



Divertikulose / Divertikulitis: eine vermeidbare Krankheit?

Ludwig T. Heuss



Spital Zollikerberg
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Spektrum

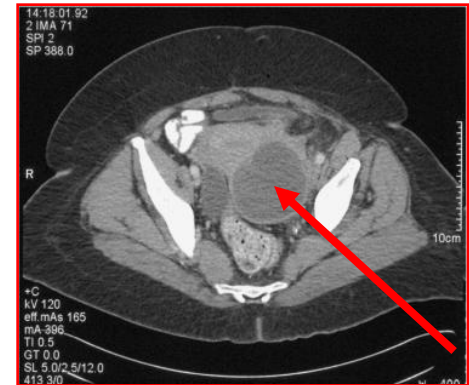
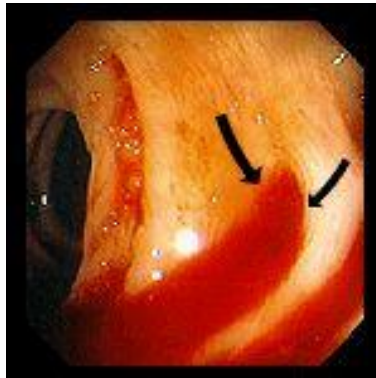
Spektrum der Divertikelkrankheit

Divertikulose

Divertikel-
blutung

Divertikulitis

Komplizierte Divertikulitis



Gastroenterologe

Hausarzt / Internist

Chirurg



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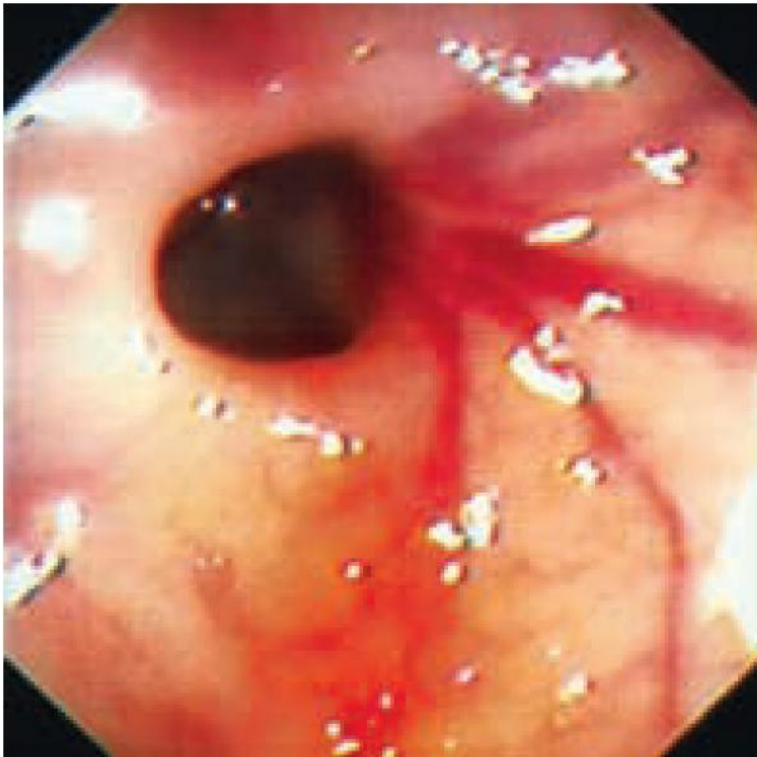
Einführung

- (Alexis Littré 1700)
- Jean Cruvelhier 1849

- Ernst Graser 1899 “falsche Darmdivertikel” MMW



Nachbarschaft Divertikel / Gefäß



Einführung

- (Alexis Littré 1700)
- Jean Cruvelhier 1849
- Ernst Graser 1899 “falsche Darmdivertikel” MMW
- Begriff “Diverticulosis” – erstmals 1914
- Akute Divertikulitis zu Beginn des 20 Jahrhunderts



Definitionen

- **Kolondivertikel:** Herniation der Mucosa und Muscularis mucosae durch die Kolonwand.
- **Divertikulose:** Vorhandensein von Divertikeln ohne Entzündung
- **Divertikelkrankheit:** Vorhandensein symptomatischer Divertikel
- **Diverticulitis:** Entzündung und Infektion assoziiert mit Divertikeln.

Pathologie

- Echte Divertikel:
 - enthalten alle Wandschichten
 - Rechtsseitig
 - Asiaten

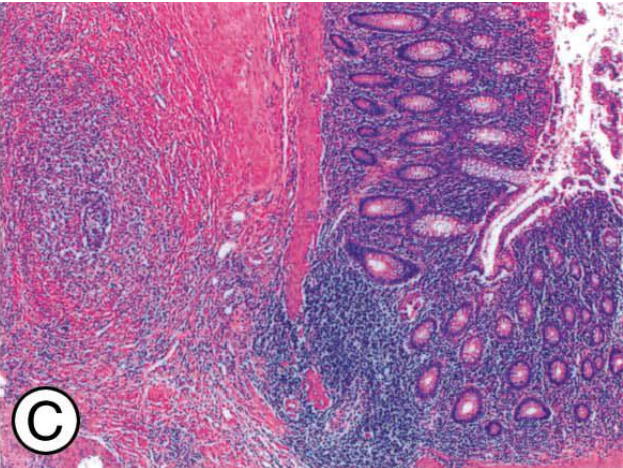
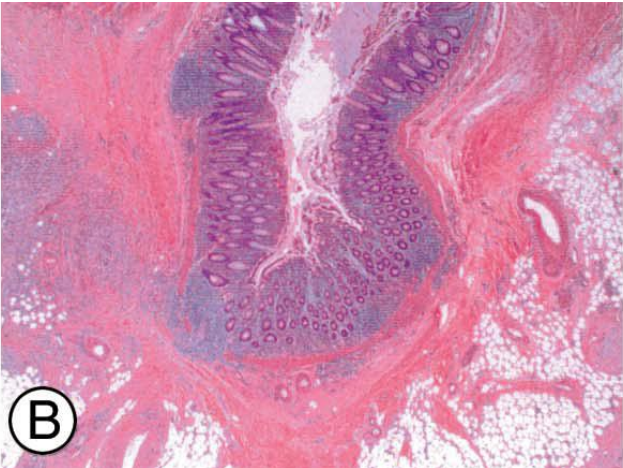
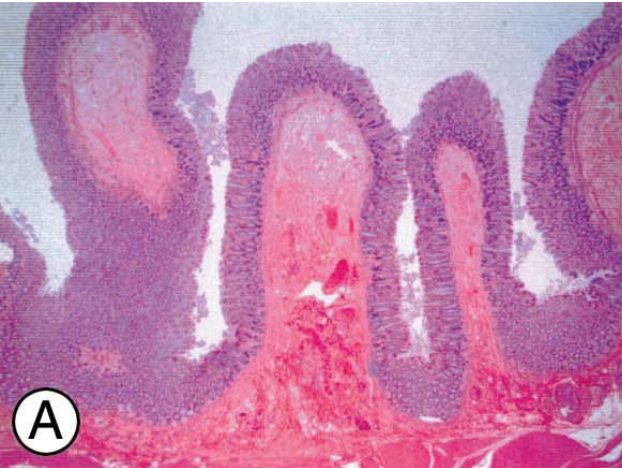
- Pseudodivertikel:
 - Ausstülpungen der Mucosa und Submucosa durch die muscularis mucosae
 - Linksseitig
 - Kaukasier



