Einstein Montefiore | Center for Continuing Professional Development

ACTIVITY INFORMATION SHEET FOR REGULARLY SCHEDULED SERIES (RSS)

ELECTRONIC EDUCATION DOCUMENTATION SYSTEMS (eeds)

Date: August 27, 2020

Presenter: Daniel Behin, MD

Activity Title: Medicine Grand Rounds: COVID-19 and the GI Tract

Location: Zoom Conference

DISCLOSURES

This activity is made possible in part by an educational grant: **N/A**

Course Director's/Moderator's

Dr Elizabeth Kitsis has no relevant financial relationships with an ACCME-defined commercial interest within the past 12 months.

Presenter's

Dr Behin has no relevant financial relationships with an ACCME-defined commercial interest within the past 12 months.

OBJECTIVES

- Understand GI involvement in systemic COVID-19 infection
- Recognize GI manifestations of COVID-19 infection
- Be aware of GI tract imaging abnormalities associated with COVID-19 infection
- Analyze current concepts and limitations supporting the spread of COVID-19 via the GI tract
- Appreciate the literature supporting H2RAs to alter outcomes in COVID-19 infection

COVID-19 and the GI Tract

Daniel Behin, MD

Medical Grand Rounds

8/27/2020

Objectives

- To recognize GI manifestations of COVID-19 infection
- To understand GI involvement in systemic COVID-19 infection
- To be aware of GI tract imaging abnormalities associated with COVID-19 infection
- To analyze current concepts and limitations supporting the spread of COVID-19 via the GI tract
- To appreciate the literature supporting H_2RAs to alter outcomes in COVID-19 infection

GI Manifestations

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Clinical Characteristics of Coronavirus Disease 2019 in China

W. Guan, Z. Ni, Yu Hu, W. Liang, C. Ou, J. He, L. Liu, H. Shan, C. Lei, D.S.C. Hui, B. Du, L. Li, G. Zeng, K.-Y. Yuen, R. Chen, C. Tang, T. Wang, P. Chen, J. Xiang, S. Li, Jin-lin Wang, Z. Liang, Y. Peng, L. Wei, Y. Liu, Ya-hua Hu, P. Peng, Jian-ming Wang, J. Liu, Z. Chen, G. Li, Z. Zheng, S. Qiu, J. Luo, C. Ye, S. Zhu, and N. Zhong, for the China Medical Treatment Expert Group for Covid-19*

Characteristic	All Patients (N= 1099)	Disease Severity		Presence of Primary Composite End Point†	
		Nonsevere (N=926)	Severe (N=173)	Yes (N=67)	No (N=1032)
Nasal congestion	53 (4.8)	47 (5.1)	6 (3.5)	2 (3.0)	51 (4.9)
Headache	150 (13.6)	124 (13.4)	26 (15.0)	8 (11.9)	142 (13.8)
Cough	745 (67.8)	623 (67.3)	122 (70.5)	46 (68.7)	699 (67.7)
Sore throat	153 (13.9)	130 (14.0)	23 (13.3)	6 (9.0)	147 (14.2)
Sputum production	370 (33.7)	309 (33.4)	61 (35.3)	20 (29.9)	350 (33.9)
Fatigue	419 (38.1)	350 (37.8)	69 (39.9)	22 (32.8)	397 (38.5)
Hemoptysis	10 (0.9)	6 (0.6)	4 (2.3)	2 (3.0)	8 (0.8)
Shortness of breath	205 (18.7)	140 (15.1)	65 (37.6)	36 (53.7)	169 (16.4)
Nausea or vomiting	55 (5.0)	43 (4.6)	12 (6.9)	3 (4.5)	52 (5.0)
Diarrhea	42 (3.8)	32 (3.5)	10 (5.8)	4 (6.0)	38 (3.7)

Symptom Timeline

February 2020

- Fever, cough, shortness of breath

April 2020

- Chills, repeated shaking with chills, muscle pain, headache, sore throat, loss of taste (dysgeusia) or smell (dysosmia)

June 2020

- Congestion, runny nose, nausea, diarrhea

Symptom Timeline

February 2020

Fever

Cough

Shortness of breath

April 2020

Chills
Muscle pain
Headache
Sore throat
Disturbed taste (dysgeusia) or smell (dysosmia)

June 2020

Congestion

Runny nose

Nausea

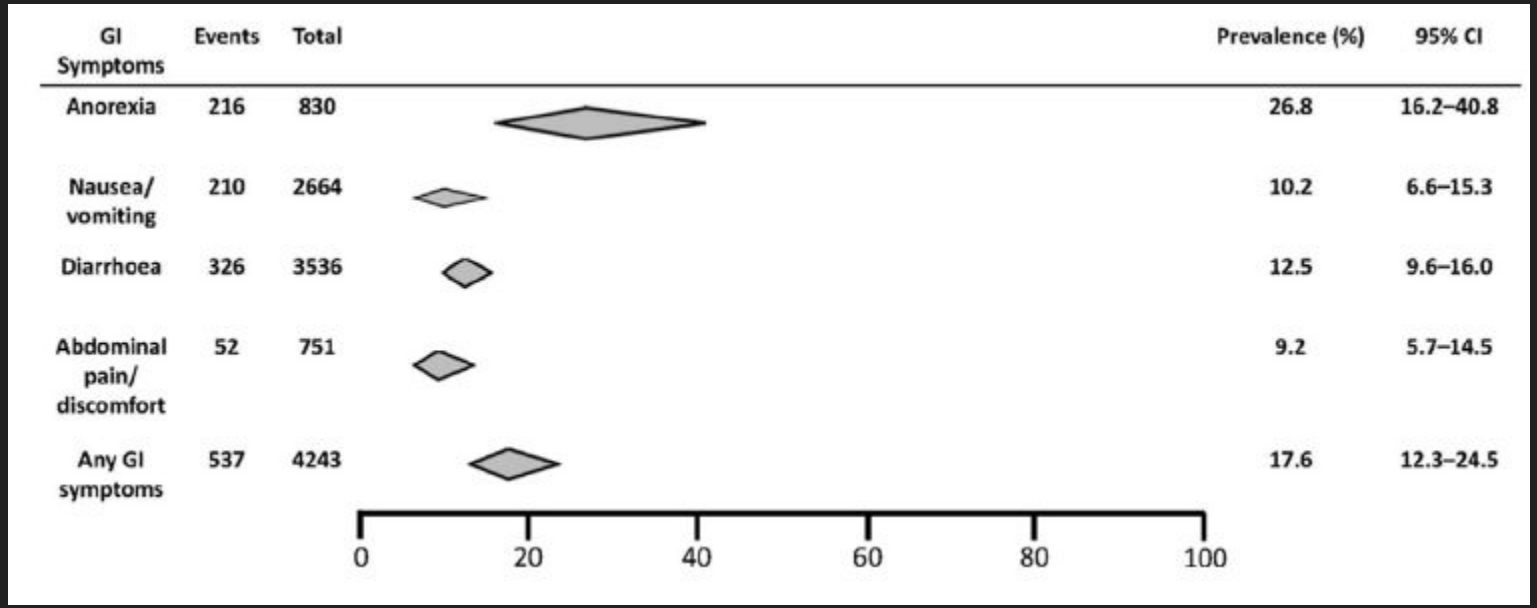
Diarrhea

Gastroenterology 2020;159:81–95

CLINICAL—ALIMENTARY TRACT

Gastrointestinal Manifestations of SARS-CoV-2 Infection and Virus Load in Fecal Samples From a Hong Kong Cohort: Systematic Review and Meta-analysis

Ka Shing Cheung,[1,2,*] **Ivan F. N. Hung**,[1,3,*] Pierre P. Y. Chan,[4] K. C. Lung,[5] Eugene Tso,[6] Raymond Liu,[4] Y. Y. Ng,[7] Man Y. Chu,[8] Tom W. H. Chung,[9] Anthony Raymond Tam,[1] Cyril C. Y. Yip,[9] Kit-Hang Leung,[9] Agnes Yim-Fong Fung,[3] Ricky R. Zhang,[1,3] Yansheng Lin,[2] Ho Ming Cheng,[1] Anna J. X. Zhang,[3] Kelvin K. W. To,[3,9] Kwok-H. Chan,[3,9] Kwok-Y. Yuen,[3] and Wai K. Leung[1]



GI symptoms are more common in severe COVID disease (17%) then in non-severe COVID disease (11%)

48.1% of stool samples were + for viral RNA

- Detected as early as 3 days into illness
- 70% of patients has + stool RNA despite negative respiratory RNA

Journal Pre-proof

Are Gastrointestinal Symptoms Specific for COVID-19 Infection? A Prospective Case-Control Study from the United States

Alan Chen, MD, Amol Agarwal, MD, Nishal Ravindran, MD, Chau To, MD, Talan Zhang, MS, Paul J. Thuluvath, MD., FRCP

Prospective case-control study at a single hospital in Maryland
Telephone survey of patients who tested + or - for COVID swab

GI Sxs in COVID-19 Infection: A Telephone Survey

COVID	-	+
Nausea	26%	30%
Anorexia	26%	53%
Diarrhea	30%	50%
Abd pain	19%	26%
Dysgeusia	14%	67%

Anorexia + diarrhea + dysgeusia = 99% specific for COVID-19 infection

NARRATIVE REVIEWS

Fasiha Kanwal, Section Editor

Diarrhea During COVID-19 Infection: Pathogenesis, Epidemiology, Prevention, and Management

Ferdinando D'Amico,[*,‡] Daniel C. Baumgart,[§,a] Silvio Danese,[*,‖] and Laurent Peyrin-Biroulet[‡,a]

Check for updates

Evaluated 21 studies looking at 3042 patients

- Diarrhea ranged from 2% to 35%
- Duration to admission was longer if they have GI symptoms
- Average of 3 non-dehydrating BMs/day
- Greater percentage of GI symptoms in severe disease

Clinical Gastro and Hep 2020

Gastrointestinal Symptoms and Coronavirus Disease 2019: A Case-Control Study From the United States

Yael R. Nobel,[1] Meaghan Phipps,[1] Jason Zucker,[2] Benjamin Lebwohl,[1] Timothy C. Wang,[1] Magdalena E. Sobieszczyk,[2] and Daniel E. Freedberg[1]

[1]Division of Digestive and Liver Diseases, Columbia University Irving Medical Center–New York Presbyterian Hospital, New York, New York; and [2]Division of Infectious Diseases, Columbia University Irving Medical Center–New York Presbyterian Hospital, New York, New York

Retrospective case-control study of 278 COVID-19 positive and 238 COVID-19 negative patient

GI symptoms at the time of testing, more like to test positive for COVID-19

No GI symptoms, patients are equally likely to test positive or negative

GI symptoms were associated with a 70% relative increased risk of testing positive

Gastroenterology 7/2020

AGA Institute Rapid Review of the GI and Liver Manifestations of COVID-19, Meta-Analysis of International Data, and Recommendations for the Consultative Management of Patients with COVID-19

Authors: Shahnaz Sultan*[1], Osama Altayar*[2], Shazia M. Siddique[3], Perica Davitkov[4], Joseph D. Feuerstein[5], Joseph K. Lim[6], Yngve Falck-Ytter[4], Hashem B. El-Serag[7] on behalf of the AGA

Meta-analysis of 47 studies including 10,890 patients throughout the world

Most studies were based on hospitalized patients

	China	Outside China
Diarrhea	5.8%	18.3%
N/V	5.2%	14.9%
Abdominal pain	2.7%	5.3%

Diarrhea is the only presenting symptom in <10% of patients
2-10 BMs per day
Usually self-resolves, lasts 4 days

A(dys)geusia vs a(dys)nosmia

Ageusia - Loss of taste

Anosmia - Loss of smell

COVID-19 and anosmia: A review based on up-to-date knowledge

Xiangming Meng[a,*], Yanzhong Deng[b], Zhiyong Dai[a], Zhisheng Meng[c]

