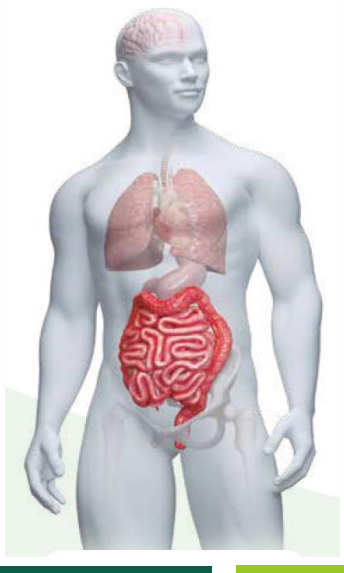
Infeccions Gastrointestinals



Rubén Fuentes, J. C. Ágreda, M. Andrade.
Medicina Familiar i Comunitària

EAP Breda-Hostalric, IAS, Girona.

1. Diarrees agudes i cròniques.
2. Diarrea Covid.
3. Helicobacter pylori.

Temàtica a actualitzar

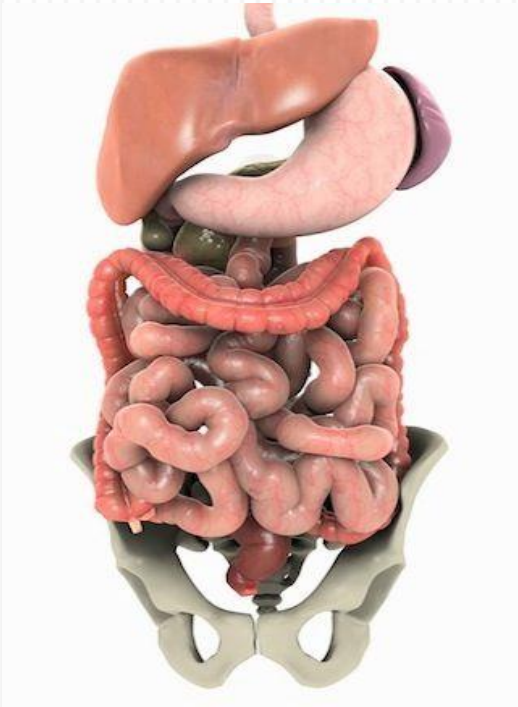
Actualització sobre Diarrees

Diarrea. Definició.

La Diarrea constitueix una patologia freqüent amb un ampli diagnòstic diferencial, essent un símptoma molt freqüent a la consulta d'Atenció Primària (AP).

Diarrees. Fisiopatologia.

- Menjar 2 litres
- Tracte gastrointestinal Intestí gruixut
- Femtes
- Missatgers neuro endocrins
- Peristaltisme
- Flora bacteriana intestinal

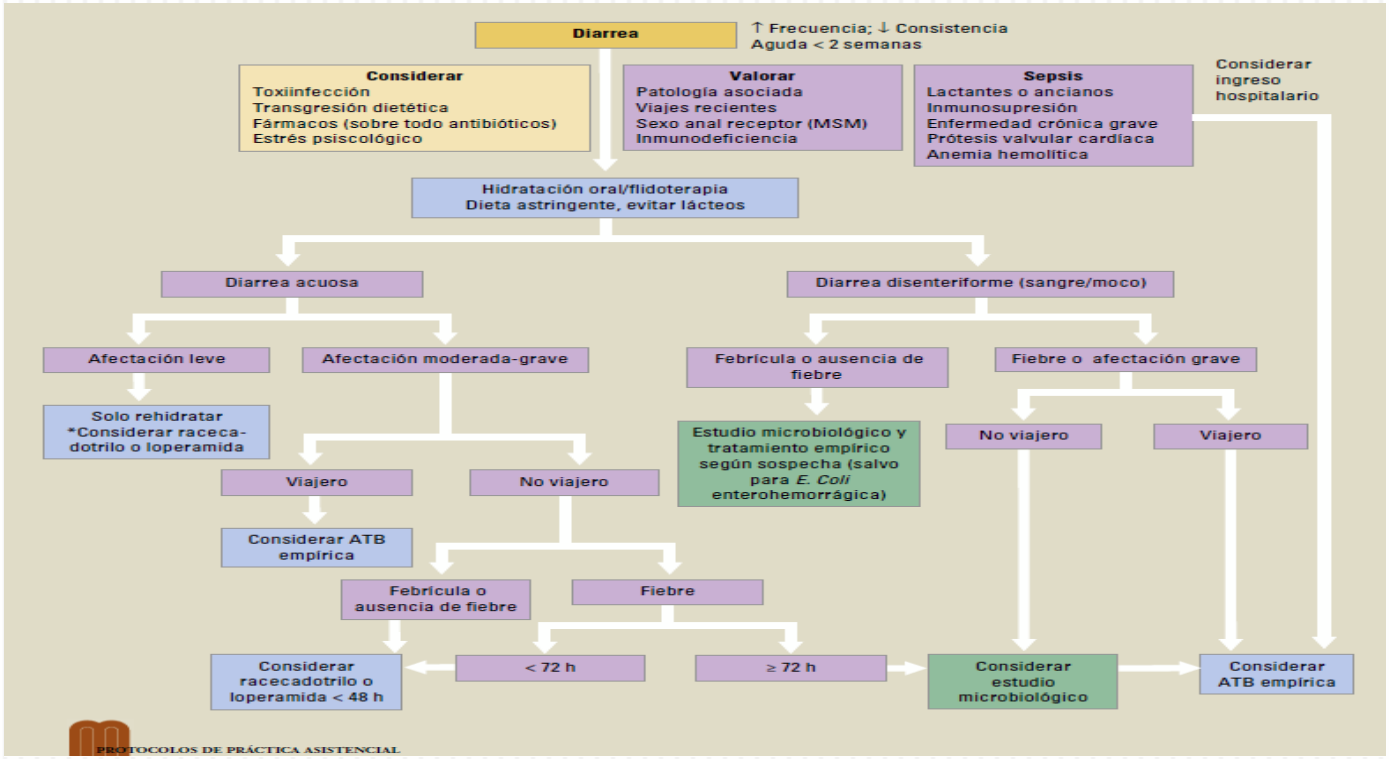


Diarrea

Diarrea aguda

Definició: Qualsevol variació significativa a les característiques de les deposicions respecte a l'hàbit previ del pacient (volum o freqüència), i amb una disminució de la consistència d'aquestes, considerant-se aguda quan la durada és inferior a dues setmanes.