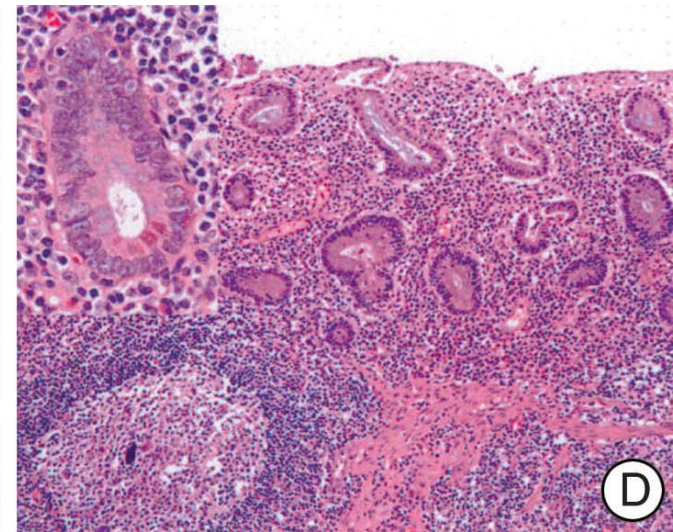
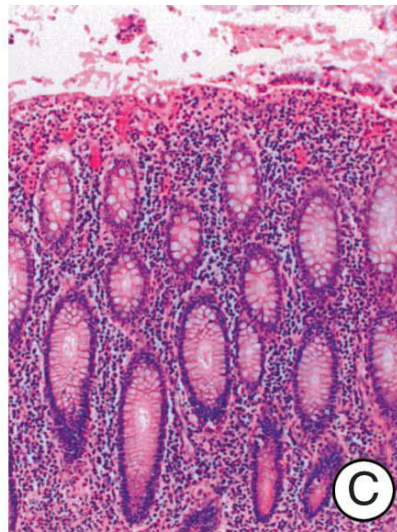
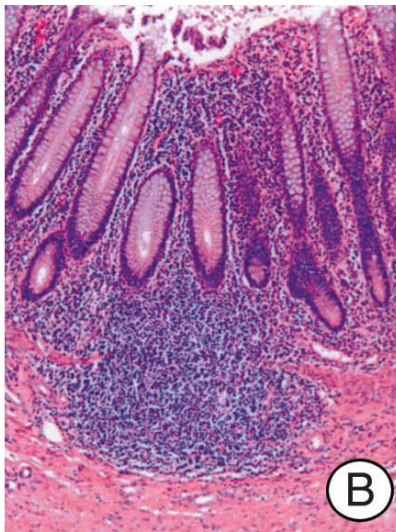
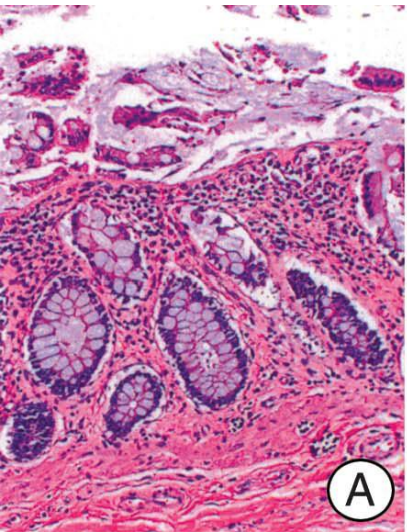
Pathologie



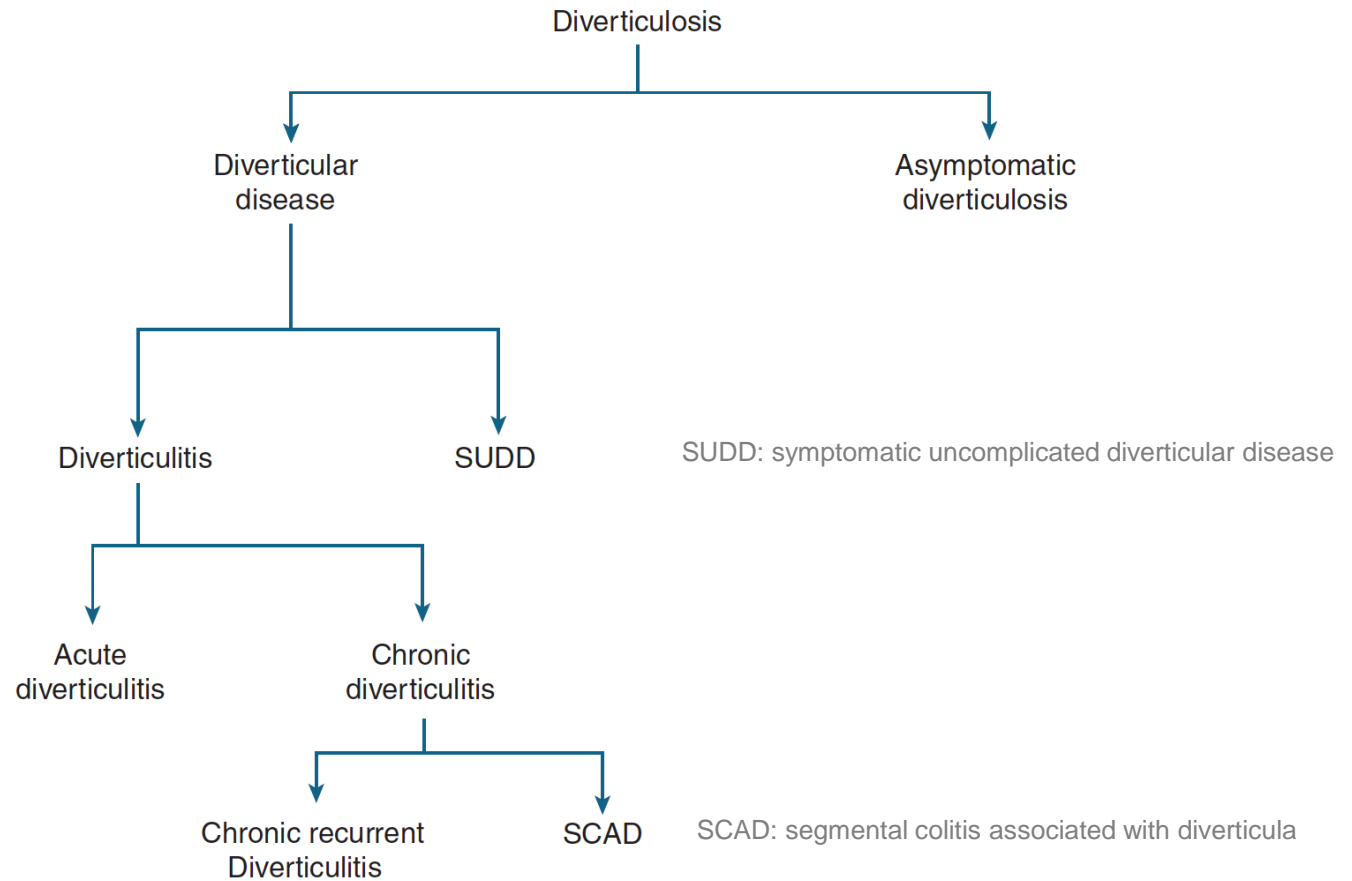
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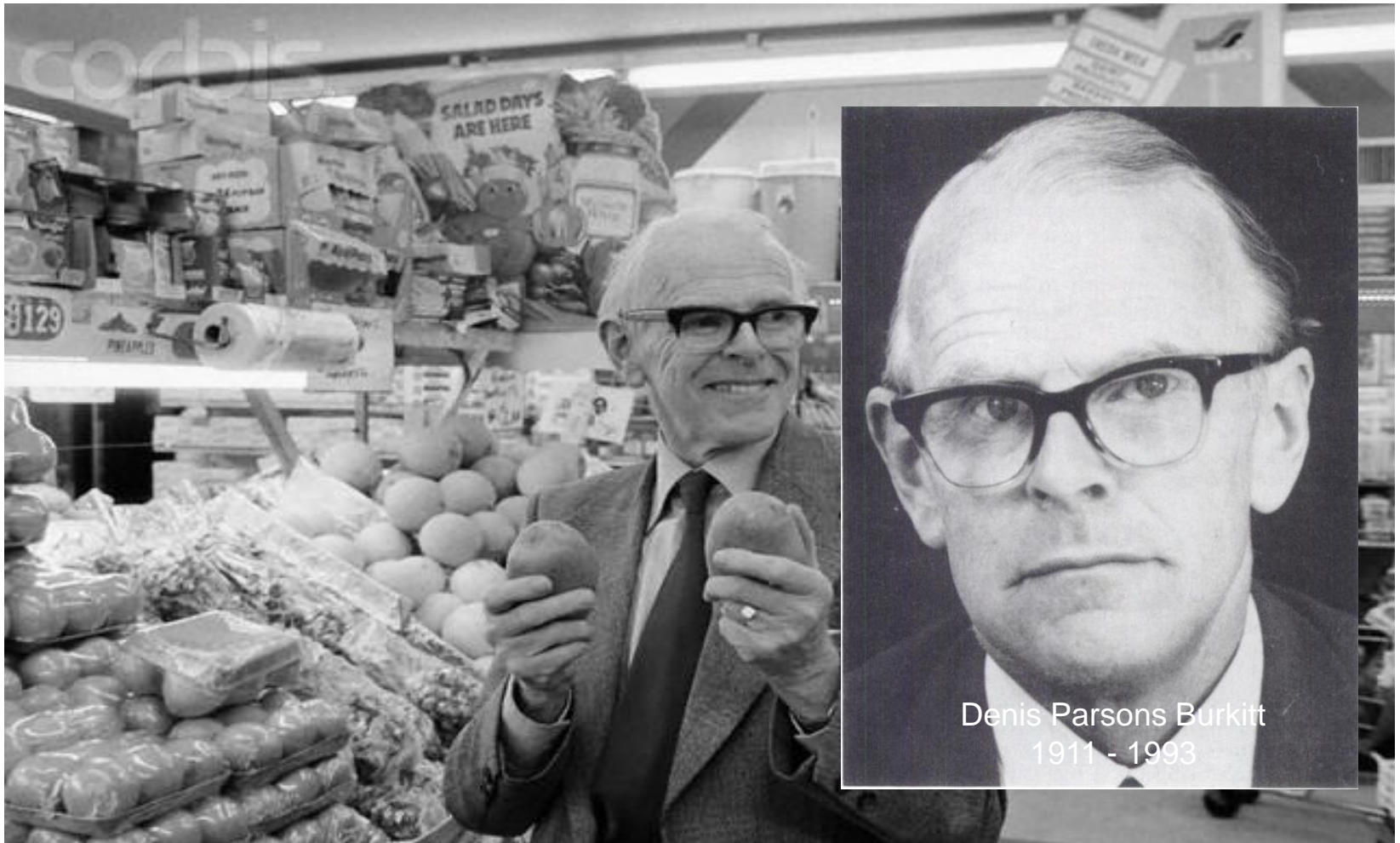
Taxonomie 2012



Merkmale

- Relativ junge Erkrankung
- Intuitiv mit Drucksteigerung verbunden
- Von Entzündungsprozessen begleitet (zT minimal)

Epidemiologie



Denis Parsons Burkitt
1911 - 1993



For Debate...