[a] Department of Otolaryngology, Wuxi Huishan District People's Hospital, 2 Zhanqian North Road, Luoshe Town, Huishan District, Wuxi 214187, PR China
[b] Department of Anesthesiology, Wuxi Huishan District People's Hospital, 2 Zhanqian North Road, Luoshe Town, Huishan District, Wuxi 214187, PR China
[c] Faculty of Information Engineering and Automation, Kunming University of Science and Technology, No.727 South Jingming Road, Chenggong District, Kunming 650500, PR China

Many coronaviruses cause anosmia

Up to 50% of patients can develop olfactory dysfunction

Anosmia begins 4-5 days after sx onset - 98% improvement by day 28

Higher incidence in European and American countries, rare in China

Can be the only presenting sx

Virally-induced olfactory nerve damage vs local inflammation of nasal cavity

Am J Otolaryngol 2020

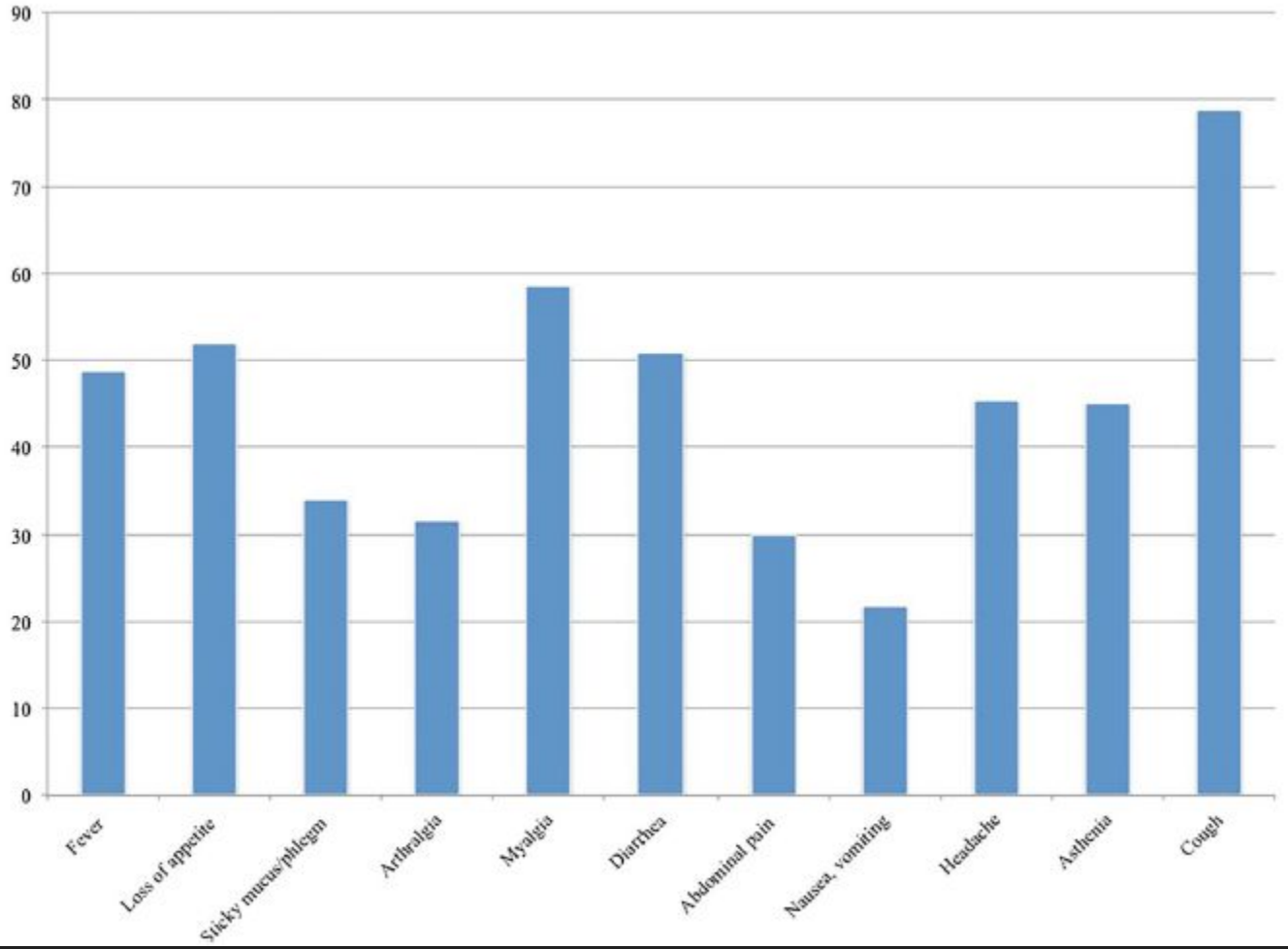
Olfactory and gustatory dysfunctions as a clinical presentation of mild-to-moderate forms of the coronavirus disease (COVID-19): a multicenter European study

Jerome R. Lechien[1,2,3,4] · Carlos M. Chiesa-Estomba[1,5] · Daniele R. De Siati[1,6] · Mihaela Horoi[4] · Serge D. Le Bon[4] · Alexandra Rodriguez[4] · Didier Dequanter[4] · Serge Blecic[7] · Fahd El Afia[1,3] · Lea Distinguin[1,3] · Younes Chekkoury-Idrissi[1,3] · Stéphane Hans[3] · Irene Lopez Delgado[1,8] · Christian Calvo-Henriquez[1,9] · Philippe Lavigne[1,10] · Chiara Falanga[1,11] · Maria Rosaria Barillari[1,11] · Giovanni Cammaroto[1,12] · Mohamad Khalife[13] · Pierre Leich[14] · Christel Souchay[14] · Camelia Rossi[15] · Fabrice Journe[2] · Julien Hsieh[1,16] · Myriam Edjlali[17,18] · Robert Carlier[18] · Laurence Ris[19] · Andrea Lovato[20] · Cosimo De Filippis[20] · Frederique Coppee[21] · Nicolas Fakhry[1,22] · Tareck Ayad[1,10] · Sven Saussez[1,2,4,13]

417 cases of mild to mod COVID-19 + infections from 12 European hospitals

- 85.6% of patients had either anosmia or hyponosmia
- Occurred before other symptoms in 12% of cases
- Most recovered by day 8
- 79% of patients w/o rhinorrhea had anosmia or hyposmia

Euro Archives of Oto-Rhino-Laryngology 4/2020


90
80
70
60
50
40
30
20
10
0
Fever
Loss of appetite
Sticky mucus/phlegm
Arthralgia
Myalgia
Diarrhea
Abdominal pain
Nausea, vomiting
Headache
Asthenia
Cough

85.6% of patients had either anosmia or hyponosmia

Occurred before other symptoms in 12% of cases

Most recovered by day 8

79% of patients w/o rhinorrhea had anosmia or hyposmia

Taste Changes (Dysgeusia) in COVID-19: A Systematic Review and Meta-analysis

Muhammad Aziz,[1] Abhilash Perisetti,[2] Wade M. Lee-Smith,[3] Mahesh Gajendran,[4] Pardeep Bansal,[5] and Hemant Goyal[6]

[1]Department of Internal Medicine, University of Toledo, Toledo, OH; [2]Department of Gastroenterology and Hepatology, University of Arkansas for Medical Sciences, Little Rock, AR; [3]University of Toledo Libraries, Toledo, OH; [4]Paul L. Foster School of Medicine, Texas Tech University Health Sciences Center El Paso, El Paso, TX; [5]Division of Gastroenterology, Moses Taylor Hospital and Reginal Hospital of Scranton, Scranton, PA; and [6]The Wright Center for Graduate Medical Education, Scranton, PA

5 articles totalling 817 patients

49.8% of patients had dysguesia/aguesia

Gastroenterology 2020

SCIENCE ADVANCES | RESEARCH ARTICLE

CORONAVIRUS

Non-neuronal expression of SARS-CoV-2 entry genes in the olfactory system suggests mechanisms underlying COVID-19–associated anosmia

David H. Brann[1*], Tatsuya Tsukahara[1*], Caleb Weinreb[1*], Marcela Lipovsek[2], Koen Van den Berge[3,4], Boying Gong[5], Rebecca Chance[6], Iain C. Macaulay[7], Hsin-Jung Chou[6], Russell B. Fletcher[6†], Diya Das[6,8‡], Kelly Street[9,10], Hector Roux de Bezieux[5,11], Yoon Gi Choi[12], Davide Risso[13], Sandrine Dudoit[3,5], Elizabeth Purdom[3], Jonathan Mill[14], Ralph Abi Hachem[15], Hiroaki Matsunami[16], Darren W. Logan[17], Bradley J. Goldstein[15], Matthew S. Grubb[2], John Ngai[6,12,18§], Sandeep Robert Datta[1‖]

Damage to non-neuronal supporting cells may lead to disruption of signalling to the brain or olfactory sensory neuron death

Vascular damage may lead to hypoperfusion and inflammation leading to olfactory bulb dysfunction

Science Advances, 7/2020

Pancreatic Injury Patterns in Patients With Coronavirus Disease 19 Pneumonia

Fan Wang,[1,2,*] **Haizhou Wang**,[1,2,*] **Junli Fan**,[3,*] **Yongxi Zhang**,[4,*] Hongling Wang,[1,2] and Qiu Zhao[1,2]

[1]Department of Gastroenterology, Zhongnan Hospital of Wuhan University, Wuhan, China; [2]Hubei Clinical Center and Key Lab of Intestinal and Colorectal Diseases, Wuhan, China; [3]Department of Laboratory Medicine, Zhongnan Hospital of Wuhan University, Wuhan, China; and [4]Department of Infectious Disease, Zhongnan Hospital of Wuhan University, Wuhan, China

Evaluated 52 patients who were + for COVID-19

Injury was defined as an elevated amylase or lipase level

17% suffered from pancreatic injury

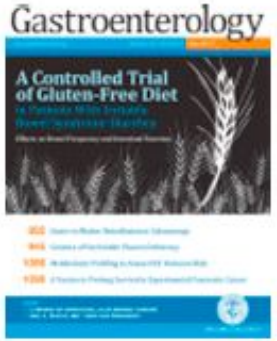
The patients with pancreatic injury had more severe illness

Gastroenterology 7/2020

Journal Pre-proof

Emerging phenotype of SARS-CoV2 associated pancreatitis.