Diarrees Agudes. Algorisme diagnòstic



Protocol diagnòstic i terapèutic de la diarrea aguda. Sánchez del Arco R.T; Machín J.M; Medicine, 2019; 12 (87): 5135-9.

Diarrea Crònica

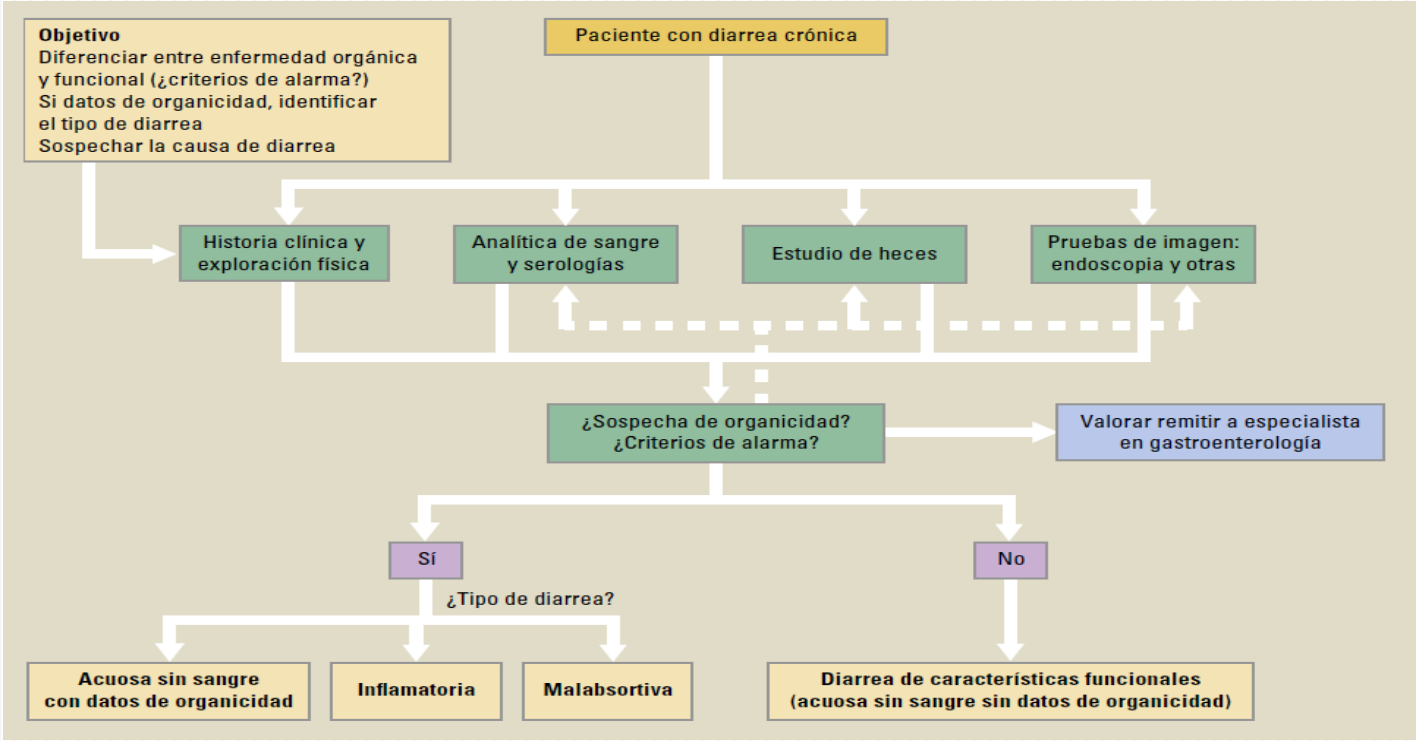
Escala de Bristol

	TIPO 1	Trozos duros separados, que pasan con dificultad	ESTREÑIMIENTO IMPORTANTE
	TIPO 2	Como una salchicha compuesta de fragmentos	LIGERO ESTREÑIMIENTO
	TIPO 3	Con forma de morcilla con grietas en la superficie	NORMAL
	TIPO 4	Como una salchicha o serpiente, lisa y blanda	NORMAL
	TIPO 5	Trozos de masa pastosa con bordes definidos	FALTA DE FIBRA
	TIPO 6	Fragmentos pastosos, con bordes irregulares	LIGERA DIARREA
	TIPO 7	Acuosa, sin pedazos sólidos, totalmente líquida	DIARREA IMPORTANTE

Definició: És una disminució de la consistència de la femta respecte a l'hàbit deposicional previ (que pot variar entre els tipus 5 i 7 de l'escala de Bristol) o augment de la freqüència defecatòria (més de tres deposicions al dia) de més de 4 setmanes de durada.