Diverticular Disease of the Colon: A Deficiency Disease of Western Civilization

NEIL S. PAINTER, DENIS P. BURKITT

British Medical Journal, 1971, 2, 450–454

We present a hypothesis as to the cause of diverticulosis coli which is consistent with its geographical distribution, its recent emergence as a medical problem, and its changing incidence. Diverticulosis appears to be a deficiency disease caused by the refining of carbohydrates which entails the removal of vegetable fibre from the diet. Consequently we consider it to be preventable.

Diverticulitis first became a clinical problem at the turn of the century, and the term “diverticulosis” first appeared in 1914. As recently as 1916 the disease was not important enough to merit a mention in textbooks.¹

Though the present incidence of diverticulosis is unknown it is certainly endemic in our aged citizens. This dramatic increase in incidence occurred in only 70 years and cannot possibly be

years later it is unlikely that perforated diverticulitis was common at that time.

Our nineteenth-century predecessors described diverticula and their complications accurately, but they regarded them as curiosities. Their concept of the pathogenesis of diverticula was surprisingly correct, and not until a century later, when cine-radiography and pressure recording became available, were diverticula shown to be the result of functional obstruction due to segmentation dividing the colon into “little bladders.” These become “trabeculated,” with the colonic muscles thrown into ridges of varying thickness before the herniation of the mucosa takes place.¹²⁻¹⁷

Modern workers have only confirmed what Gross³ believed—namely, that diverticula were caused by obstruction “by which the muscular fibres are separated from each other so as to permit the mucous membrane to protrude.” Uehara¹⁸



Painter & Burkitt (1971)

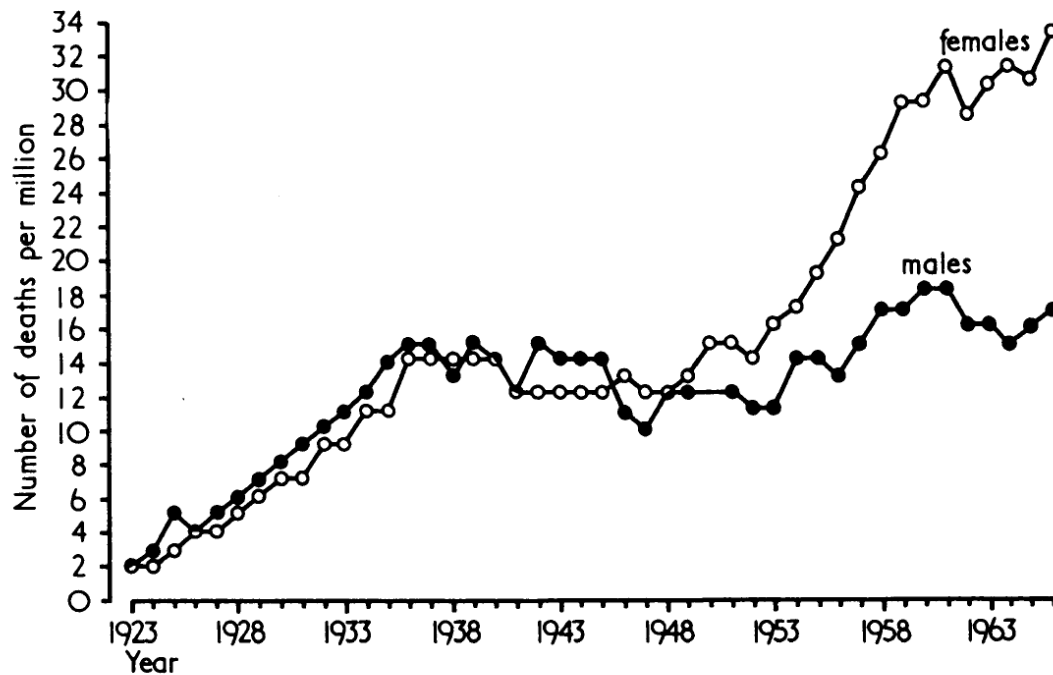


FIG. 2—Crude death rate for diverticular disease: Registrar General's statistical review of England and Wales 1923-66. (From Cleave, Campbell, and Painter.⁶³)

Epidemiologie

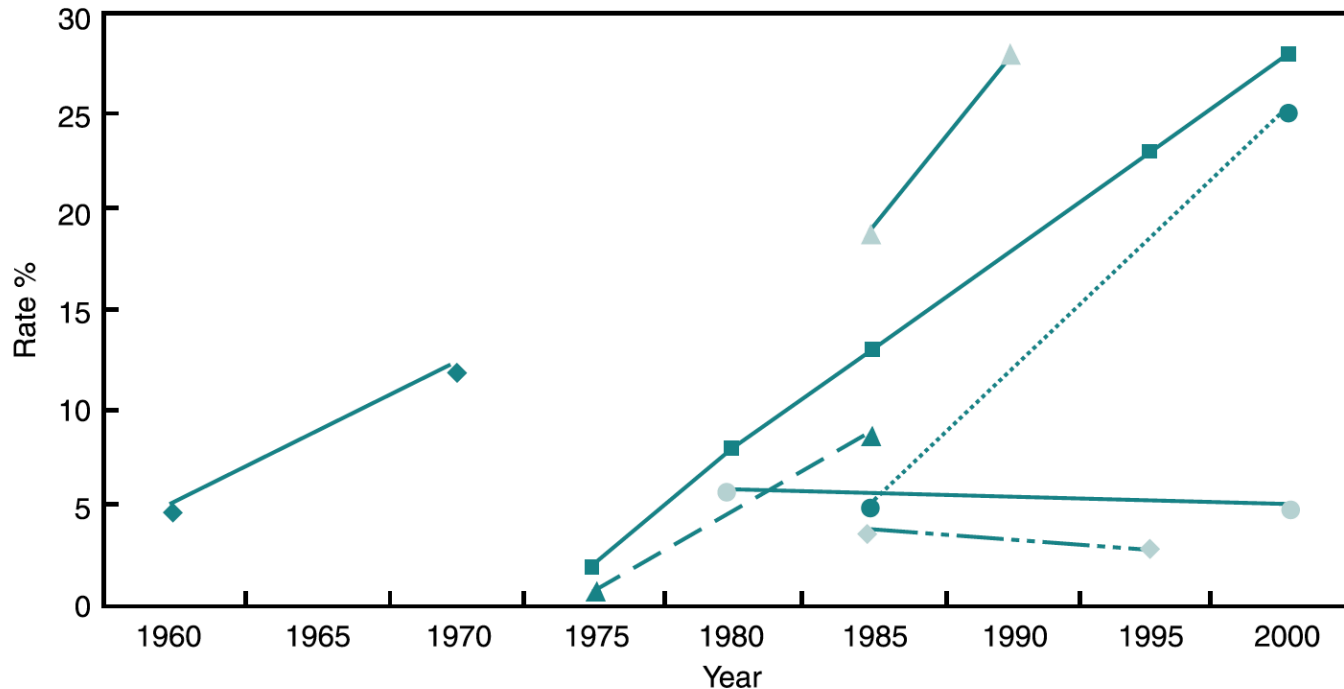


Figure 1. Graph shows the changing prevalence of diverticulosis over time. Only countries with at least two time points reported have been included. ◆, Finland; ▲, Israel; ◇, Jordan; ○, Kenya; △, Singapore; ●, Hong Kong; ■, Japan.