Peter Szatmary, Ankur Arora, Michael Godwin Thomas Raraty, Declan Francis Joseph Dunne, Ryan David Baron, Christopher Michael Halloran



5 young, overweight, COVID + men with CT-proven pancreatitis

Mild pancreatic and duodenal inflammation

Profound SIR

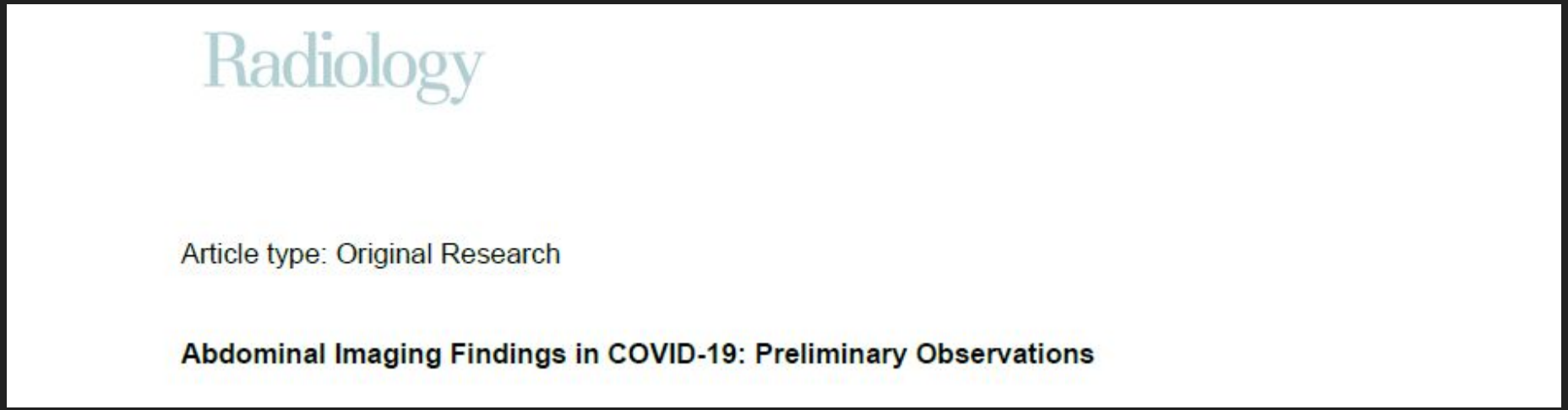
Surprising low amylase levels

Nasal epithelium

Respiratory Epithelium
- Humidify air
- Continuous with epithelium of respiratory tract
- Contain high levels of ACE2 and TMPRSS2

Olfactory Epithelium
- Odor detection
- No ACE2 in sensory neurons (SN), but in cells that support SN, reserved stem cells

Imaging

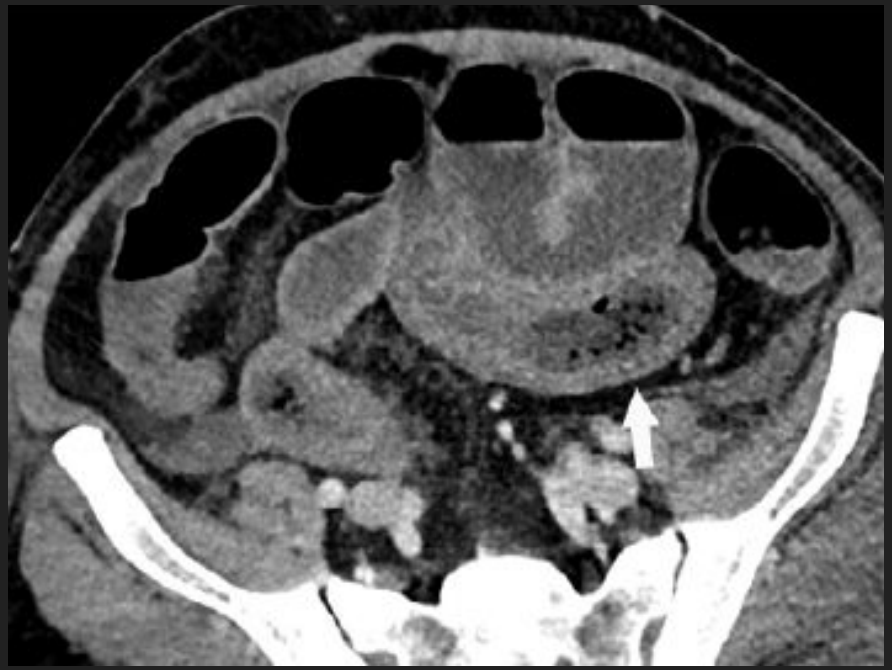


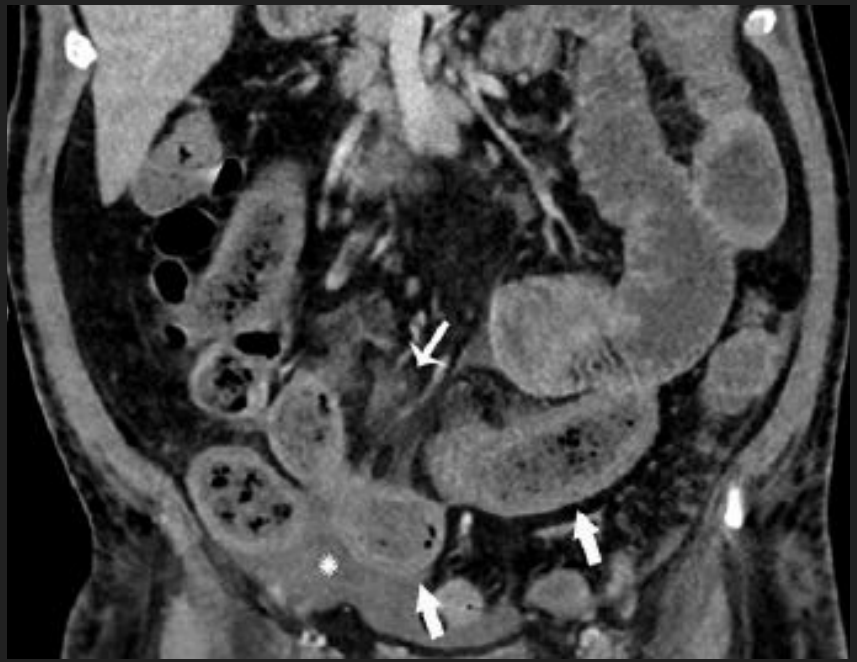
Evaluated CT scan, x-ray, US and MRI studies on 134 in-pts with COVID-19

Bowel findings in 31% included:

- Bowel wall thickening (29%)
- Pneumatosis or portal venous gas (20%)
- Perforation

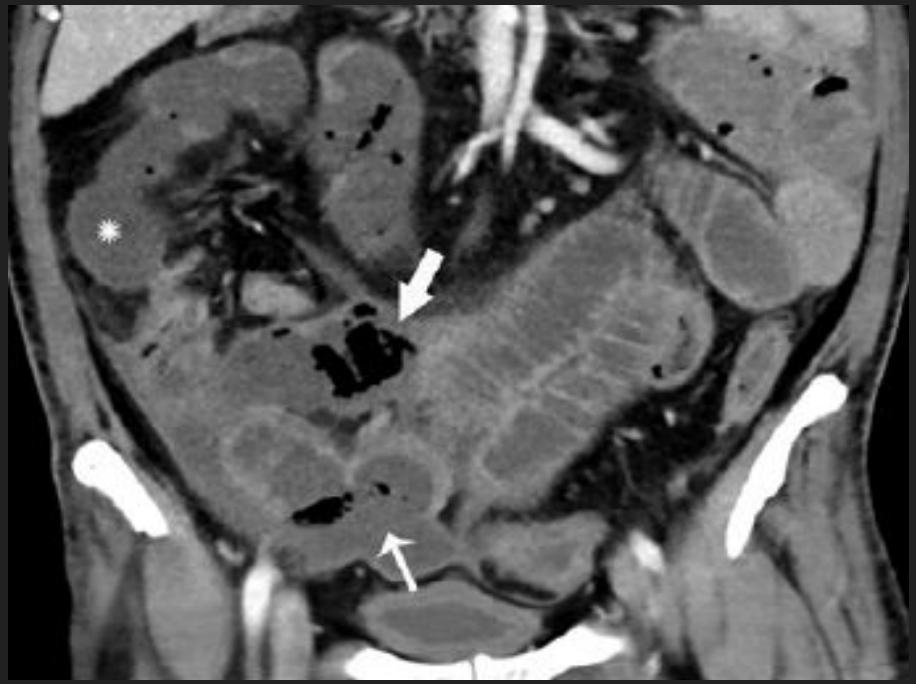
Bhayana, R, Som, A. May 2020

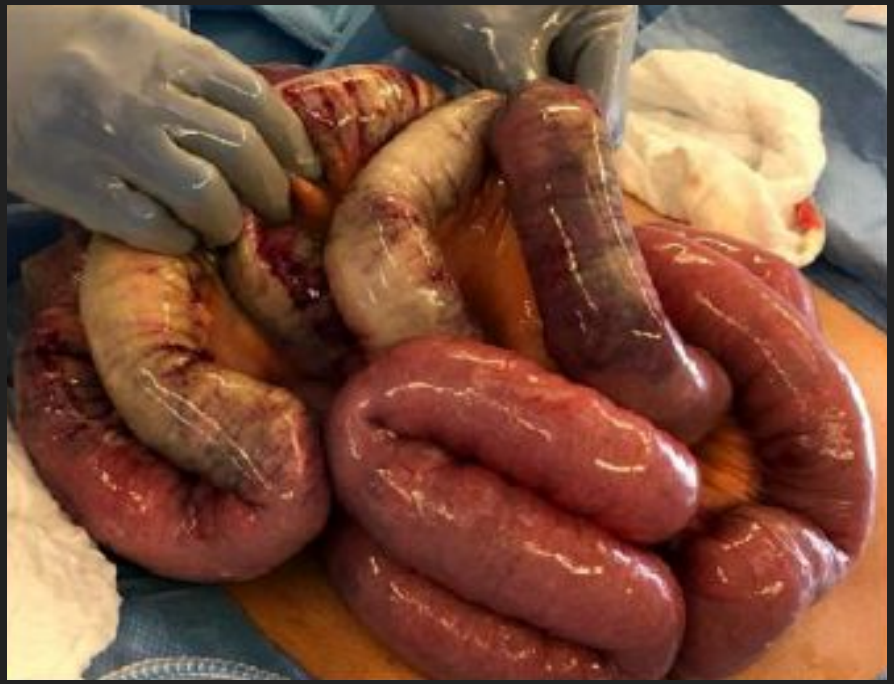




Pts with pneumatosis and portal venous gas @ ex-lap

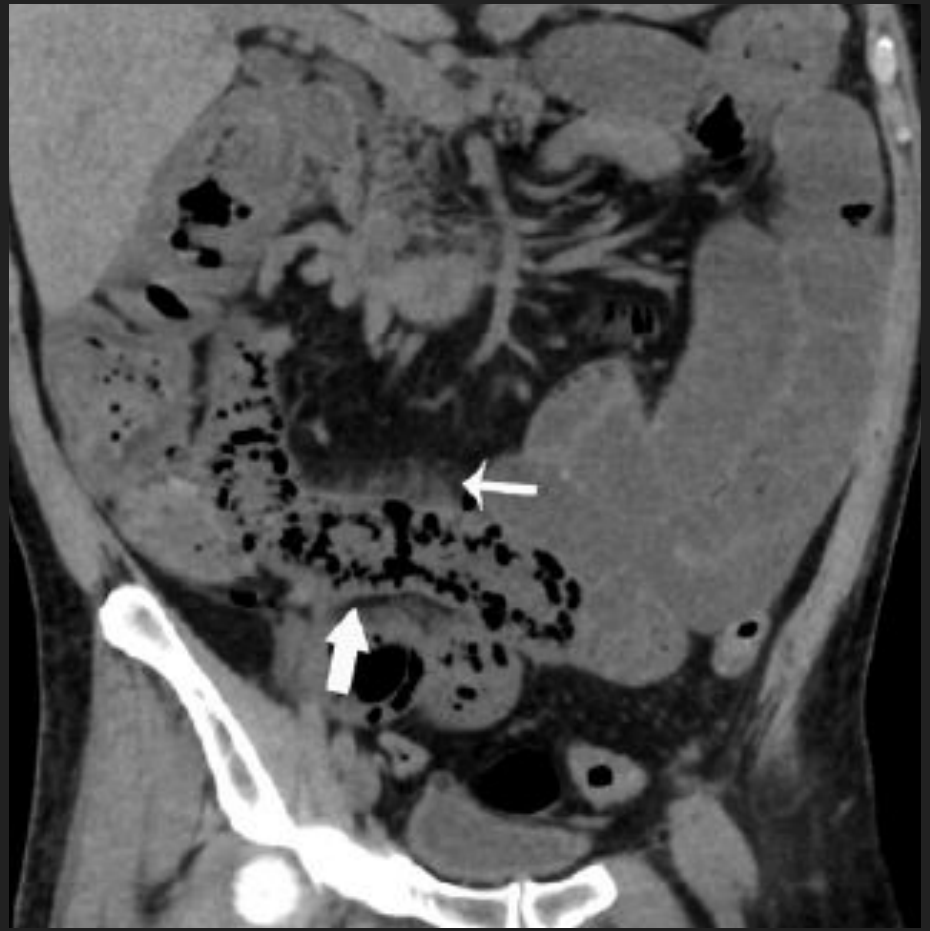
- necrotic bowel in half of patients.