Heaton KW, Lewis SJ. Stool form scale as a useful guide to intestinal transit time [internet]. Scandinavian Journal of Gastroenterology. 1997;32(9):920-4

Diarrea Crònica. Algorisme diagnòstic



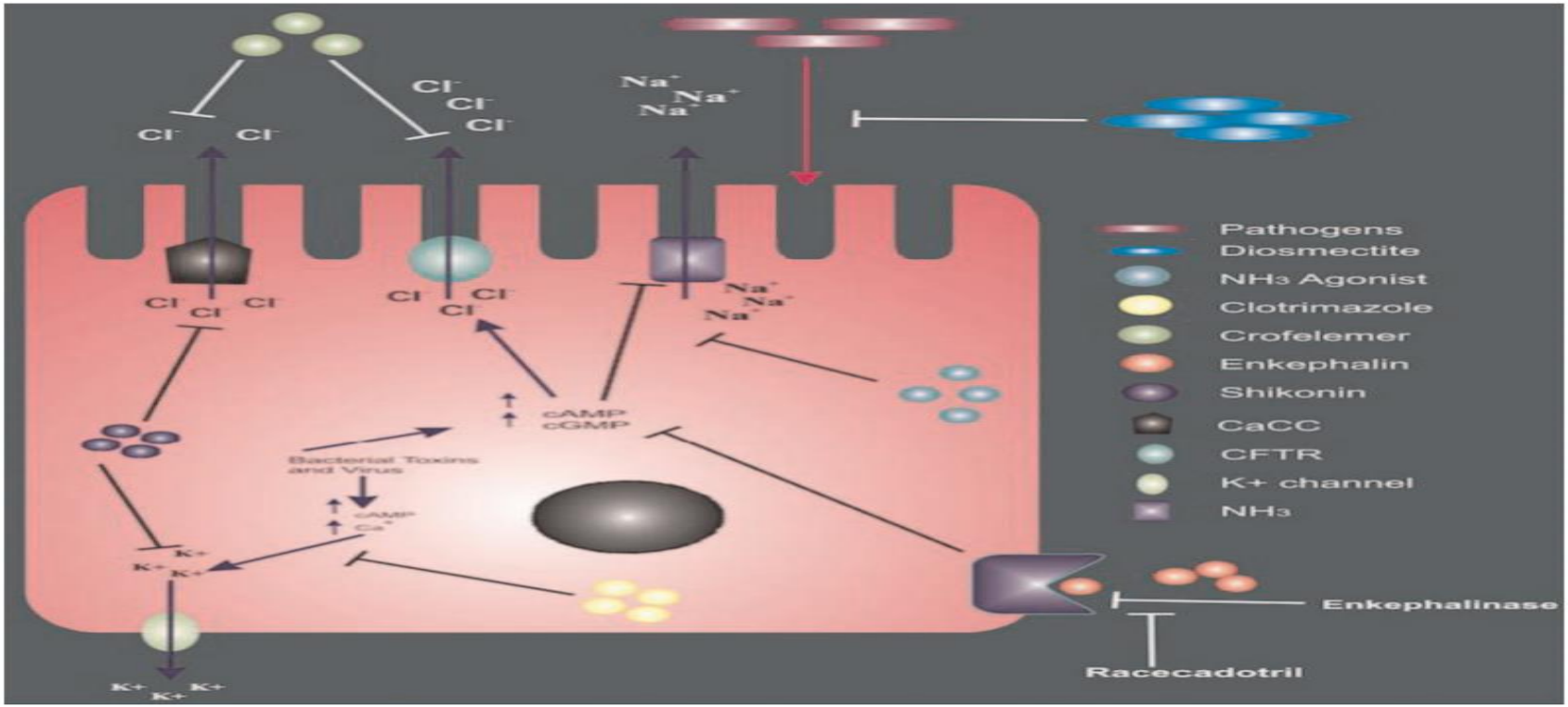
Protocol diagnòstic etiopatogènic de la diarrea crònica. Igualada Escribano, L. ; Santos Rodríguez, A.; García Centeno, P. Machín J.M; Medicine, 2020; 13 (1): 38-44.

Diarrea Crònica

Quan derivar…

1. Davant l'aparició de signes d'alarma (organicitat?)
2. Diarrea Greu
3. Sospita EII
4. Diagnòstic…?
5. Fallada a la terapèutica.

Diarrees. Tractament.



The Cutting Edge of Gastroenteritis: Advances in Understanding of Enteric Infection; Dalia Arostegui and Thomas Wallach; Journal of Pediatric Gastroenterology and Nutrition; 74 (2): 180-185

Diarrees. Tractament.