Pathophysiologie

1408

THE LANCET, DECEMBER 30, 1972



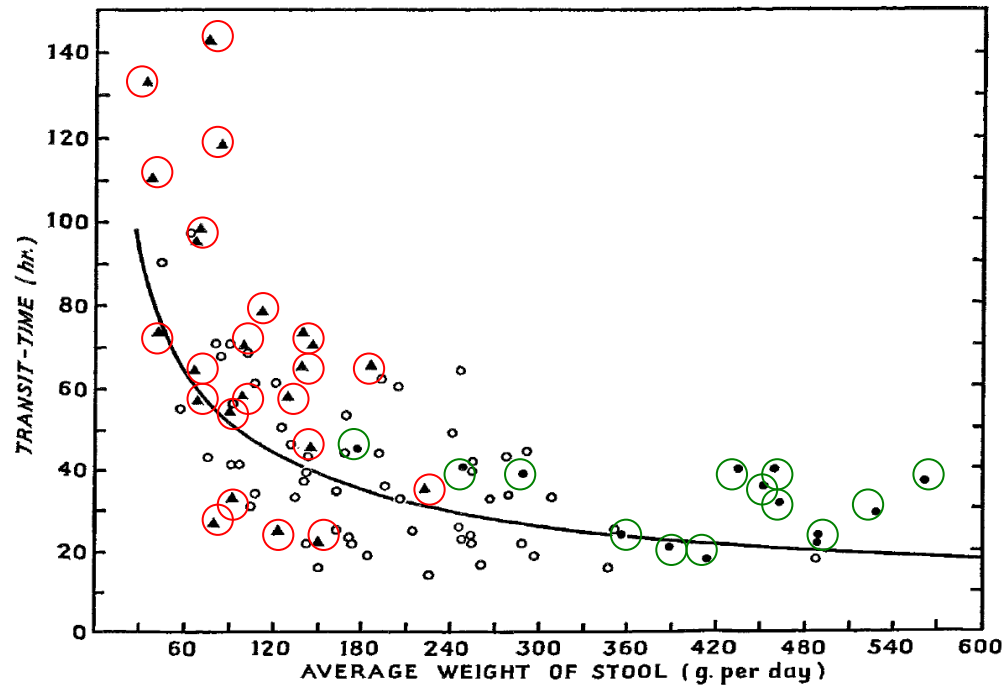
TABLE I—APPROXIMATE DAILY CONSUMPTION OF FIBRE IN THE U.S.A. (g./person/day)

	1880		1970		Changes in fibre intake
	Food	Fibre	Food	Fibre	
<i>Starches:</i>					
Cereals	480	3.2*	120	0.3	-90%
Potatoes	300	1.1	120	0.5	-45%
Legumes	60	1.0	60	1.0	None
Starchy fibre	..	5.3	..	1.8	-66%
<i>Fruit and vegetables</i>	275	2.8	325	3.3	+20%
Total fibre	..	8.1	..	5.1	-37%

* Assumed fibre content of bread 0.7 g. per 100 g. (i.e., about 85% extraction; roller mills had only just started in U.S.A.).
Prepared by Dr. H. C. Trowell from material of Antar et al.¹⁰

been argued on historical and epidemiological grounds

Pathophysiologie

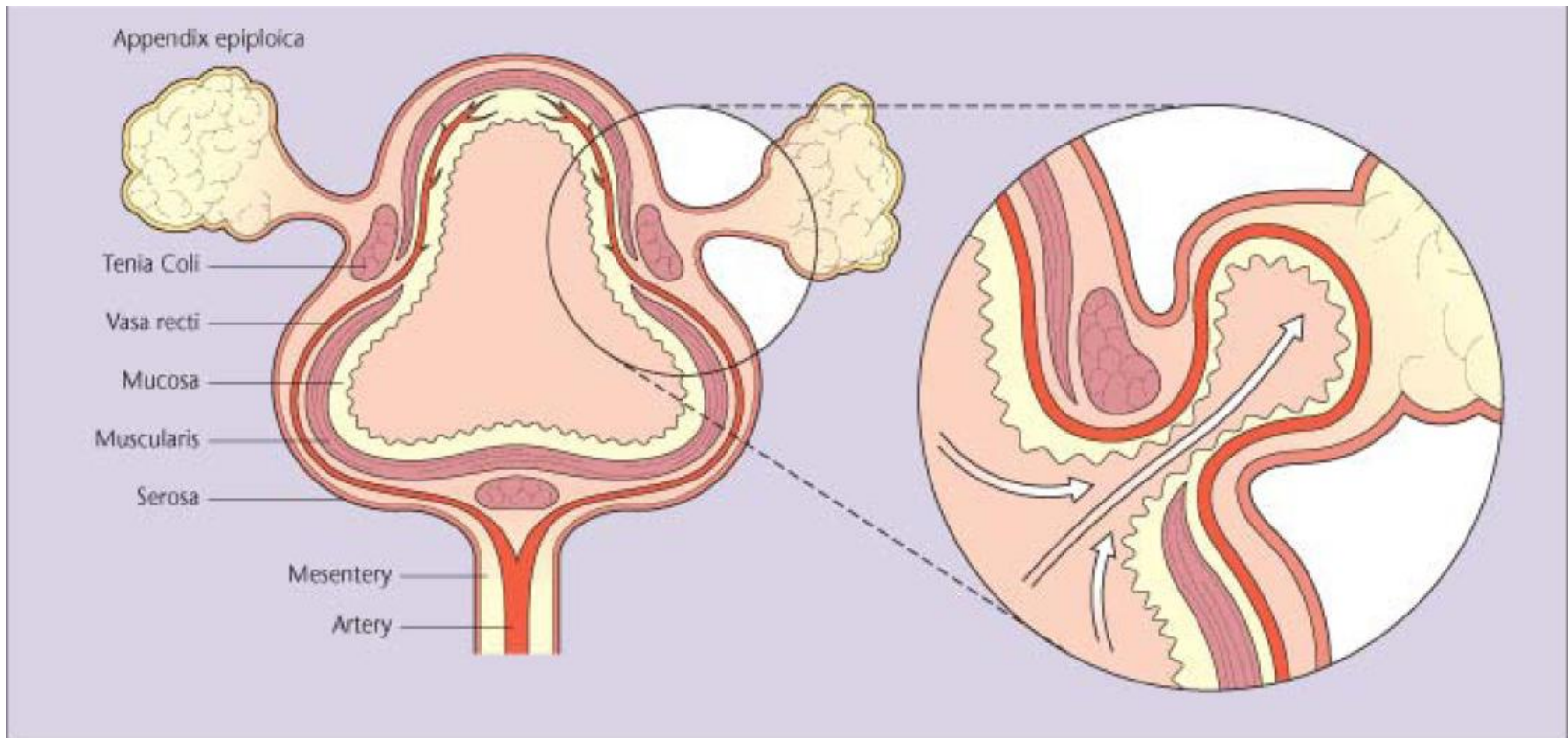


Relation between fibre intake, transit-time, and stool weight.

- = Vegetarians, vegans, and African boarding-school (mixed diet).
- = African villagers (high-residue diet).
- ▲ = English boarding-school and British Navy (low-residue diet).

The curve (which is based on more data than the points shown here) is:
 $\log(\text{time}) = 2.81633 - 0.56057 \log(\text{weight})$.

Pathophysiologie



Pathophysiologie

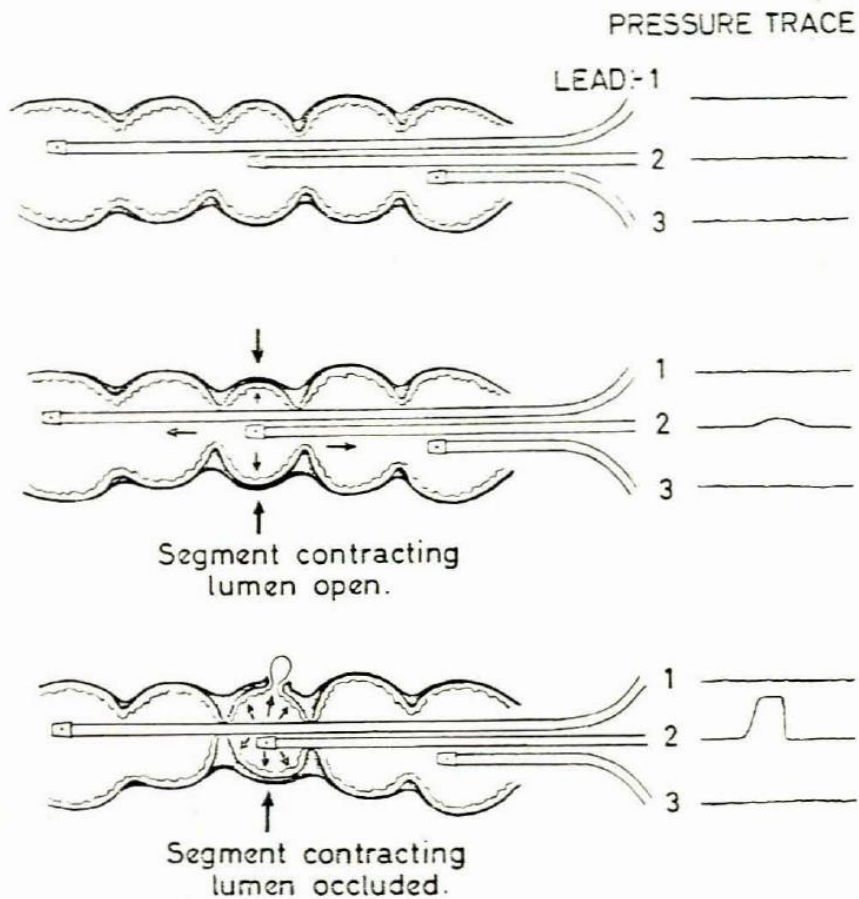
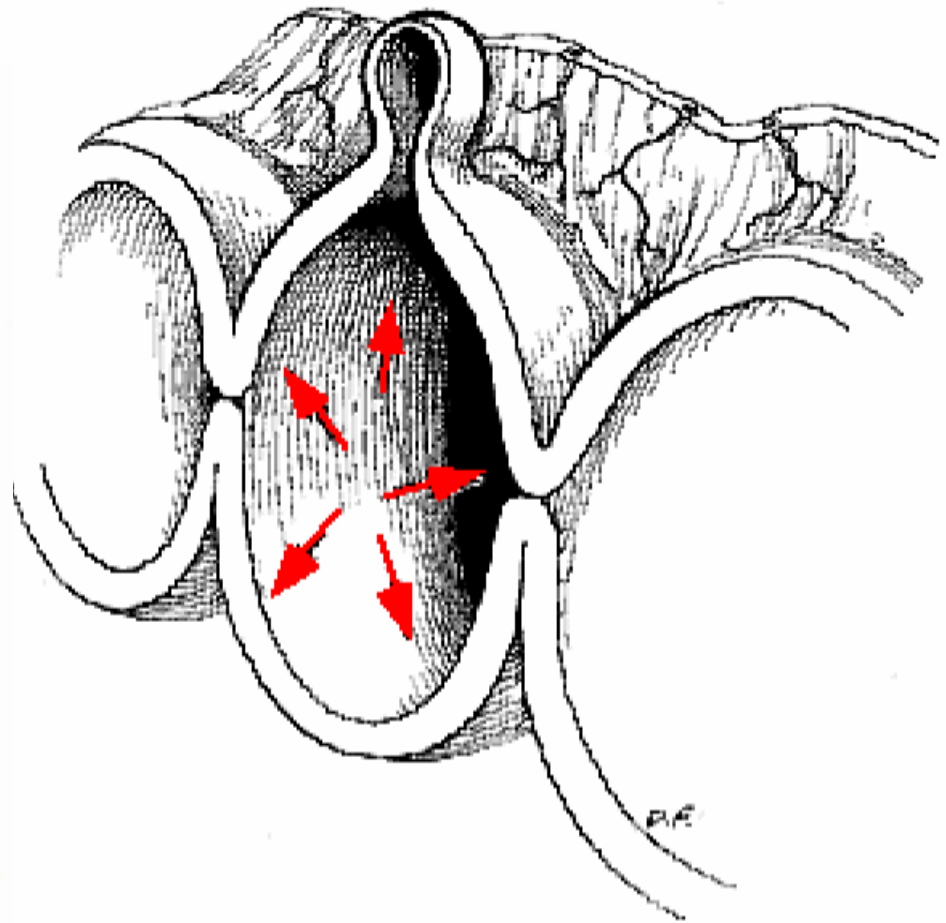


