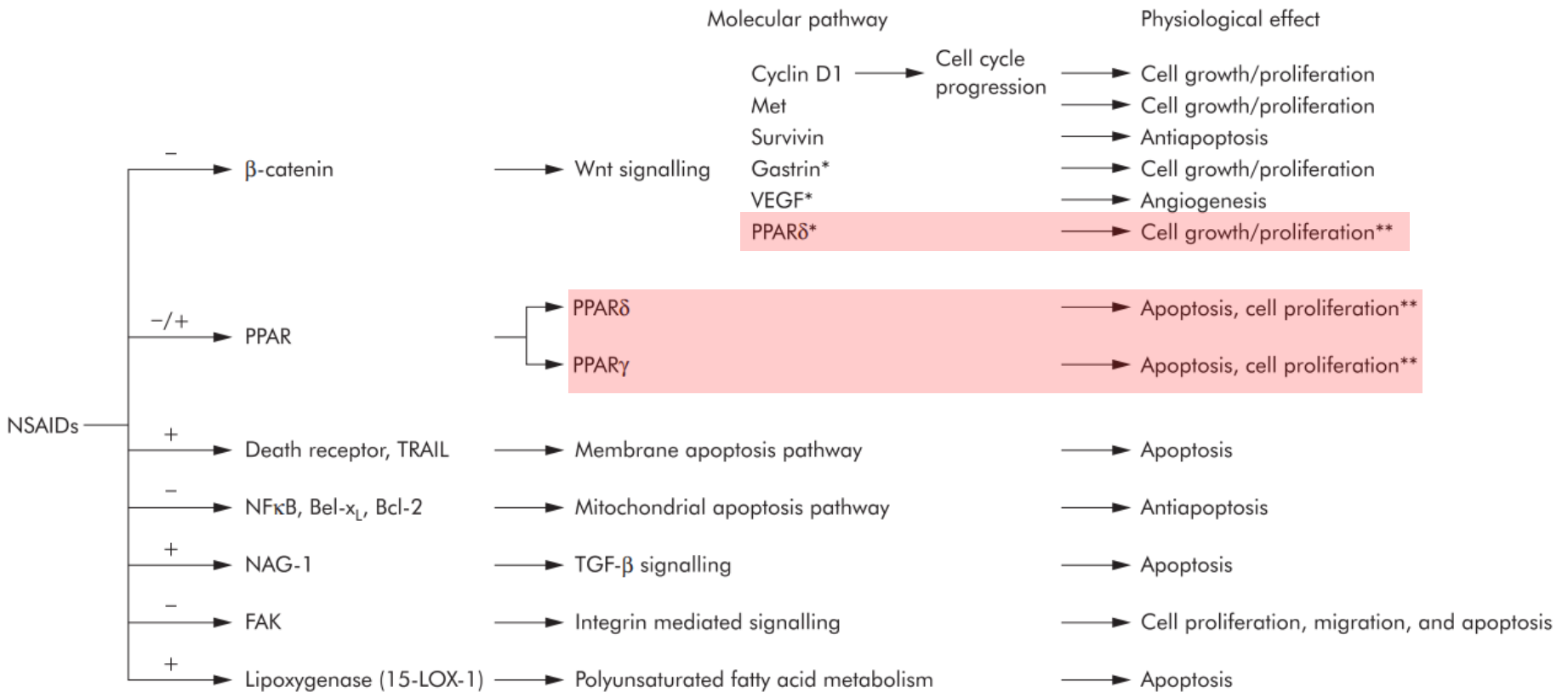
Medicatie? Preventie?



Physiological effect



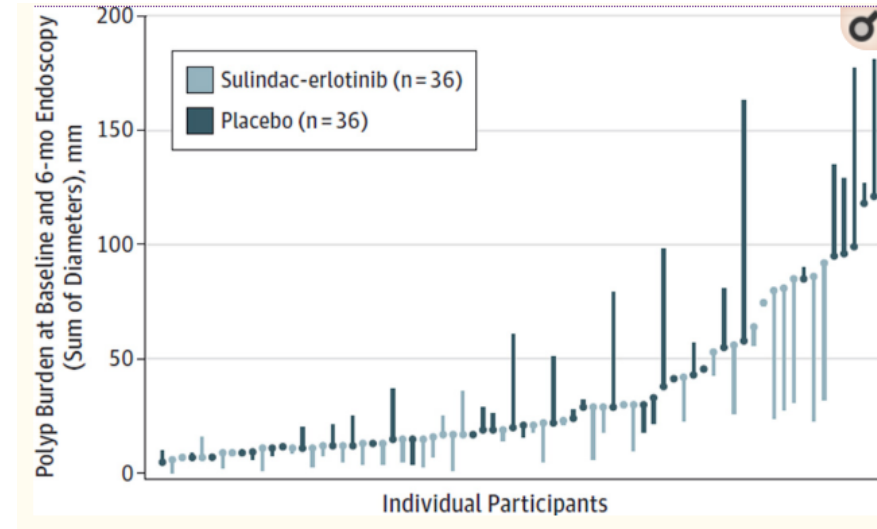
Medicatie? Preventie?



Cardiovasculaire risico's (cfr terugtrekking Vioxx® 2014)

Medicatie? Preventie?

Outcome	Baseline	6-mo Follow-up	Median Change	Between-Group Difference (95% CI)	PValue
Median Duodenal Polyp Burden, mm					
Sulindac-erlotinib	29.0	19.5	-8.5	-19.0 (-32.0 to -10.9)	<.001
Placebo	23.0	31.0	8.0		
Median Duodenal Polyp Count, No.					
Sulindac-erlotinib	13.5	10.0	-2.8	-8.0 (-12.2 to -4.7)	<.001
Placebo	10.5	17.0	4.3		



83% neveneffecten: rash, mucositis, diarree en misselijkheid

Verder onderzoek nodig

Conclusies

- Duodenale poliepen bij FAP zijn heel frequent in vergelijking met algemene bevolking
- Screening is cruciaal en afhankelijk van aantal en type poliepen
- Verschillende behandelingsmogelijkheden, opnieuw afhankelijk van aantal en type
- Preventie van evolutie mogelijk, momenteel nog niet praktisch/veilig

Vragen?