TABLE 1. AGE therapeutics

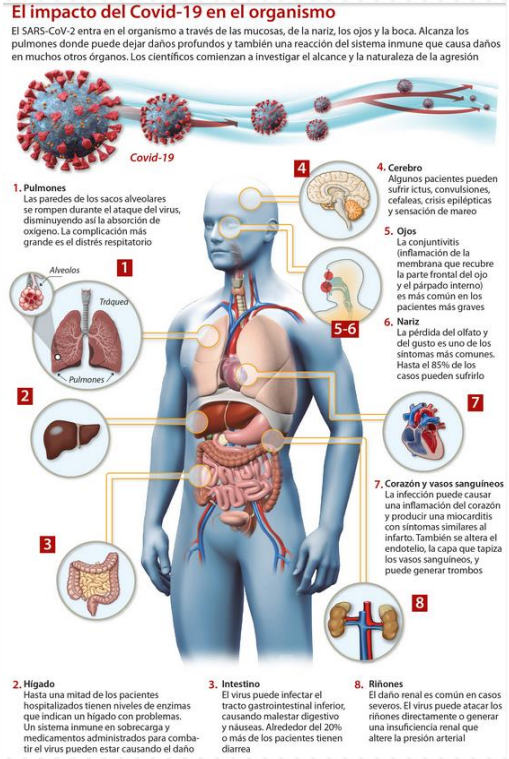
Drug name	Mechanism of action/drug effect	Dosage (PO)	Availability
Odansetron	5-HT3 receptor antagonist Antiemetic agent	8–15 kg: 2 mg × 1 >15 and ≤30 kg: 4 mg × 1 >30 kg: 8 mg × 1 (Harriet lane)	Available in United States
Racecadotril	Enkephalinase inhibitor Antisecretory Antidiarrheal agent	1.5 mg/kg three TID for children 100 mg TID for adults (Guarino et al, 2013)	Not available in United States
Loperamide	Opioid-receptor agonist Antimotility agent Antidiarrheal agent	Contraindicated in patients less than 2 y 9–11 y (>27–43 kg): 2 mg PO TID ≥12 y and adult: 4 mg/dose × 1, followed by 2 mg/dose after each stool Max dose for adolescents 8 mg/24 h and for adults 16 mg/24 h (Harriet lane)	Available in United States
Diosmectite	Natural aluminomagnesium silicate clay with absorbent properties Antidiarrheal agent	3 g in each sachet 1–12 mo old- 6 g/day (2 sachets) 13–36 mo and older — 12 g/day (4 sachets) (Guarino et al 2009)	Available in United States
Crofelemer	Binds to CFTR and CaCC inhibiting chloride secretion Anti-secretory	125 mg PO BID (Gao et al 2017)	Available in United States
NHE3 agonists	Anti-secretory	N/A	Experimental
Clotrimazole	Anti-secretory by inhibiting cAMP chloride channels and Ca^{2+} mediated potassium channels	N/A	Experimental
Shikonin	Anti-secretory by inhibiting chloride channel activity	N/A	Experimental

The table reviews relevant therapeutic agents for acute gastroenteritis, noting mechanism, dose (and origin of dose), as well as availability in the United States. CFTR = Cystic Fibrosis Transmembrane Conductance Regulator, cACC = Calcium Activated Chloride Channel, cAMP = Cyclic adenosine monophosphate.

The Cutting Edge of Gastroenteritis: Advances in Understanding of Enteric Infection; Dalia Arostegui and Thomas Wallach; Journal of Pediatric Gastroenterology and Nutrition; 74 (2): 180-185

Actualització sobre Diarrea Covid

Diarrea Covid. Impacte.



La pandèmia de la COVID-19 ha comportat múltiples avenços científics i des de l'aspecte mèdic ens ha col·locat en una cruïlla de nous patiments sistèmics que arriben com a seqüela de la inflamació que passa en aquesta malaltia.

Review article: Gastrointestinal features in COVID-19 and the possibility of faecal transmission. Yuan Tian, et al; Aliment Pharmacol Ther. 2020;51:843–851.

Diarrea COVID. Impacte.

Almenys 50 efectes a llarg termini s'han descrit a la literatura del recentment anomenat COVID-19 persistent; s'ha informat que com a mínim 80% dels pacients que han tingut infecció per SARS-COV-2 desenvoluparà un o més símptomes a futur.

Així mateix, les manifestacions gastrointestinals han sorgit com a complicacions clíniques importants i cada dia hi ha més evidència sobre aquest problema al qual ens enfrontarem en el futur.

Los síntomas gastrointestinales tempranos en COVID-19 podrían indicar transmisión fecal - Medscape - 21 de marzo de 2020.

Diarrea Covid. Impacte.

Review article

P.C. KONTUREK[1], I.A. HARSCH[1], M.F. NEURATH[1], Y. ZOPF[2]

COVID-19 - MORE THAN RESPIRATORY DISEASE: A GASTROENTEROLOGIST'S PERSPECTIVE

[1]Department of Internal Medicine II, Thuringia-Clinic Saalfeld, Teaching Hospital of the University of Jena, Germany
[2]Department of Medicine 1, Erlangen-Nuremberg, Germany

Severe acute respiratory syndrome-coronavirus-2 (SARS-CoV2) outbreak is the most dramatic event since World War II. Originating as a cluster of unexplained cases of pneumonia, it turned out that this viral disease termed COVID-19 is not only a respiratory infection, but a systemic disease associated with a number of extrapulmonary complications. One of the medical disciplines that is strongly affected by this viral infection is gastroenterology. COVID-19 causes in some patients typical symptoms of enteritis such as diarrhea or abdominal pain. There is also evidence that this infection may lead to liver and pancreatic injury. Since the SARS-CoV2 virus was detected in stool, a fecal-oral route of transmission is possible. Moreover, viral receptor angiotensin converting enzyme 2 (ACE2) is highly expressed in the gastrointestinal tract and enables the invasion of the gastrointestinal epithelium as demonstrated *in vitro* and *in vivo*. COVID-19 pandemic has an impact on the daily practice and the workflows in endoscopy leading to a dramatic decrease of screening and surveillance procedures. COVID-19 impacts the therapy of patients with inflammatory bowel disease (IBD), particularly those using high doses of corticosteroids, immunosuppressive agents and biologics. Patients with preexisting liver disease, especially metabolic associated liver fatty disease (MALFD) with fibrosis or liver cirrhosis, are at high risk for severe COVID-19. As long as no active vaccine against SARS-CoV2 is available, gastroenterologists have to be aware of these problems that affect their daily routine practice.