Fig. 2. Segmentation and the generation of high localized intracolonic pressures.



Laplace Gesetz

$$K = p * r / 2 * d$$

Sigma hat kleinsten Durchmesser



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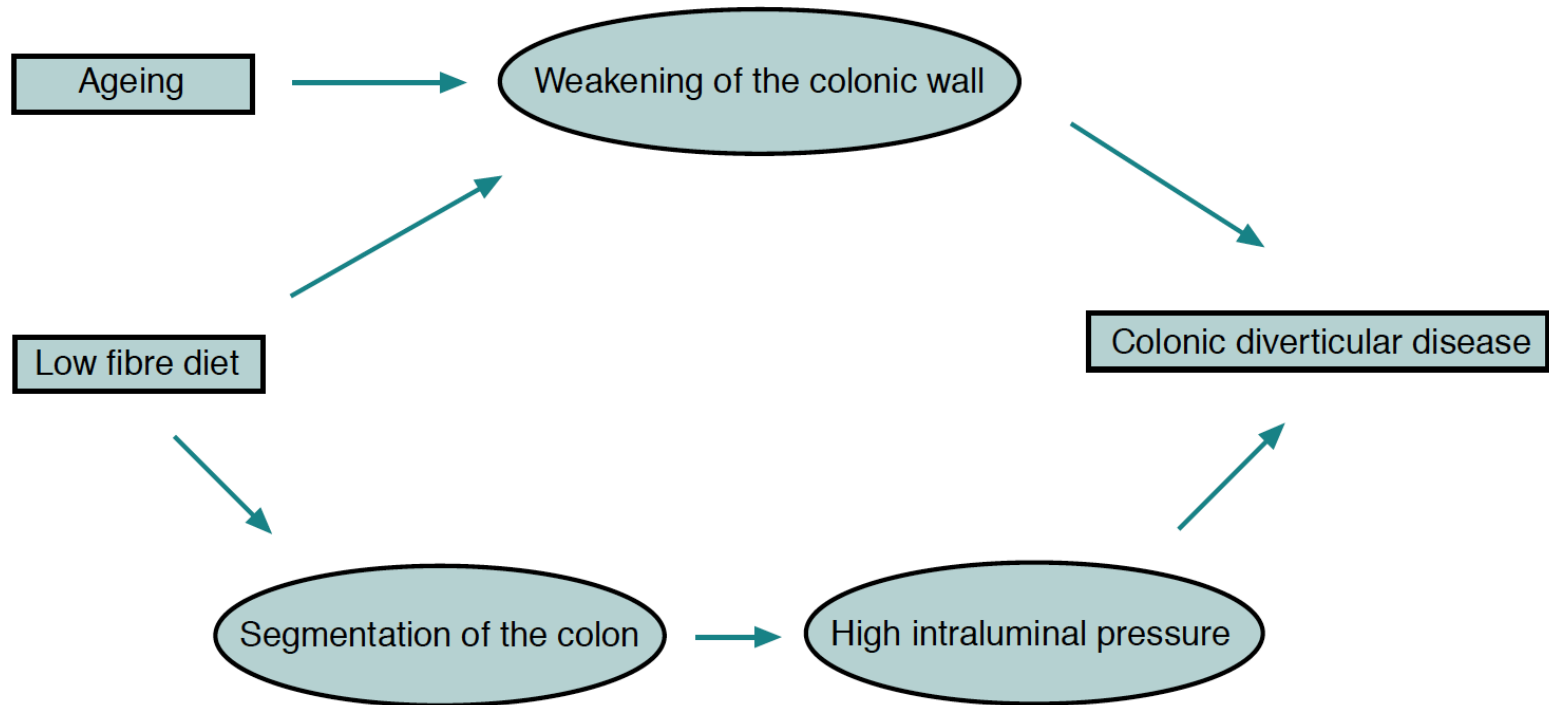
Proof of concept

Effects of High-residue Diet on Established Disease

If a lack of fibre causes diverticulosis then the symptoms of diverticular disease might be alleviated by replacing the fibre, in the form of bran, in the diet. This has proved to be the case in a trial of 70 patients with the disease. Bran has relieved or abolished abdominal aching and pain and distension in over 80% of patients. Even severe colic which first was diagnosed as left renal colic disappeared on a high-residue diet. It is not yet known whether this diet prevents diverticulitis, but the symptoms of painful diverticular disease are usually diminished or abolished by adding bran to the diet.⁷⁴



Pathophysiologie (klass. Konzept)



Painter & Burkitt (1971)



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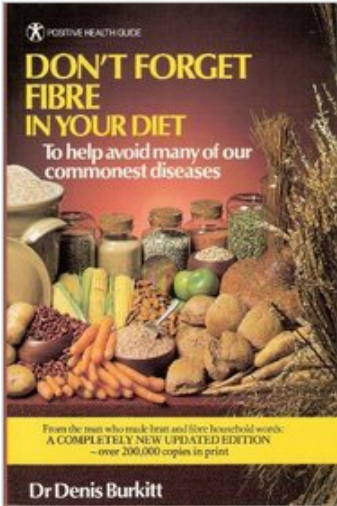
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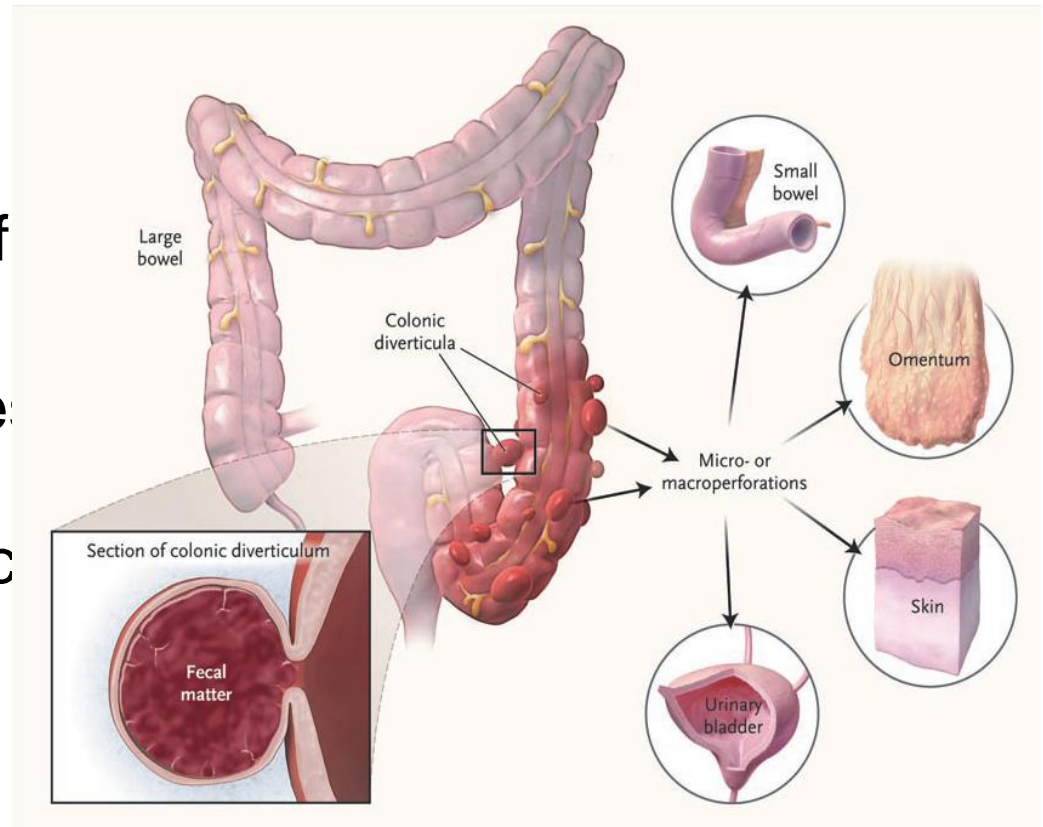
Pathophysiologie der Diverticulitis