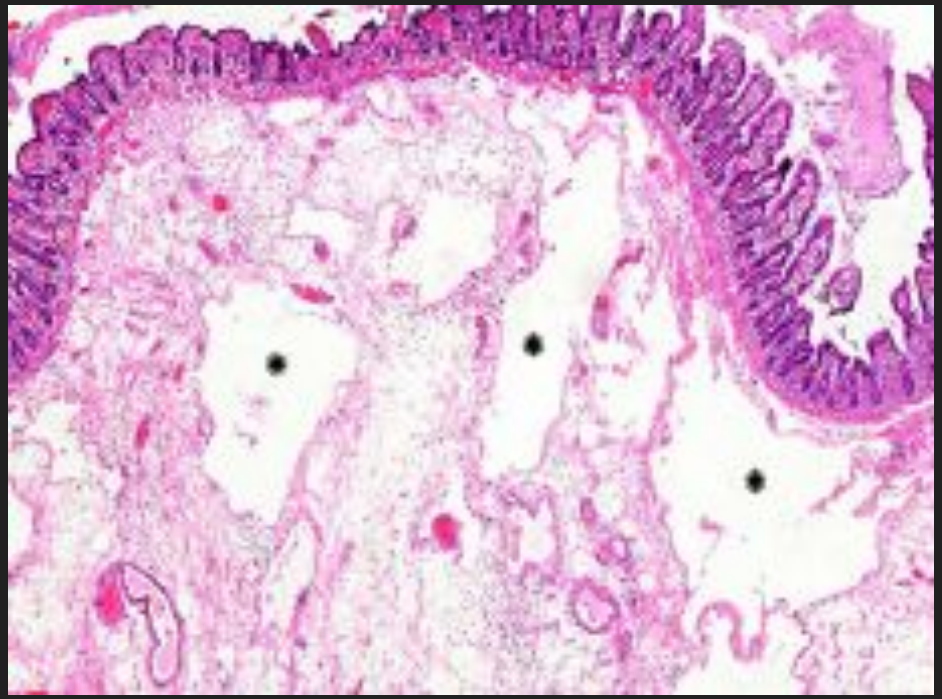


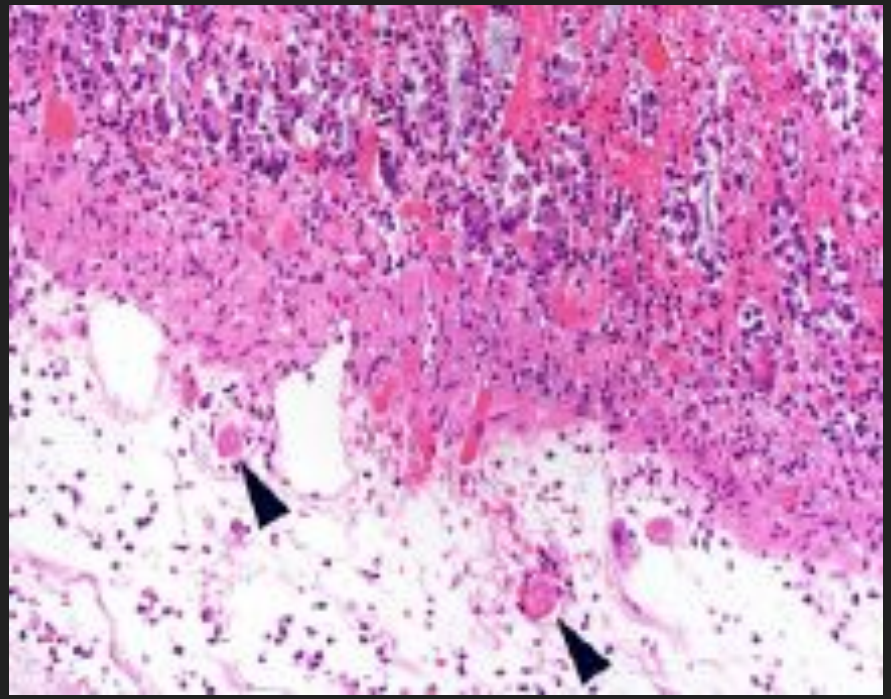


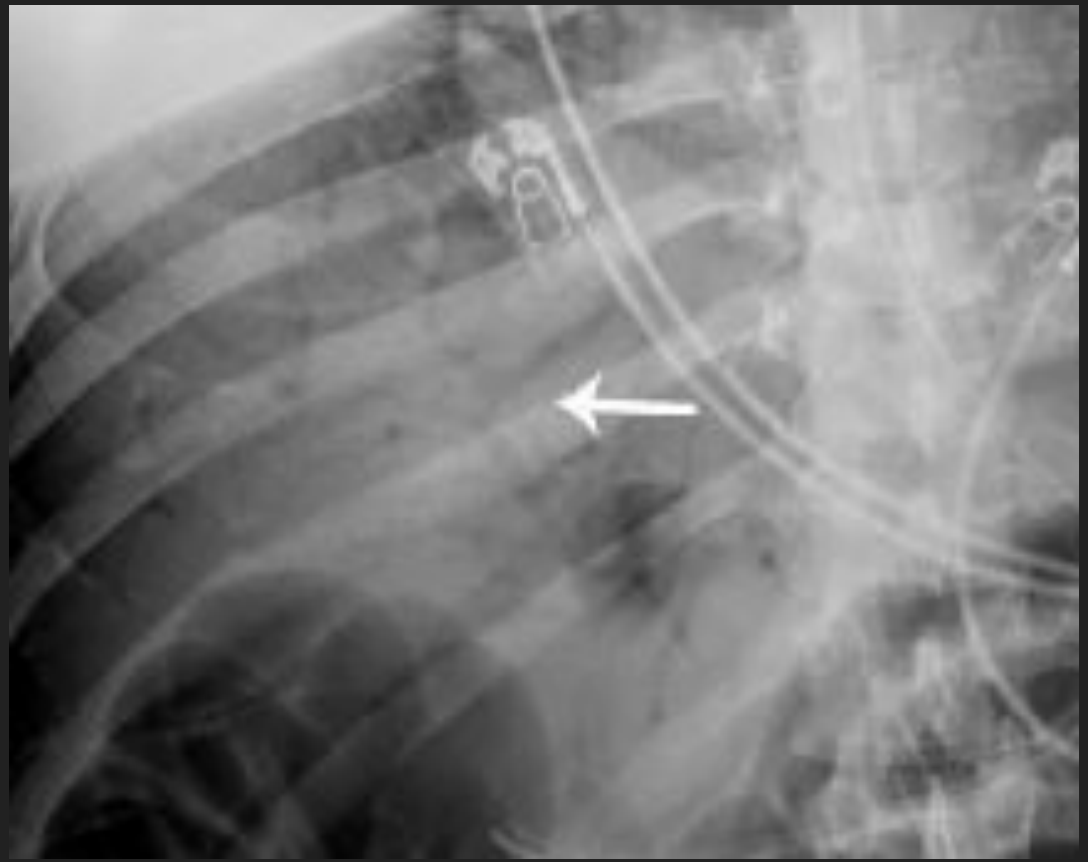
Necrotic bowel had a yellow appearance vs a purple dusky appearance

Pathology revealed ischemia with multifocal necrosis and occasional fibrin thrombi in submucosal arterioles





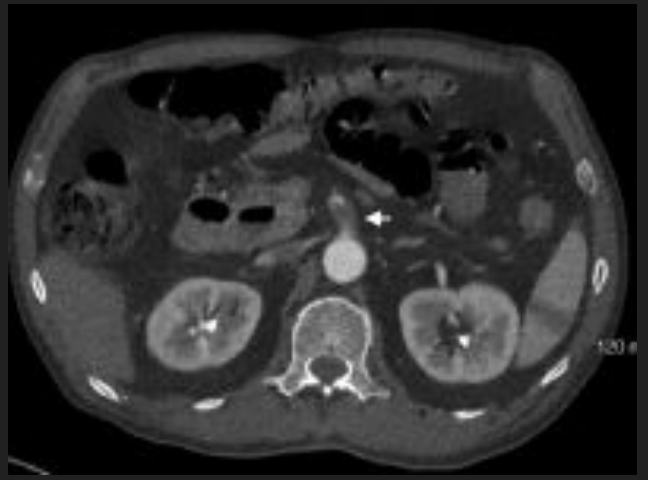


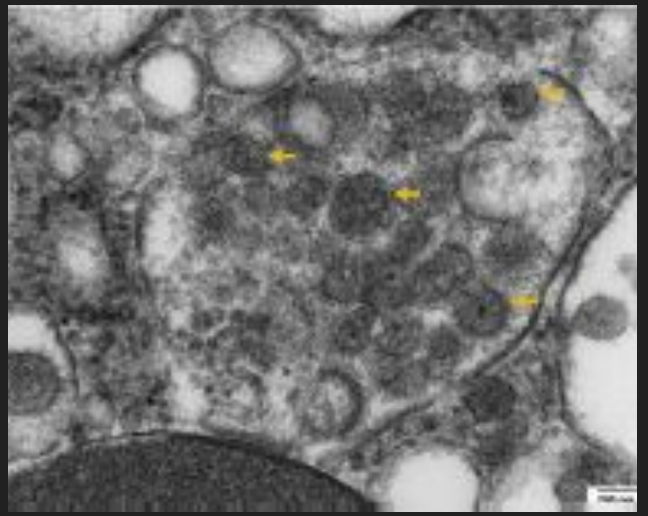


A 69 y/o man with COVID presenting with abdominal pain and constipation

Imaging revealed a thrombus in the proximal segment of the SMA

Electron microscopy revealed viral particles clustered within cisternal spaces in enterocytes