Key words: *SARS-CoV2, pandemic, COVID-19, gastrointestinal manifestations, anti-inflammatory therapy, gut microbiota, endoscopy, inflammatory bowel disease, liver disease*

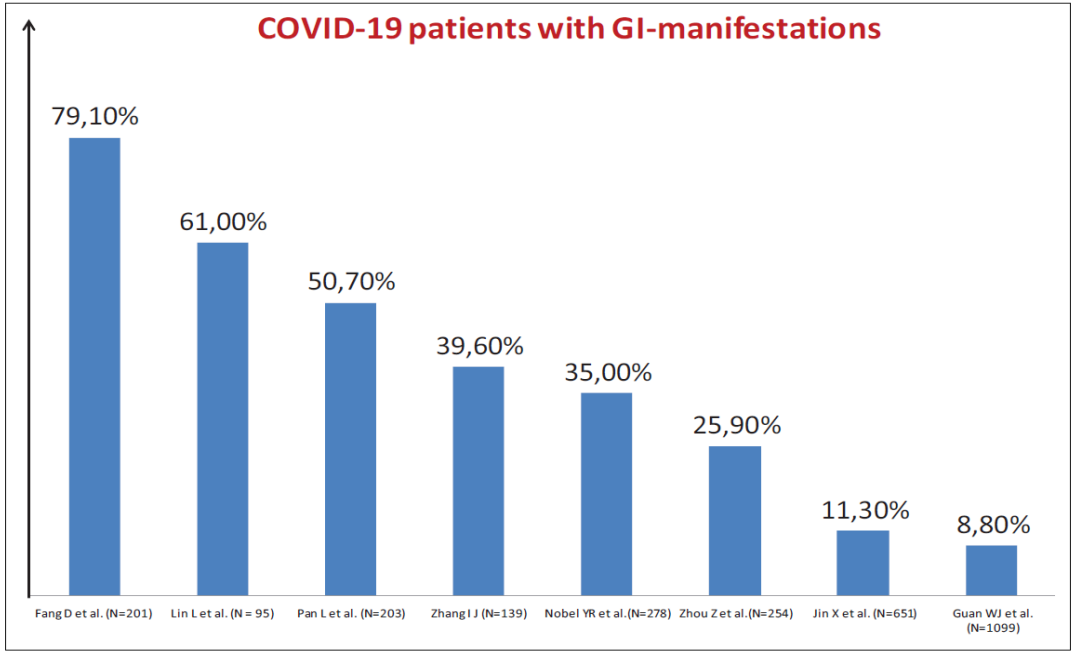


Fig. 5. Frequency of GI complications in different clinical studies.

Covid-19 - More Than Respiratory Disease: A Gastroenterologist's Perspective; Konturek, Et Al; Journal Of Physiology And Pharmacology 2020, 71, 2, 179-189

Diarrea COVID. Fisiopatologia.

- Encara no es coneix amb precisió el mecanisme fisiopatològic que genera els símptomes Gastrointestinals (GI) a COVID-19, però, l'evidència suggereix que l'expressió de l'enzim convertidor d'angiotensina (ACE2) indueix un procés inflamatori al Tracte Gastrointestinal (TGI).

- D'altra banda, l'evidència d'ARN viral en la matèria fecal recomana replicació al TGI.

- Així mateix, s'ha reportat disbiosi intestinal, amb possibilitat d'increment de patògens oportunistes.

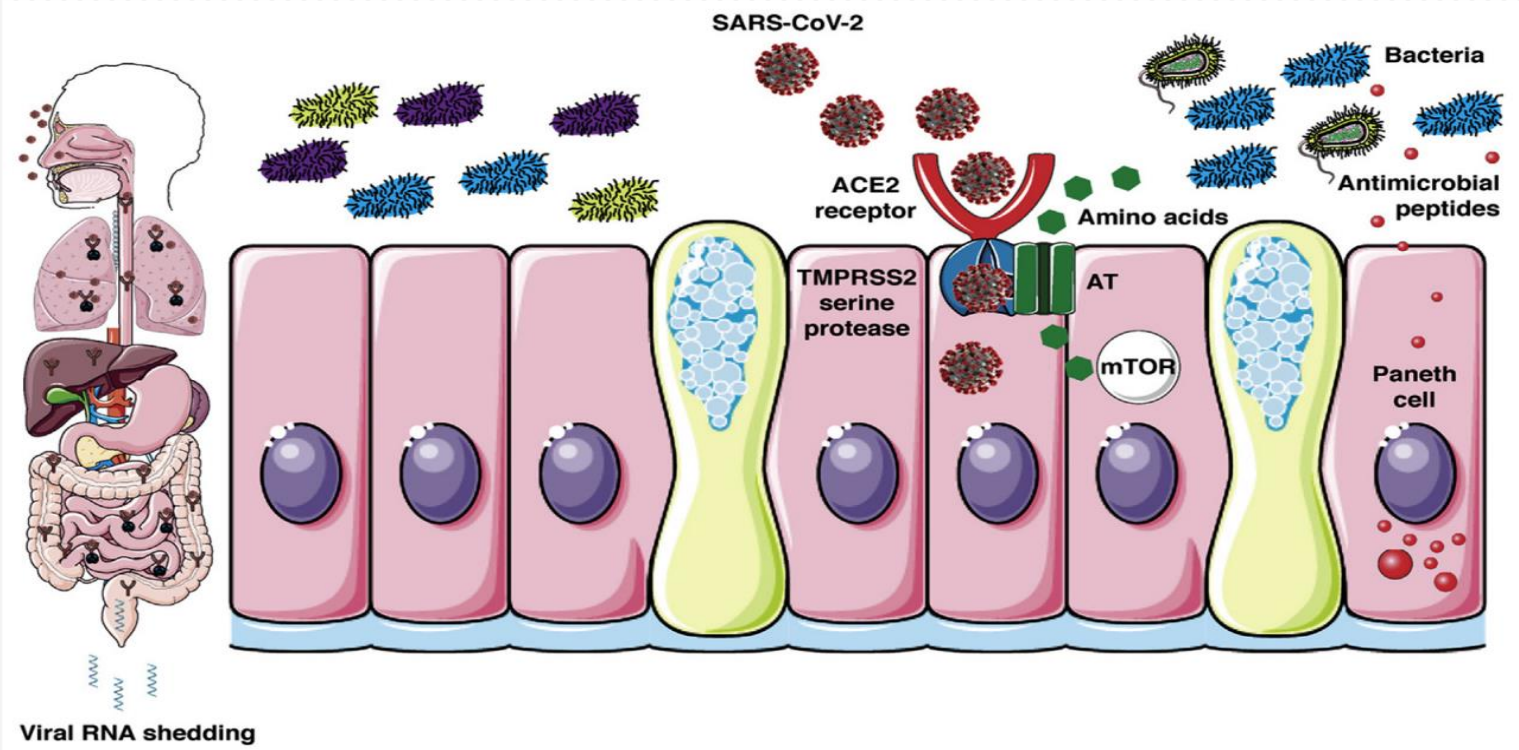
Mini-examen clínico: ¿Cuánto sabe sobre el diagnóstico y manejo del trastorno funcional digestivo pos-COVID-19? - Medscape - 24 de feb de 2022.