- Erhöhter intraluminaler Druck oder Nahrungspartikel erodieren die Divertikelwand -> Entzündung und fokale Nekrose -> Perforation
- Klinische Manifestation entsprechend Grösse der Perforation und Reaktion des Körpers



Komplizierte Diverticulitis

- Abszess
- Obstruktion
- Diffuse Peritonitis (f Perforation)
- Fisteln, z.B., kolove, kolovaginal, koloenterisch, koloc



Changing concepts of diverticular disease

	Klassischer Typus (kaukasisch)	Neuer Typus (asiatisch)
Lokalisation	links	bilateral
Muskelabnormität	Vorhanden	fehlend
Intraluminaler Druck	Abnorm hoch	normal
Bindegewebe	Normal	abnorm
Entzündl. Komplikation	Häufig	selten
Blutung	Selten	häufig

Guidelines

Organisation	Year	Fibers recommended preventing Divert Disease	Original research cited	n
Am Coll Gast	1999	Yes		
Eur Ass End Surg	1999	Yes		
Am Soc Col Rect Surg	2006	Not mentioned		
World Gast Org	2007	Yes		

Gear et al.

	N	Fiber intake (g/day)	Prevalence of colonic diverticulosis in a barium follow-through study (%)
Vegetarians	56	41.5 ± 12.6	12
Non-vegetarians	264	21.4 ± 8.2	33

Fiber and prevention of diverticulosis

Table 1. Dietary Fiber and Risk of Asymptomatic Diverticulosis

Study	Year	Design	Diverticulosis cases (n)	Findings
Gear ⁵	1979	Case control	95	Diverticulosis less prevalent in vegetarians who on average consumed more fiber
Lin ⁶	2000	Case control	86 (100% right sided)	No significant association between fruit and vegetable intake and diverticulosis in high vs low comparison of 3 categories. Vegetable: OR, 0.55 (95% CI, 0.19–1.61) Fruit: OR, 0.56 (95% CI, 0.18–1.72)
Song ⁷	2010	Cross-sectional	103 (85% right sided)	No significant difference in mean dietary fiber score in cases vs controls (mean score 7.0 vs 7.1, respectively)
Peery ¹³	2011	Cross-sectional	878	Increased risk of diverticulosis in high vs low quartile of fiber intake. OR, 1.30 (95% CI, 1.13–1.50)



Peery et al. (2012)

A High-Fiber Diet Does Not Protect Against Asymptomatic Diverticulosis

ANNE F. PEERY,* PATRICK R. BARRETT,* DOYUN PARK,**‡ ALBERT J. ROGERS,* JOSEPH A. GALANKO,*
CHRISTOPHER F. MARTIN,* and ROBERT S. SANDLER*

**Department of Medicine, University of North Carolina School of Medicine, Chapel Hill, North Carolina; ‡Department of Medicine, Albert Einstein College of Medicine, Bronx, New York*

- Erste Kolonoskopie-basierte Studie (Screening)
- 2104 Personen (30-80 Jahre)
- 878 Fälle mit Divertikeln; 1226 Kontrolle
- Teilanalyse der „Diet and Health Studies“ III-V
- Telefon Interview innerhalb 3 Mte nach Koloskopie

Peery et al. (2012)

Table 2. Crude and Adjusted^a (95% CI) Prevalence Ratios for Diverticulosis by Diet and Physical Activity

	Quartile				P for trend
	1	2	3	4	
Total fiber					
Crude	1	0.93 (0.80–1.08)	1.06 (0.92–1.22)	1.09 (0.94–1.25)	.004
Adjusted	1	1.03 (0.89–1.19)	1.14 (1.00–1.31)	1.30 (1.13–1.50)	
Fiber from beans					
Crude	1	0.96 (0.83–1.11)	1.11 (0.96–1.27)	1.00 (0.86–1.15)	.31
Adjusted	1	0.94 (0.82–1.09)	1.10 (0.96–1.26)	1.10 (0.95–1.27)	
Fiber from grains					
Crude	1	1.01 (0.87–1.17)	1.11 (0.96–1.28)	1.09 (0.94–1.26)	.011
Adjusted	1	1.01 (0.88–1.17)	1.16 (1.01–1.33)	1.25 (1.09–1.45)	
Fiber from fruits and vegetables					
Crude	1	0.84 (0.73–0.98)	1.05 (0.92–1.20)	0.90 (0.78–1.04)	.431
Adjusted	1	0.87 (0.76–1.01)	1.12 (0.98–1.28)	1.06 (0.92–1.22)	
Insoluble fiber					
Crude	1	0.84 (0.72–0.97)	0.96 (0.84–1.11)	1.03 (0.90–1.18)	.07
Adjusted	1	0.92 (0.79–1.06)	1.05 (0.92–1.22)	1.24 (1.08–1.42)	
Soluble fiber					
Crude	1	0.86 (0.74–1.00)	1.05 (0.91–1.20)	1.04 (0.91–1.20)	.038
Adjusted	1	0.92 (0.80–1.07)	1.12 (0.98–1.28)	1.24 (1.07–1.42)	
Total fat					
Crude	1	0.96 (0.84–1.11)	0.92 (0.80–1.06)	0.96 (0.83–1.11)	.445
Adjusted	1	0.96 (0.83–1.10)	0.91 (0.79–1.05)	0.97 (0.84–1.12)	
Red meat					
Crude	1	1.00 (0.86–1.15)	1.05 (0.91–1.21)	1.03 (0.89–1.19)	.862
Adjusted	1	0.95 (0.83–1.10)	1.00 (0.87–1.15)	1.04 (0.90–1.19)	
Physical activity					
Crude	1	0.88 (0.76–1.01)	0.81 (0.70–0.94)	0.85 (0.74–0.98)	.539
Adjusted	1	0.95 (0.83–1.10)	0.92 (0.80–1.06)	1.02 (0.89–1.18)	

^aAdjusted for age, race, and body mass index.



Peery et al. (2012)

Table 4. Crude and Adjusted^a (95% CI) Prevalence Ratios for Number of Diverticula by Diet and Physical Activity Comparing Highest Quartile to Lowest

	All cases (n = 878)	Few diverticula (n = 354)	Many diverticula (n = 246)
Total fiber			
Crude	1.09 (0.94–1.25)	1.02 (0.79–1.33)	1.25 (0.90–1.72)
Adjusted	1.30 (1.13–1.50)	1.17 (0.89–1.54)	1.81 (1.30–2.52)
Fiber from beans			
Crude	1.00 (0.86–1.15)	0.90 (0.70–1.17)	1.09 (0.78–1.53)
Adjusted	1.10 (0.95–1.27)	0.97 (0.74–1.26)	1.34 (0.95–1.88)
Fiber from grains			
Crude	1.09 (0.94–1.26)	1.19 (0.91–1.57)	1.10 (0.80–1.50)
Adjusted	1.25 (1.09–1.45)	1.31 (0.99–1.72)	1.49 (1.09–2.04)
Fiber from fruits and vegetables			
Crude	0.90 (0.78–1.04)	0.98 (0.75–1.29)	0.77 (0.56–1.06)
Adjusted	1.06 (0.92–1.22)	1.07 (0.81–1.43)	1.06 (0.77–1.46)
Insoluble fiber			
Crude	1.03 (0.90–1.18)	1.00 (0.78–1.29)	1.10 (0.80–1.51)
Adjusted	1.24 (1.08–1.42)	1.15 (0.88–1.50)	1.64 (1.18–2.28)
Soluble fiber			
Crude	1.04 (0.91–1.20)	0.93 (0.72–1.20)	1.22 (0.88–1.70)
Adjusted	1.24 (1.07–1.42)	1.06 (0.81–1.40)	1.74 (1.24–2.45)
Total fat			
Crude	0.96 (0.83–1.11)	0.98 (0.76–1.26)	1.00 (0.74–1.34)
Adjusted	0.97 (0.84–1.12)	0.99 (0.76–1.30)	1.02 (0.75–1.38)
Red Meat			
Crude	1.03 (0.89–1.19)	1.04 (0.80–1.35)	1.02 (0.74–1.41)
Adjusted	1.04 (0.90–1.19)	1.04 (0.80–1.36)	1.07 (0.78–1.47)
Physical activity			
Crude	0.85 (0.74–0.98)	0.84 (0.65–1.09)	0.91 (0.66–1.27)
Adjusted	1.02 (0.89–1.18)	0.94 (0.72–1.22)	1.24 (0.89–1.72)

^aAdjusted for age, race, and body mass index.