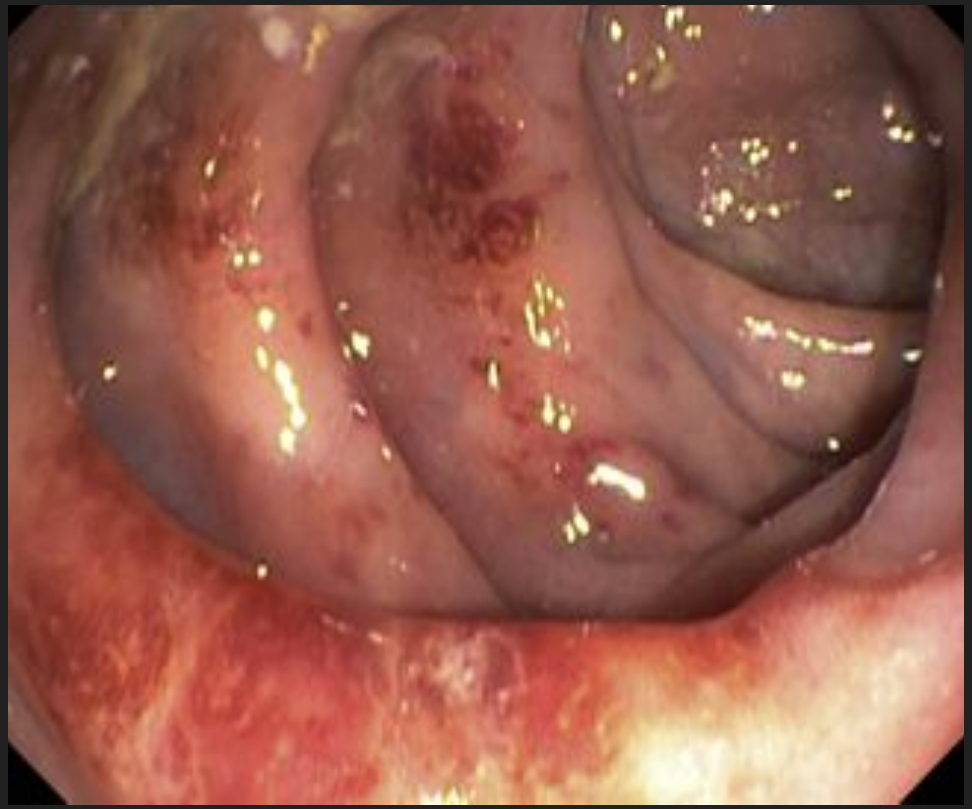


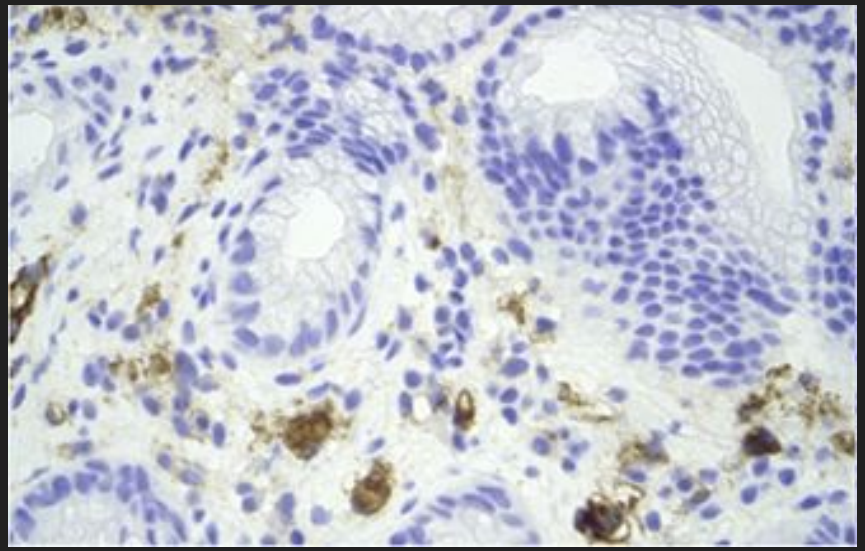
Mitchell, J. Clinical Gastro Hep July 2020

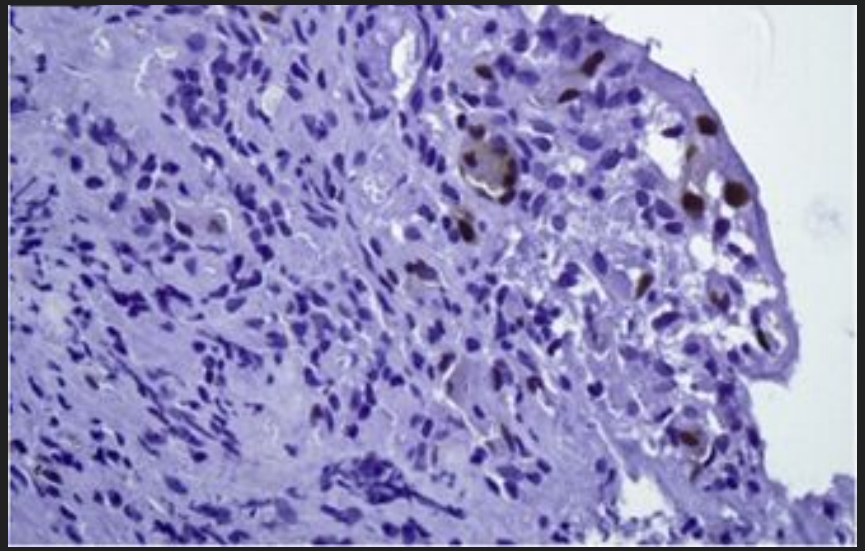
Clinical Gastroenterology and Hepatology 2020;■:■–■

Endoscopic Findings in Patients Infected With 2019 Novel Coronavirus in Lombardy, Italy

Sara Massironi,[*] Chiara Viganò,[*] Lorenzo Dioscoridi,[‡] Elisabetta Filippi,[§,¶¶] Michela Pagliarulo,[‖] Guido Manfredi,[¶] Clara Benedetta Conti,[#] Clementina Signorelli,[**] Alessandro Ettore Redaelli,[‡‡] Giulia Bonato,[‡] Elena Iiritano,[¶] Roberto Frego,[‡‡] Nicola Zucchini,[§§] Marco Ungari,[‖‖] Marianna Pedaci,[¶] Francesca Bono,[§§] Camillo Di Bella,[§§] Elisabetta Buscarini,[¶] Massimiliano Mutignani,[‡] Roberto Penagini,[§] Marco Emilio Dinelli,[‡‡] and Pietro Invernizzi[*]







GI Transmission

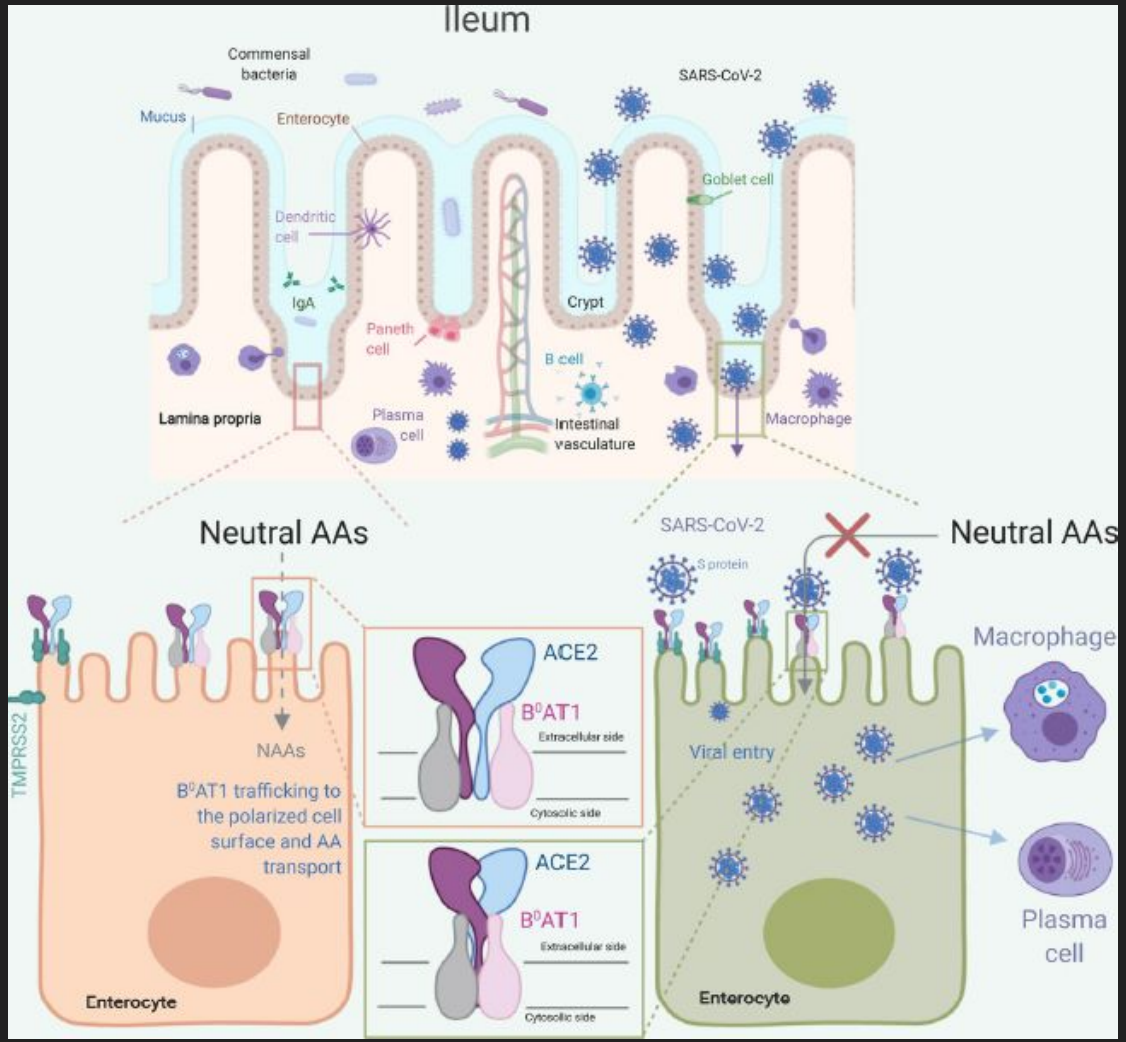
How Does COVID-19 Enter the GI?

In 2003, ACE2 was identified as the receptor for SARS-CoV

Newer reports show SARS-CoV-2 engages ACE2 as entry receptor and employs serine protease TMPRSS2 for cell entry

In humans, ACE2 is expressed in airway, kidney cells, small intestine (mostly ileum, jejunum) and to a lesser extent, the colon

- Ileal ACE2+TMPRSS2+ cells are absorptive enterocytes
- Highest expression of ACE2 in the body is in the brush border of enterocytes


Ileum
Commensal bacteria
Mucus
Enterocyte
SARS-CoV-2
Goblet cell
Dendritic cell
IgA
Crypt
Paneth cell
B cell
Lamina propria
Plasma cell
Intestinal vasculature
Macrophage
Neutral AAs
SARS-CoV-2
S protein
Neutral AAs
Macrophage
ACE2
B0AT1
Extracellular side
Cytosolic side
TMPRSS2
NAAs
B0AT1 trafficking to the polarized cell surface and AA transport
Viral entry
Enterocyte
Enterocyte
Plasma cell

RESEARCH ARTICLE

CORONAVIRUS

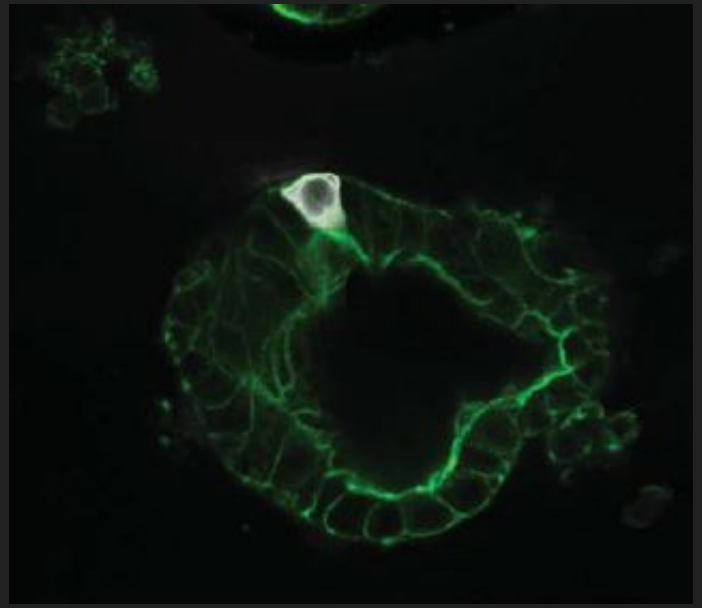
SARS-CoV-2 productively infects human gut enterocytes