Diarrea COVID. Fisiopatologia.

- Posterior a l'entrada del SARS-Cov-2 a les cèl·lules epitelials del TGI a través R-ACE2, ocorre una resposta inflamatòria intensa que incrementa la permeabilitat intestinal, que té com a conseqüència l'alliberament de diverses citocines pro inflamatòries (IL-6) i increment de marcadors inflamatoris (Cal-p).
- Es tradueix en una resposta exagerada més en pacients sotmesos a algun estrès psicològic.

Mini-examen clínico: ¿Cuánto sabe sobre el diagnóstico y manejo del trastorno funcional digestivo pos-COVID-19? - Medscape - 24 de feb de 2022.

Diarrea Covid. Fisiopatologia



Diarrhea during COVID-19 Infection: Pathogenesis, Epidemiology, Prevention, and Management; D'Amico F, Et al; Clinical Gastroenterology and Hepatology, 2020; 18: 1663-1672.

Diarrea Covid. Fisiopatologia.

- Desregulació intestinal (> permeabilitat, mala absorció sals biliars).
- Modificació en cèl·lules senceres endocrines
- Hipersensibilitat visceral
- Alteració del metabolisme de la seròtina
- Disbiosi

Un altre punt a destacar els factors individuals involucren predisposiciógenètica i presència d'alteracions psicològiques preexistents, com **ansietat o depressió.**

Mini-examen clínico: ¿Cuánto sabe sobre el diagnóstico y manejo del trastorno funcional digestivo pos-COVID-19? - Medscape - 24 de feb de 2022.

Diarrea Covid. Diagnòstic.

Quin criteri són indispensables per al diagnòstic de trastorn funcional digestiu post-COVID-19?

Complir els criteris de Roma IV per a qualsevol trastorn funcional Digestiu en els 3 mesos previs, amb inici dels símptomes almenys 6 mesos previs al diagnòstic associats amb:

a. Infecció prèvia per COVID-19 confirmada per reacció en cadena de la polimerasa de temps real de SARS-CoV-2.
b. Inici de símptomes immediatament després de la resolució de la infecció per COVID-19.

Mini-examen clínico: ¿Cuánto sabe sobre el diagnóstico y manejo del trastorno funcional digestivo pos-COVID-19? - Medscape - 24 de feb de 2022.

Diarrea Covid. Diagnòstic.

El criteri indispensable per fer el diagnòstic de trastorn funcional digestiu Post-COVID-19 és no tenir dades de trastorn funcional digestiu previ a la infecció.

Mini-examen clínico: ¿Cuánto sabe sobre el diagnóstico y manejo del trastorno funcional digestivo pos-COVID-19? - Medscape - 24 de feb de 2022.

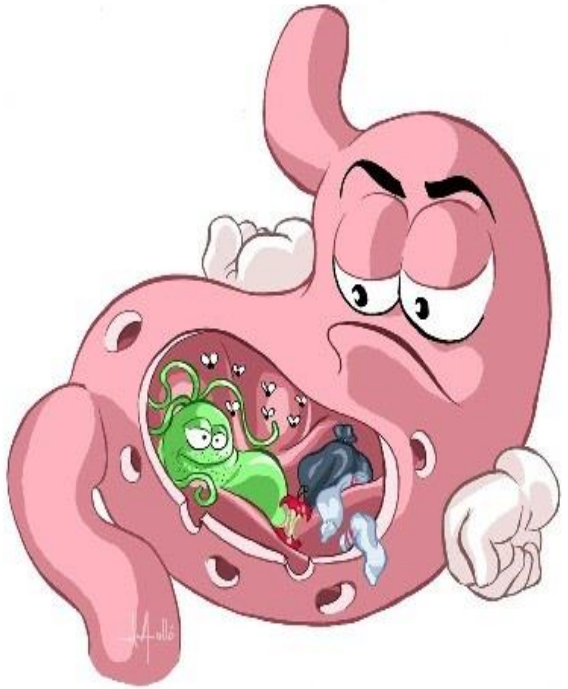
Actualització sobre Helicobacter pylori

Recomanació diagnòstica H. Pylori

TABLA 2

Recomendaciones sobre el diagnóstico de la infección por *H. pylori*

Para el diagnóstico no invasivo de la infección por *H. pylori,* se recomienda la prueba del aliento con C^{13} según el protocolo europeo que incluye la administración previa de ácido cítrico
Como alternativa a la prueba del aliento se recomienda la prueba de antígeno en heces, siempre que se utilice un metido de ELISA monoclonal
No se recomienda el uso sistemático de la serología para el diagnóstico de la infección por *H. pylori*
Tanto para pruebas invasivas como no invasivas se recomienda suspender los inhibidores de la bomba de protones dos semanas antes de su realización
Tanto para pruebas invasivas como no invasivas es necesario suspender la antibioterapia cuatro semanas antes de su realización
Se recomienda comprobar la curación de la infección por *H. pylori* en todos los casos
Para la comprobación de la curación, se aconseja la prueba no invasiva del aliento con C^{13} según el protocolo europeo que incluye la administración previa de ácido cítrico
No se recomienda el uso de la serología como método para comprobar la erradicación tras el tratamiento
La curación de la infección se valorará al menos cuatro semanas después de finalizar el tratamiento de la infección.