Peery et al. (2012)

Table 5. Crude and Adjusted (95% CI) Prevalence Ratios for Diverticulosis by Bowel Habits

	Bowel habits				<i>P</i> for trend
	<7 BM/week	7 BM/week	8–14 BM/week	>15 BM/week	
Crude	1.00 (referent)	1.33 (1.13–1.58)	1.50 (1.25–1.80)	1.57 (1.26–1.95)	.<.001
Adjusted ^a	1.00 (referent)	1.34 (1.04–1.72)	1.59 (1.22–2.07)	1.70 (1.24–2.34)	

BM, bowel movements.

^aAdjusted for age, tobacco use.



Peery et al. (2012)

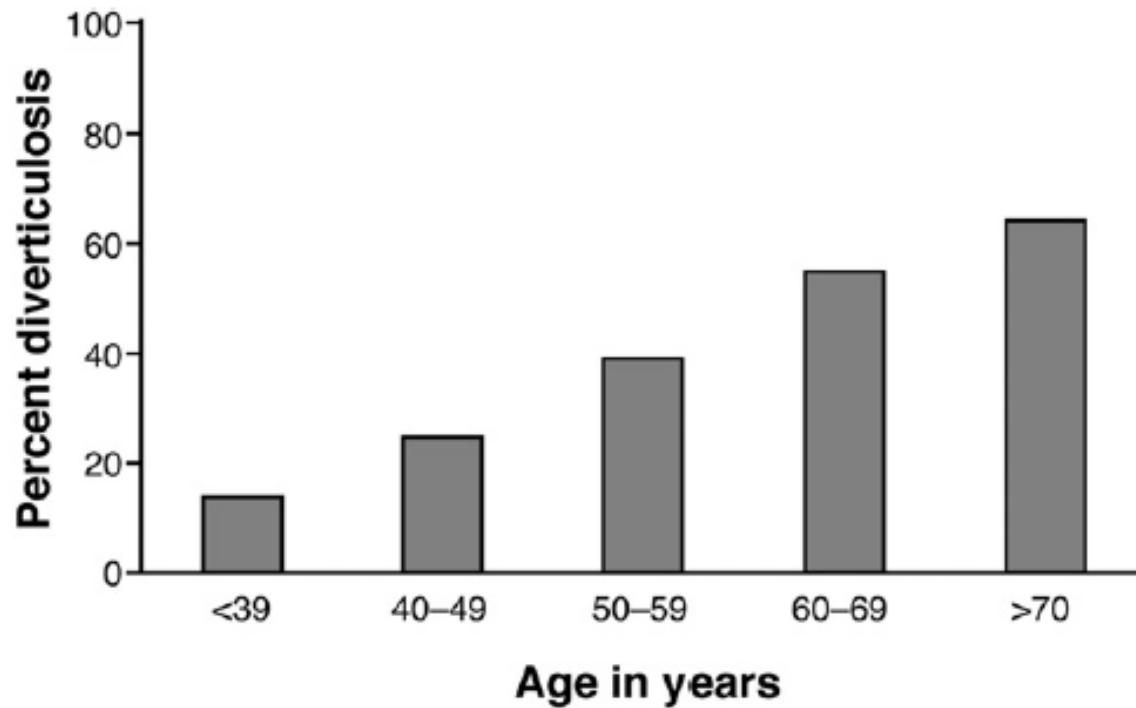


Figure 1. Prevalence of diverticulosis by age (n = 878).

Widerlegung des Dogmas

In conclusion, we found that a high-fiber diet and more frequent bowel movements were associated with an increased rather than a decreased prevalence of diverticulosis. Our data demonstrated no association between fat, red meat, physical activity, and diverticulosis. Based on our results, previous hypotheses regarding diverticulosis risk factors and diet recommendations to patients should be reconsidered.



Obesity, Metabolic Syndrome and the risk of colonic diverticulosis

- Retrospektive Studie
- 3175 Patienten (40-85)
- 17.4% Divertikulose
- Kolonoskopie

	OR	p value	95% CI
Age	1.070	<0.001	1.056–1.083
Male gender	1.737	<0.001	1.346–2.241
Obesity (BMI >30)	1.394	0.006	1.099–1.769
Diabetes mellitus (history)	0.488	0.007	0.289–0.825
Hypothyroidism (history)	2.403	0.005	1.303–4.431

Guidelines

Organisation	Year	Fibres recommended in preventing recurrence of Diverticulitis	Original research cited	n
Am Coll Gast	1999	Not mentioned		
Eur Ass End Surg	1999	Yes	none	
Am Soc Col Rect Surg	2006	Yes	Larson (1976) Painter (1982)	132 -
World Gast Org	2007	Not mentioned		



Ünlü et al. (2012)

**A systematic review of high-fibre dietary therapy
in diverticular disease**

Dietary fibre to prevent recurrence of diverticulitis:

No dietary fibre study met the inclusion criteria of this
systematic review question



Aldoori et al. 1998

A Prospective Study of Dietary Fiber Types and Symptomatic Diverticular Disease in Men^{1,2}

Relative risk (RR) of symptomatic diverticular disease in quintiles of soluble and insoluble fiber components:
the HPFS, 1988–1992

	Quintiles					P-value for trend
	1	2	3	4	5	
Soluble fiber, median g/d	4.10	5.10	5.90	6.90	8.60	
Cases, <i>n</i>	72	78	78	69	65	
RR ¹ (95% CI)	1.00	1.03 (0.75–1.43)	1.00 (0.72–1.38)	0.83 (0.59–1.17)	0.82 (0.59–1.16)	0.05
Multivariate RR ² (95% CI)	1.00	1.05 (0.76–1.45)	1.04 (0.75–1.44)	0.91 (0.65–1.29)	0.90 (0.62–1.29)	0.40
Insoluble fiber, median g/d	10.10	13.0	15.20	17.90	22.70	
Cases, <i>n</i>	83	78	70	77	54	
RR ¹ (95% CI)	1.00	0.89 (0.65–1.22)	0.78 (0.57–1.07)	0.80 (0.59–1.10)	0.55 (0.39–0.78)	0.001
Multivariate RR ² (95% CI)	1.00	0.91 (0.66–1.24)	0.80 (0.58–1.10)	0.87 (0.63–1.20)	0.63 (0.44–0.91)	0.02

¹ Adjusted for age and total energy.

² Adjusted for age, physical activity and energy-adjusted total fat.

HPFS, Health Professionals Follow-up Study; CI, confidence interval.



Spital Zollikerberg
Ihr Schwerpunktspital im Grünen

Crowe et al. 2011

Diet and risk of diverticular disease in Oxford cohort of European Prospective Investigation into Cancer and Nutrition (EPIC): prospective study of British vegetarians and non-vegetarians

- Kohorte von 47033 Personen, davon 33% Vegetarier
- Diät mittels validiertem Fragebogen erhoben
- Nach 11.6 Jahren:
 - 812 Fälle von Diverticulitis (Hosp. oder Tod)
 - Vegetarier: 31% tieferes Risiko



Crowe et al. 2011

Table 4| Relative risk of diverticular disease by diet group in EPIC-Oxford study

	Cases	Unadjusted*		Adjusted†	
		Relative risk (95% CI)	P value	Relative risk (95% CI)	P value
Vegetarian status:					
No	710	1.00	<0.001‡	1.00	0.001‡
Yes	102	0.62 (0.50 to 0.77)		0.70 (0.56 to 0.87)	
Diet group:					
Meat eater	633	1.00	<0.001	1.00	0.003
No meat but some fish	77	0.83 (0.65 to 1.06)		0.91 (0.71 to 1.16)	
Vegetarian or vegan	102	0.60 (0.48 to 0.75)		0.69 (0.55 to 0.86)	
Diet group:					
Meat eater	633	1.00	<0.001	1.00	0.001
No meat but some fish	77	0.83 (0.65 to 1.06)		0.90 (0.71 to 1.16)	
Vegetarian	98	0.65 (0.52 to 0.81)		0.73 (0.58 to 0.92)	
Vegan	4	0.22 (0.08 to 0.59)		0.28 (0.10 to 0.74)	

*Stratified by sex, method of recruitment, and region of residence.