Mart M. Lamers[1]*, Joep Beumer[2]*, Jelte van der Vaart[2]*, Kèvin Knoops[3], Jens Puschhof[2], Tim I. Breugem[1], Raimond B. G. Ravelli[3], J. Paul van Schayck[3], Anna Z. Mykytyn[1], Hans Q. Duimel[3], Elly van Donselaar[3], Samra Riesebosch[1], Helma J. H. Kuijpers[3], Debby Schipper[1], Willine J. van de Wetering[3], Miranda de Graaf[1], Marion Koopmans[1], Edwin Cuppen[4,5], Peter J. Peters[3], Bart L. Haagmans[1]†, Hans Clevers[2]†‡

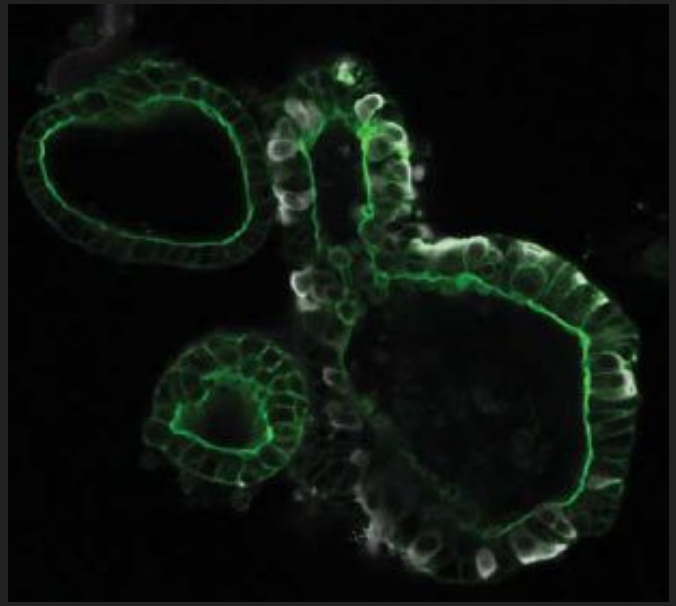
In-vitro study using organoids derived from adult stem cells infected with SARS-CoV-2

Science, 7/2020

SARS-CoV-2 infected-enterocytes

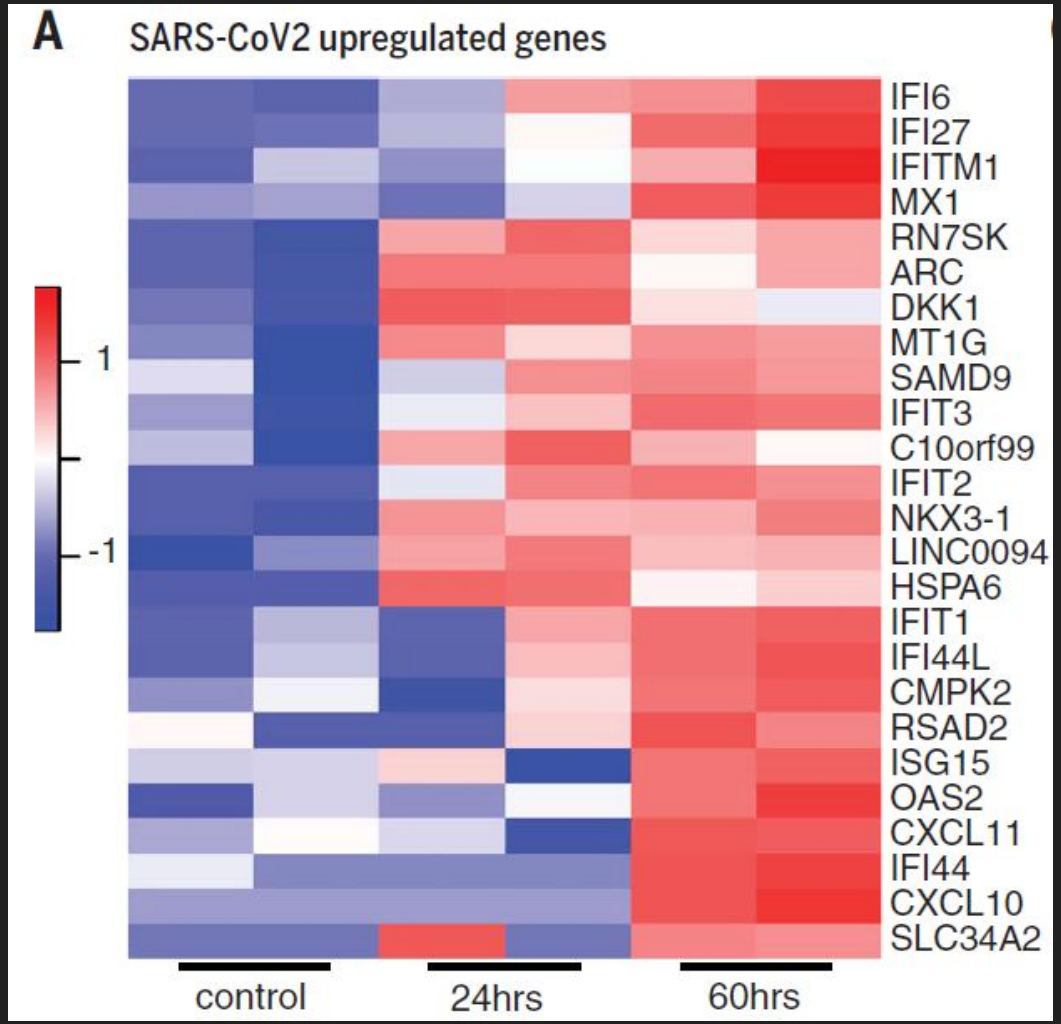


24 hours



60 hours

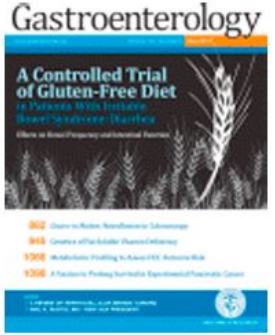
- Gene expression changes induced by CoV-1 and CoV-2
- Infection elicited a broad signature of cytokine- and interferon-stimulated genes
- Upregulation also is seen in other GI viral infections



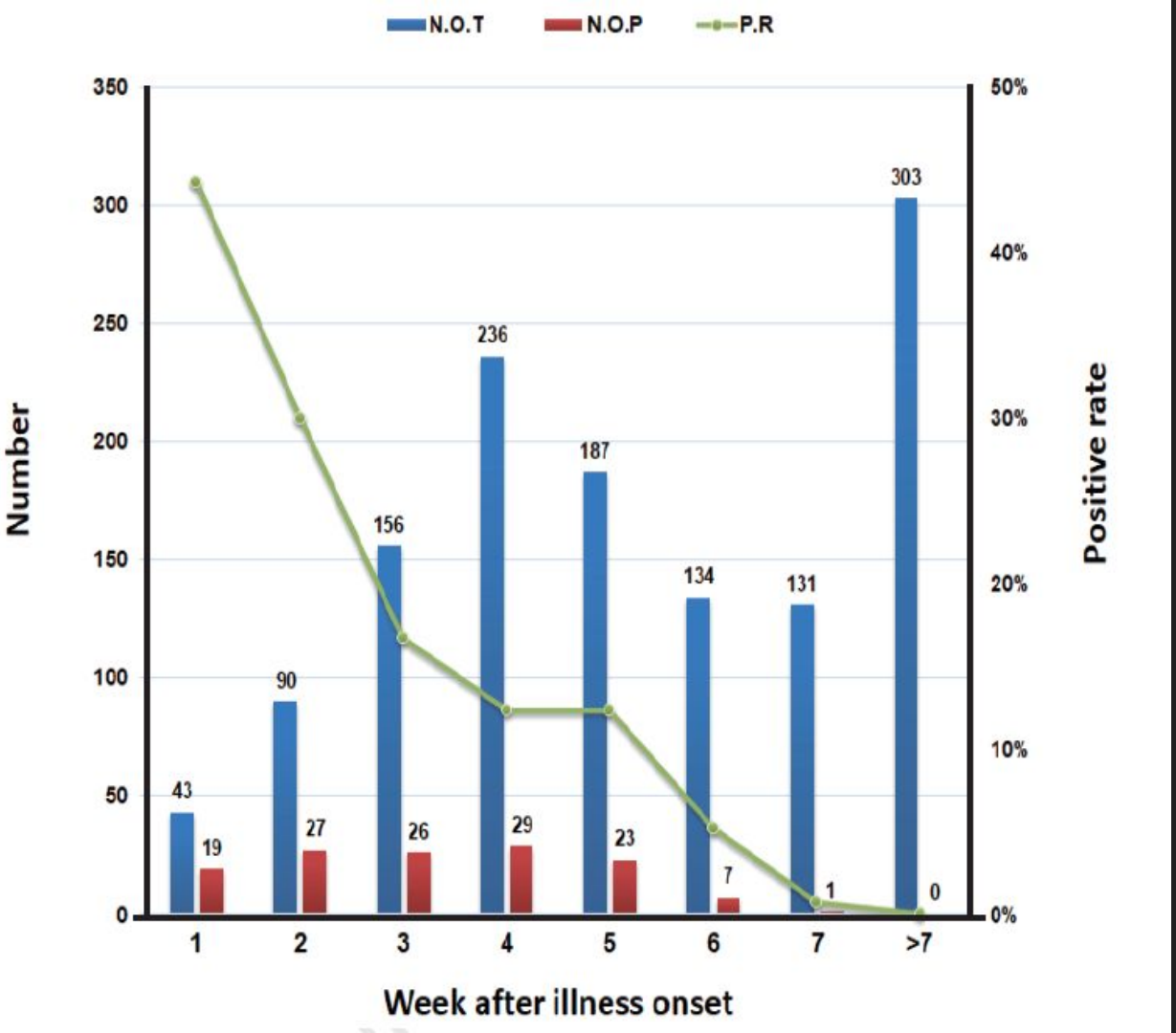
Journal Pre-proof

The Time Sequences of Oral and Fecal Viral Shedding of Coronavirus Disease 2019 (COVID-19) Patients

Fang Zhao, Yang Yang, Zhaoqin Wang, Liang Li, Lei Liu, Yingxia Liu



Retrospective review evaluating 401 patients with COVID-19 in fecal and respiratory swabs for more than 7 weeks


N.O.T
N.O.P
P.R
Number
Positive rate
Week after illness onset
350
300
250
200
150
100
50
0
50%
40%
30%
20%
10%
0%
43
19
90
27
156
26
236
29
187
23
134
7
131
1
303
0
1
2
3
4
5
6
7
>7