Protocolo practica asistencial. A. Lanas-Gimeno, S. Martínez Domingo; Medicine, 2020; 13 (2): 106-10.

La realitat a H. pylori

Journal of Microbiology, Immunology and Infection 54 (2021) 1184–1187

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Short Communication

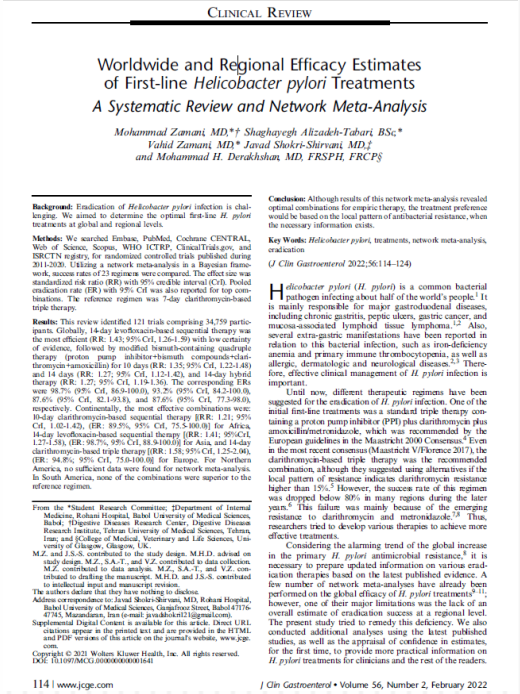
Multidrug resistance: The clinical dilemma of refractory *Helicobacter pylori* infection

Chia-Jung Kuo [a,b,c], Cheng-Han Lee [a], Ming-Ling Chang [a,b], Cheng-Yu Lin [a], Wey-Ran Lin [a,b], Ming-Yao Su [a,b,j], Cheng-Hsun Chiu [b,c,d,e], Chi-Nan Tseng [g,h], Yu-Shan Wu [i], Cheng-Tang Chiu [a,b,c,**], Chih-Ho Lai [e,f,k,l,*]

In conclusion, the prevalence of antimicrobial resistance rates was high in refractory *H. pylori* recently, which contributed to the decrease in the eradication rate and became a therapeutic challenge in clinical practice. It is important to determine the optimum *H. pylori* eradication strategy according to the results of antibacterial susceptibility analysis. The results of our current study provide the resistance patterns for refractory *H. pylori* infection and may lead to a better selection of effective antimicrobial agents and treatment outcomes.

Worldwide and Regional Efficacy Estimates of First-line Helicobacter pylori Treatments. A Systematic Review and Network Meta-Analysis. Zamani M. et al; J Clin Gastroenterol 2022 (february);56:114–124.

Últimes recomanacions de H. Pylori.



CLINICAL REVIEW

Worldwide and Regional Efficacy Estimates of First-line *Helicobacter pylori* Treatments

A Systematic Review and Network Meta-Analysis

Mohammad Zamani, MD,† Shaghayegh Alizadeh-Tabari, BSc,* Vahid Zamani, MD,* Javad Shokri-Shirvani, MD,‡ and Mohammad H. Derakhshan, MD, FRSPH, FRCP§*

Background: Eradication of *Helicobacter pylori* infection is challenging. We aimed to determine the optimal first-line *H. pylori* treatments at global and regional levels.

Methods: We searched Embase, PubMed, Cochrane CENTRAL, Web of Science, Scopus, WHO ICTRP, ClinicalTrials.gov, and ISRCTN registry, for randomized controlled trials published during 2011-2020. Utilizing a network meta-analysis in a Bayesian framework, success rates of 23 regimens were compared. The effect size was standardized risk ratio (RR) with 95% credible interval (CrI). Pooled eradication rate (ER) with 95% CrI was also reported for top combinations. The reference regimen was 7-day clarithromycin-based triple therapy.

Results: This review identified 121 trials comprising 34,759 participants. Globally, 14-day levofloxacin-based sequential therapy was the most efficient (RR: 1.43; 95% CrI, 1.26-1.59) with low certainty of evidence, followed by modified bismuth-containing quadruple therapy (proton pump inhibitor+bismuth compounds+clarithromycin+amoxicillin) for 10 days (RR: 1.35; 95% CrI, 1.22-1.48) and 14 days (RR: 1.27; 95% CrI, 1.12-1.42), and 14-day hybrid therapy (RR: 1.27; 95% CrI, 1.19-1.36). The corresponding ERs were 98.7% (95% CrI, 86.9-100.0), 93.2% (95% CrI, 84.2-100.0), 87.6% (95% CrI, 82.1-93.8), and 87.6% (95% CrI, 77.3-98.0), respectively. Continentally, the most effective combinations were: 10-day clarithromycin-based sequential therapy [(RR: 1.21; 95% CrI, 1.02-1.42), (ER: 89.5%, 95% CrI, 75.5-100.0)] for Africa, 14-day levofloxacin-based sequential therapy [(RR: 1.41; 95%CrI, 1.27-1.58), (ER: 98.7%, 95% CrI, 88.9-100.0)] for Asia, and 14-day clarithromycin-based triple therapy [(RR: 1.58; 95% CrI, 1.25-2.06), (ER: 94.8%; 95% CrI, 75.0-100.0)] for Europe. For Northern America, no sufficient data were found for network meta-analysis. In South America, none of the combinations were superior to the reference regimen.