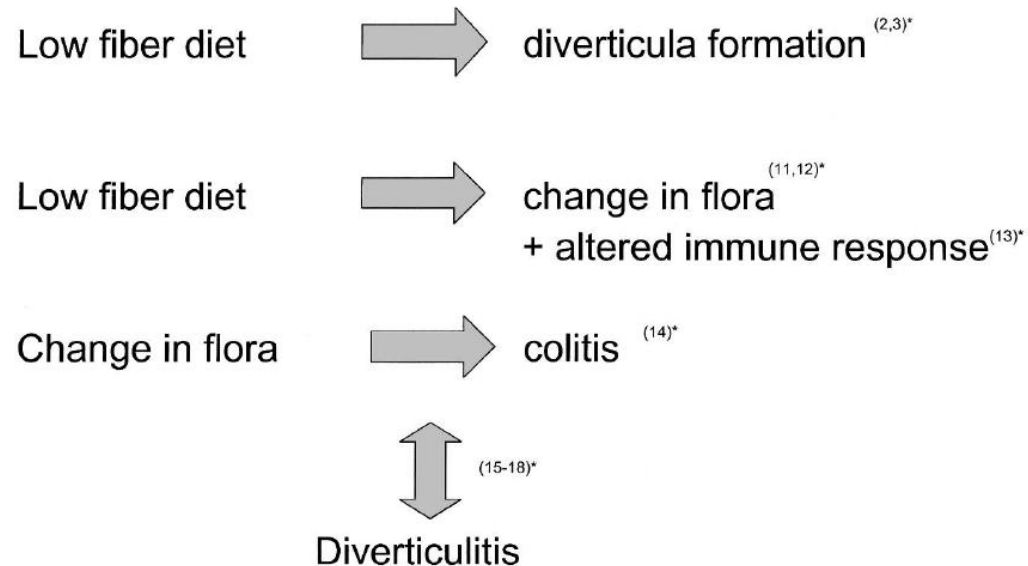
†Stratified by sex, method of recruitment, and region of residence and adjusted for smoking, education level, Townsend deprivation index, self reported hyperlipidaemia, receiving long term medical treatment, ever used oral contraceptives, ever used hormone replacement therapy, and BMI (fully adjusted model).

‡ χ^2 test.



Entstehung der Diverticulitis

Theoretical Progression from Diverticula Formation to Diverticulitis



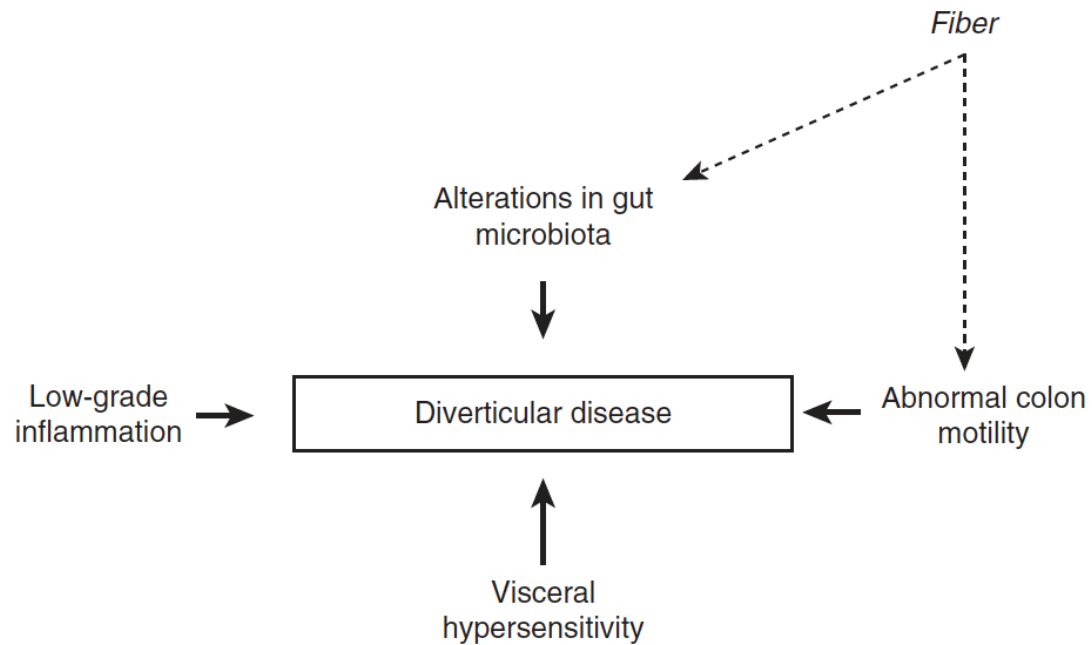
*References suggesting each step

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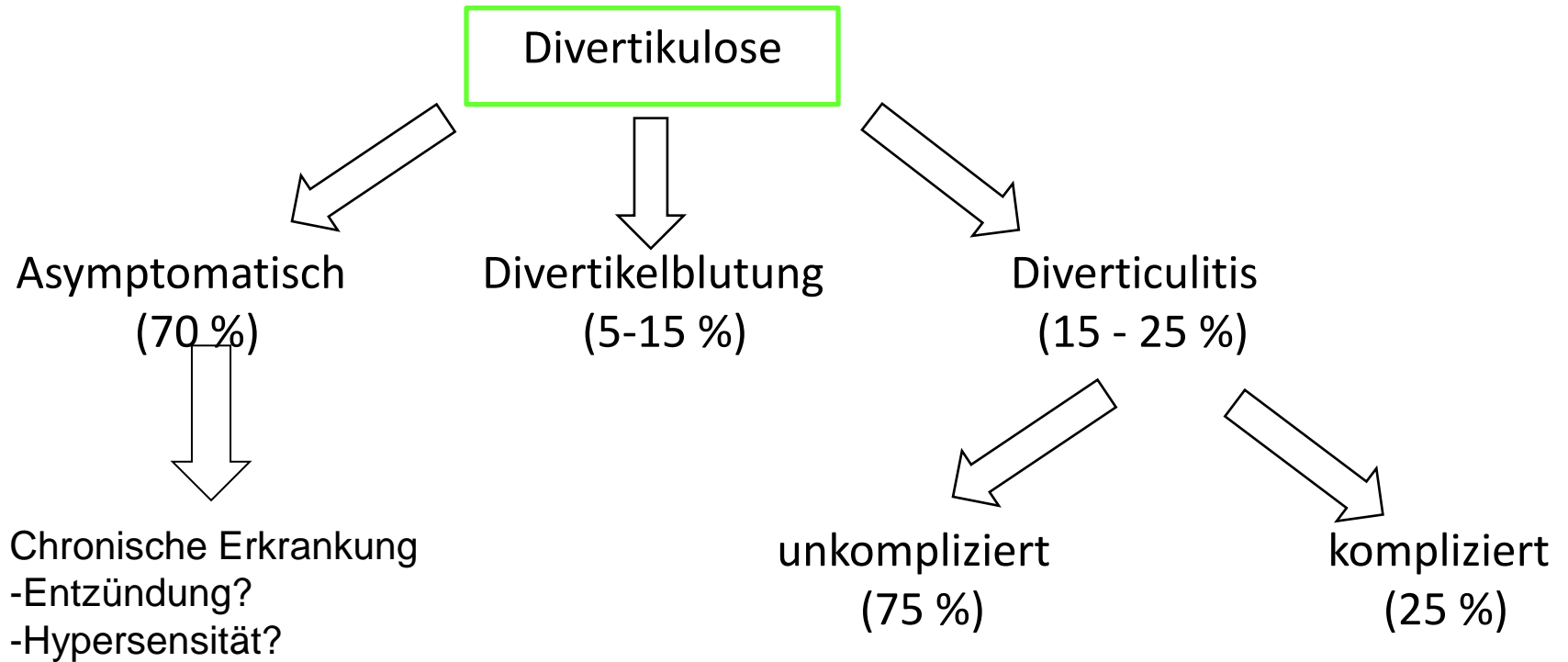
FIGURE 1. Theoretical progression from diverticula formation to diverticulitis.



Pathophysiologie



Natürlicher Verlauf?



Beyond the fibers?

- **5-ASA**
 - Systematic review of 6 RCT (818 pts)
 - Mesalamin > Placebo zur Schmerzminderung und Rezidivprophylaxe
- **Rifaximin**
 - Metaanalysis of 4 RC (1660 pts)
 - NNT für Symptombesserung: 3, Komplikation: 59
- **Probiotika**
 - Pilotstudie (30 pts) VSL # 3 mit 5-ASA

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Bianchi V. Aliment Pharmacol Ther 2011;33:902-10.

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Zusammenfassung Divertikulose

- Zunehmende Inzidenz und unterschiedliche geographische Prävalenz lassen **exogenen Faktor** vermuten.
- Neben mechanistischer zunehmend **andere** ätiologische Faktoren (Entzündung, Hypersens).
- Prävention der Divertikelbildung durch faserreiche Ernährung ist ein **Dogma**, für das es **keine ausreichende** Evidenz gibt.
- Schwache Evidenz für Symptomminderung.