RESEARCH ARTICLE

JOURNAL OF MEDICAL VIROLOGY WILEY

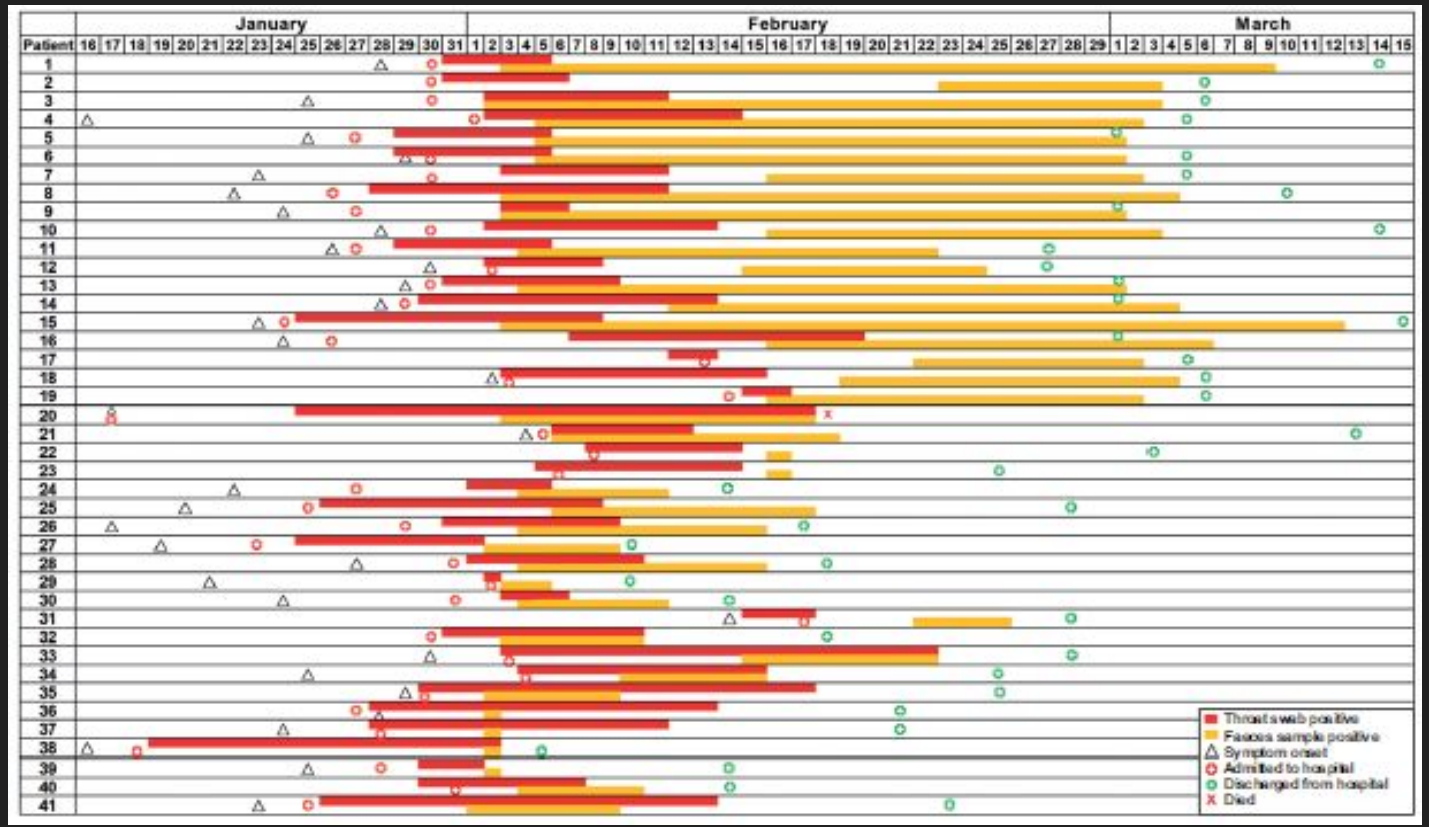
The presence of SARS-CoV-2 RNA in the feces of COVID-19 patients

Yifei Chen MD[1] | Liangjun Chen MD[2] | Qiaoling Deng MD[2] | Guqin Zhang MD[1] | Kaisong Wu MD[1] | Lan Ni MD[1] | Yibin Yang MD[1] | Bing Liu MD[1] | Wei Wang MD[1] | Chaojie Wei MD[1] | Jiong Yang MD[1] | Guangming Ye MD[2] | Zhenshun Cheng MD[1]

Retrospective review of 42 COVID-positive patients

- 20% GI symptoms
- 66% + stool RNA
- 65% remained + in stool after pharyngeal swab neg
- Pharyngeal swab + 6.5 days after SO and + 11 days in feces after SO

Lancet. Brief Correspondence (March 2020)

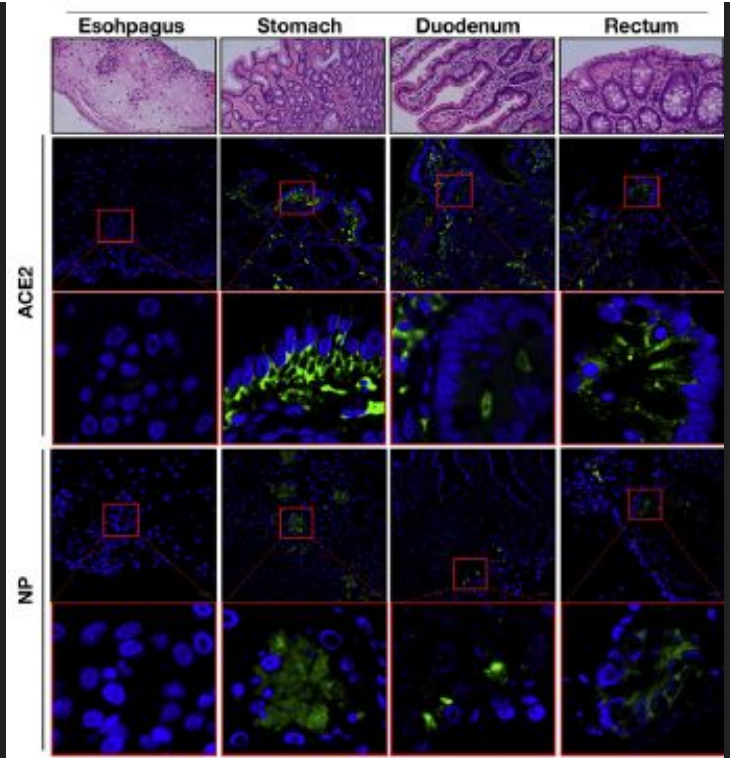


Gastroenterology 2020;158:1831–1833

BRIEF COMMUNICATIONS

Evidence for Gastrointestinal Infection of SARS-CoV-2

Fei Xiao,[1,2,3,*] Meiwen Tang,[4,*] Xiaobin Zheng,[5,*] Ye Liu,[6] Xiaofeng Li,[7] and Hong Shan[2,3,8]



Infectious SARS-CoV-2 in Feces of Patient with Severe COVID-19

Fei Xiao,[1] Jing Sun,[1] Yonghao Xu,[1] Fang Li,[1] Xiaofang Huang,[1] Heying Li, Jingxian Zhao, Jicheng Huang, Jincun Zhao

Author affiliations: Sun Yat-sen University, Zhuhai, China (F. Xiao); Guangzhou Medical University, Guangzhou, China (J. Sun, Y. Xu, F. Li, X. Huang, Jingxian Zhao, Jincun Zhao); Chinese Academy of Sciences, Guangzhou (H. Li); Guangzhou Customs District Technology Center, Guangzhou (J. Huang)

Emerging Infectious Disease - August

- Collected fecal samples from COVID + patients
- Found viral particles in stool up to 28 days after symptom onset
- Isolated the virus and infected fresh Vero E6 cells
- Transmission is possible through aerosolized feces

ORIGINAL ARTICLE

Evidence of Airborne Transmission of the Severe Acute Respiratory Syndrome Virus

Ignatius T.S. Yu, M.B., B.S., M.P.H., Yuguo Li, Ph.D., Tze Wai Wong, M.B., B.S., Wilson Tam, M.Phil., Andy T. Chan, Ph.D., Joseph H.W. Lee, Ph.D., Dennis Y.C. Leung, Ph.D., and Tommy Ho, B.Sc.

Amoy Gardens, Hong Kong

- Design of bathroom floor drains lacked a replenishment system to keep water traps filled, leading virus laden aerosols to seep into bathrooms

H_2 Receptor Antagonists

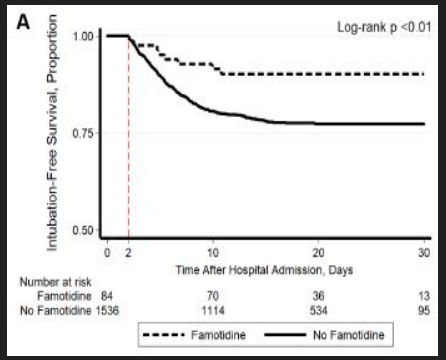
Famotidine Use Is Associated With Improved Clinical Outcomes in Hospitalized COVID-19 Patients: A Propensity Score Matched Retrospective Cohort Study

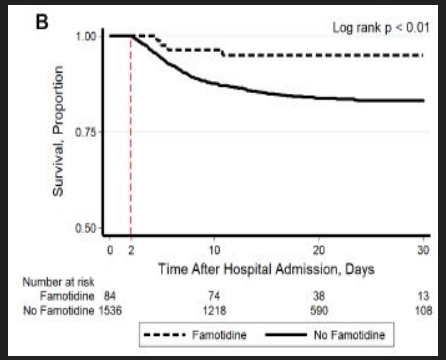
Daniel E. Freedberg,[1] Joseph Conigliaro,[2,3] Timothy C. Wang,[1] Kevin J. Tracey, MD,[4] Michael V. Callahan,[5,6] and Julian A. Abrams,[1] on behalf of the Famotidine Research Group

Intro: computer models, famotidine may inhibit a protease which is needed for viral replication

Study: 1620 patients with COVID-19

- 84 took famotidine (20-40 mgs) within 24 hours of admission
- Primary outcome was death or intubation 2-30 days





HR = 0.43 for Intubation or death

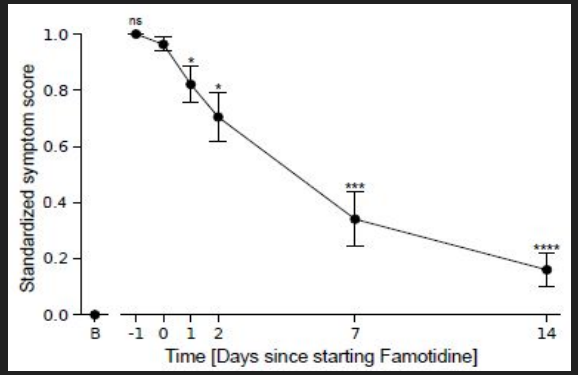
Gastroenterology May 2020

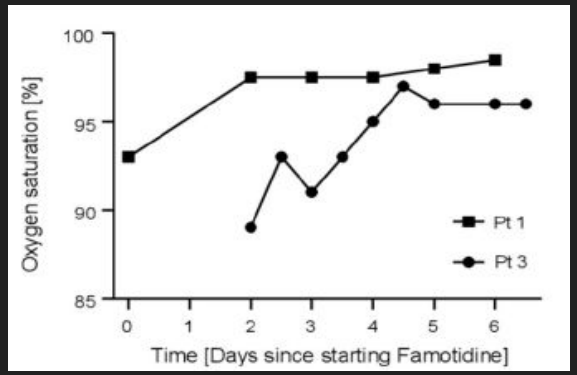
Famotidine use and quantitative symptom tracking for COVID-19 in non-hospitalised patients: a case series

Tobias Janowitz [1,2], Eva Gablenz,[1,3] David Pattinson,[4] Timothy C Wang,[5] Joseph Conigliaro,[6,7] Kevin Tracey,[7] David Tuveson [1]