Conclusion: Although results of this network meta-analysis revealed optimal combinations for empiric therapy, the treatment preference would be based on the local pattern of antibacterial resistance, when the necessary information exists.

Key Words: *Helicobacter pylori*, treatments, network meta-analysis, eradication

(*J Clin Gastroenterol* 2022;56:114–124)

Helicobacter pylori (*H. pylori*) is a common bacterial pathogen infecting about half of the world's people.[1] It is mainly responsible for major gastroduodenal diseases, including chronic gastritis, peptic ulcers, gastric cancer, and mucosa-associated lymphoid tissue lymphoma.[1,2] Also, several extra-gastric manifestations have been reported in relation to this bacterial infection, such as iron-deficiency anemia and primary immune thrombocytopenia, as well as allergic, dermatologic and neurological diseases.[3,4] Therefore, effective clinical management of *H. pylori* infection is important.

Until now, different therapeutic regimens have been suggested for the eradication of *H. pylori* infection. One of the initial first-line treatments was a standard triple therapy containing a proton pump inhibitor (PPI) plus clarithromycin plus amoxicillin/metronidazole, which was recommended by the European guidelines in the Maastricht 2000 Consensus.[4] Even in the most recent consensus (Maastricht V/Florence 2017), the clarithromycin-based triple therapy was the recommended combination, although they suggested using alternatives if the local pattern of resistance indicates clarithromycin resistance higher than 15%.[5] However, the success rate of this regimen was dropped below 80% in many regions during the later years.[6] This failure was mainly because of the emerging resistance to clarithromycin and metronidazole.[7,8] Thus, researchers tried to develop various therapies to achieve more effective treatments.

Considering the alarming trend of the global increase in the primary *H. pylori* antimicrobial resistance,[8] it is necessary to prepare updated information on various eradication therapies based on the latest published evidence. A few number of network meta-analyses have already been performed on the global efficacy of *H. pylori* treatments[9–11]; however, one of their major limitations was the lack of an overall estimate of eradication success at a regional level. The present study tried to remedy this deficiency. We also conducted additional analyses using the latest published studies, as well as the appraisal of confidence in estimates, for the first time, to provide more practical information on *H. pylori* treatments for clinicians and the rest of the readers.

From the *Student Research Committee; †Department of Internal Medicine, Rohani Hospital, Babol University of Medical Sciences, Babol; ‡Digestive Diseases Research Center, Digestive Diseases Research Institute, Tehran University of Medical Sciences, Tehran, Iran; and §College of Medical, Veterinary and Life Sciences, University of Glasgow, Glasgow, UK.

M.Z. and J.S.-S. contributed to the study design. M.H.D. advised on study design. M.Z., S.A.-T., and V.Z. contributed to data collection. M.Z. contributed to data analysis. M.Z., S.A.-T., and V.Z. contributed to drafting the manuscript. M.H.D. and J.S.-S. contributed to intellectual input and manuscript revision.

The authors declare that they have nothing to disclose.

Address correspondence to: Javad Shokri-Shirvani, MD, Rohani Hospital, Babol University of Medical Sciences, Ganjafrooz Street, Babol 47176-47745, Mazandaran, Iran (e-mail: javadshokri21@gmail.com).

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DOI: 10.1097/MCG.0000000000001641

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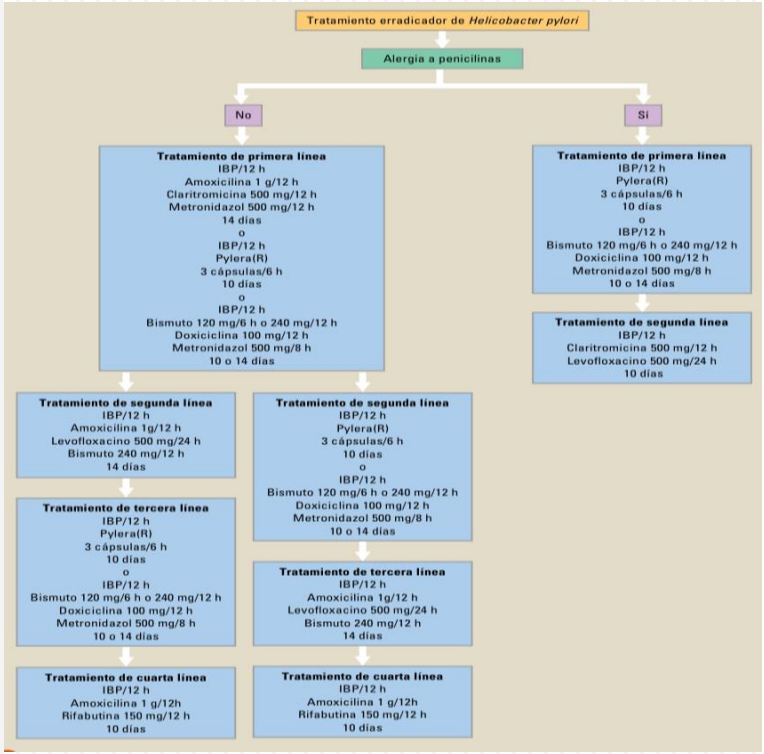
Worldwide and Regional Efficacy Estimates of First-line Helicobacter pylori Treatments. A Systematic Review and Network Meta-Analysis. Zamani M. et al; J Clin Gastroenterol 2022 (february);56:114–124.

Tractament H. Pylori



Protocol pràctica assistencial. Lanas-Gimeno, A; Martínez Domingo, S.; Medicine, 2020; 13 (2): 106-10.

Moltes gràcies