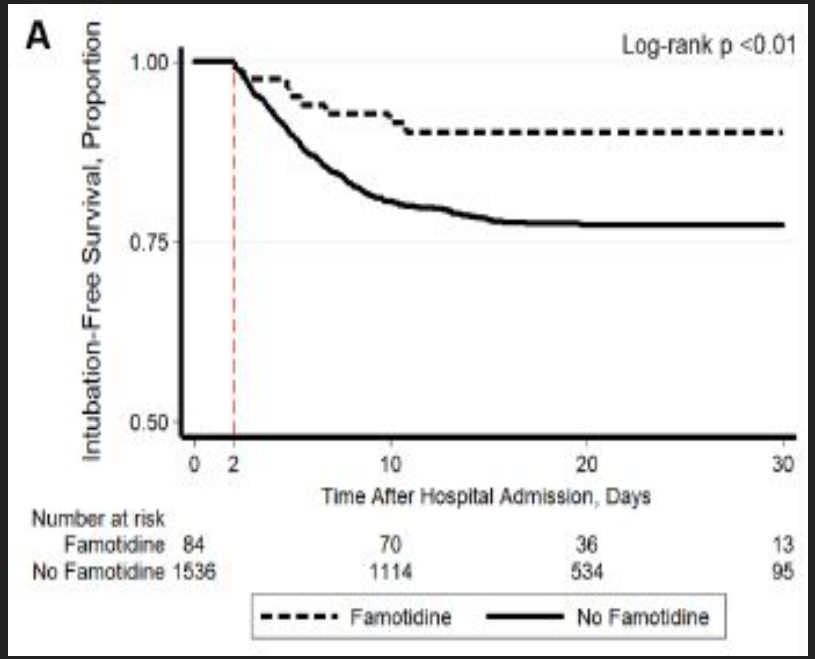
10 patients

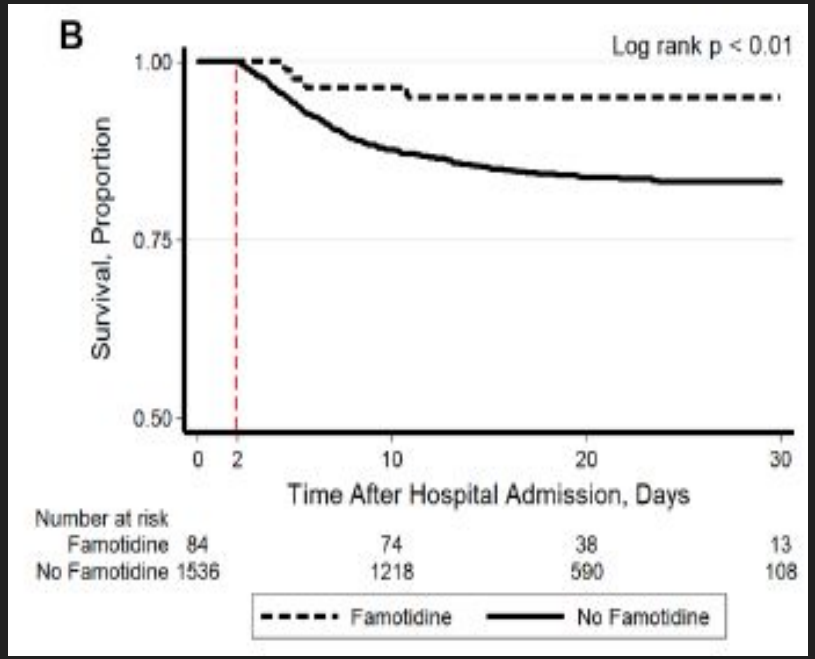
- NYS, NJ, Sweden
- High dose famotidine (80 mg TID)
- Most symptoms improved within 24 to 48 hours





Gut 6/2020





Hazard Ratio of 0.43 Intubation or death

Impact of Famotidine Use on Clinical Outcomes of Hospitalized COVID-19 Patients

Retrospective study of 878 patients, 83 (9.5%) of whom received famotidine

- Similar demographics, except famotidine pts younger by 5 years
- Only 30% were taking famotidine prior to hospitalization
- Mostly administered orally, 20mg daily
- Primary outcome: In-hospital death and intubation

Mathers, J, Seip, Richard. Am J Gastro 2020

Impact of Famotidine Use on Clinical Outcomes of Hospitalized COVID-19 Patients

	In Hospital Death	In Hospital Intubation	Death/intubation
Famotidine	14.5%	21.7%	7.2%
Non-famotidine	26%	32%	13.8%

Significant reduction in risk of in-hospital mortality OR 0.366

Impact of Famotidine Use on Clinical Outcomes of Hospitalized COVID-19 Patients

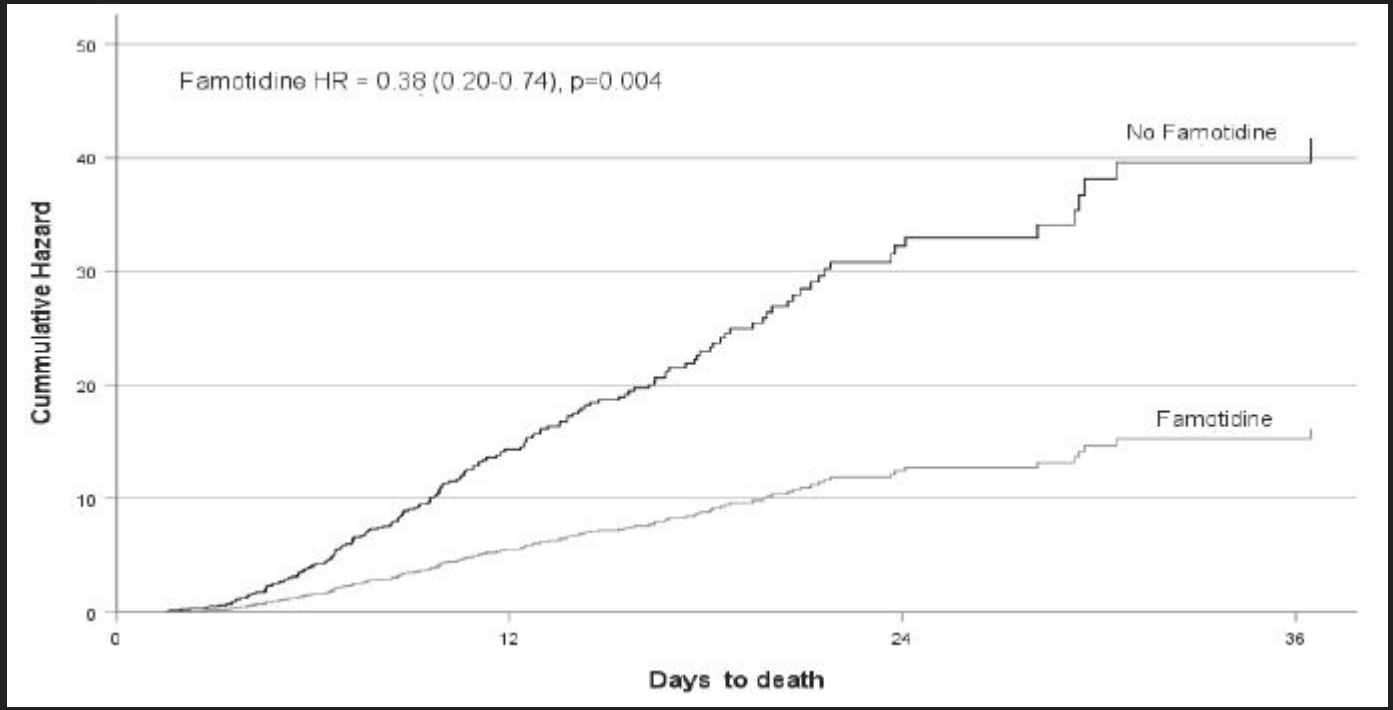


Table 3. Laboratory Findings: All Patients and In Subpopulations with and Without Famotidine

Laboratory Values, median (IQR)					
	Reference Range	**All Patients (n=772)**	**No Famotidine (n=689)**	**Famotidine (n=83)**	**p value[a]**
Hematologic					
WBC, x 109/L[b]	3.5 - 9.5	11.30(7.60-17.20)	11.30(7.60-17.40)	10.80(6.80-16.00)	0.424
Lymphocytes, x 109/L[c]	1.50 - 4.50	0.60(0.40-0.94)	0.60(0.40-0.93)	0.66(0.37-1.09)	0.666
NLR, x 109/L[b]	0.78 - 3.53	9.30(5.07-16.96)	9.43(5.05-17.25)	8.11(5.48-14.86)	0.403
Monocytes, x 109/L[c]	0.2 - 1.50	0.28(0.17-0.46)	0.29(0.18-0.46)	0.27(0.15-0.43)	0.401
Platelets, x 109/L[c]	150 - 400	164.00(119.00-212.00)	167.00(119.00-212.00)	148.00(107.00-201.00)	0.093
Eosinophils, x 109/L[b]	0 - 0.7	0.07(0.01-0.19)	0.08(0.01-0.19)	0.07(0.01-0.20)	0.273
Biochemical					
AST, U/L[b]	10 - 40	55.00(36.00-8100)	56.00(36.00-81.00)	48.00(35.00-77.00)	0.203
ALT, U/L[b]	10 - 40	38.00(21.00-71.00)	39.00(21.00-71.00)	36.00(22.00-71.00)	0.732
BUN, mg/dL[c]	20-Aug	15.00(11.00-26.00)	15.00(11.00-27.00)	14.00(11.00-19.00)	0.073
Albumin, g/dL[c]	3.5 - 5.5	2.80(2.30-3.20)	2.80(2.30-3.20)	3.00(2.50-3.40)	0.028
Infection related indices					
hsCRP, mg/L[b]	0.0 - 3.0	12.31(6.48-20.74)	12.83(6.77-21.22)	9.41(4.82-14.08)	0.002
ESR, mm/h[b]	0 -15	65.00(41.00-88.00)	67.00(41.50-88.00)	57.50(35.00-84.00)	0.19
Serum ferritin, ng/mL[b]	11 - 336	940.00(426.00-1,929.00)	964.00(452.00-1,947.00)	797.50(343.00-1,345.50)	0.076
Procalcitonin, ng/ml[b]	0.10 - 0.49	0.29(0.12-1.00)	0.30(0.13-1.06)	0.16(0.08-0.45)	0.004

Abbreviations: WBC, white blood cell count; NLR, neutrophil-to-lymphocyte ratio; AST, aspartate aminotransferase; ALT, alanine aminotransferase; BUN, blood urea nitrogen; hsCRP, high-sensitivity C-reactive protein; ESR, erythrocyte sedimentation rate

[a] Mann-Whitney U test.
[b] Maximum value used.
[C] Minimum value used.

COVID-19: Famotidine, Histamine, Mast Cells and Mechanisms

Mechanism for famotidine is on-target histamine receptor H_2 activity

Clinical COVID-19 involves dysfunctional mast cell activation

Famotidine does NOT bind papain-like protease or 3 chymotrypsin-like protease

In Vero E6 cells, famotidine showed no antiviral activity (while remdesivir and HCQ did)

Famotidine binds with much more affinity to H_2 receptor than cimetidine

Malone, R *Drug Discovery, Design, & Development 2020*

Mast cell deregulation releasing histamine, bradykinin, etc, impacting cellular and basement membrane function and tight junction integrity causing edema

Inference: COVID–19 is at least partially mediated by pathologic histamine release

Famotidine binds with much more affinity to H_2 receptor than cimetidine

PPI and COVID

PPIs are associated with ⬆ risk of enteric infections and SIBO

Online phone survey described as “national health survey”

6.4% + COVID rate

If taking PPI, OR 2.15 for daily use and 3.67 for BID use

No increase in risk with H_2 blocker

Almario, C, Chey, W, Spiegel B. *Am J Gastro* 2020

Corticosteroids, But Not TNF Antagonists, Are Associated With Adverse COVID-19 Outcomes in Patients With Inflammatory Bowel Diseases: Results From an International Registry

Erica J. Brenner,[1,*] **Ryan C. Ungaro**,[2,*] Richard B. Gearry,[3] Gilaad G. Kaplan,[4] Michele Kissous-Hunt,[5] James D. Lewis,[6] Siew C. Ng,[7] Jean-Francois Rahier,[8] Walter Reinisch,[9] Frank M. Ruemmele,[10] Flavio Steinwurz,[11] Fox E. Underwood,[4] Xian Zhang,[12] Jean-Frederic Colombel,[2] and Michael D. Kappelman[1]

IBD registry looking at the impact of COVID-19 on 525 patients with IBD

- 31% required hospitalizations
- 7% met the primary outcome - (ICU/ventilator/death)
- 3% fatality rate
- Risk factors included increased age, 2 or more comorbidities, corticosteroids and 5-ASA
- Anti-TNFs were NOT associated with severe COVID infections

Gastroenterology, 2020

CLINICAL PRACTICE UPDATES

AGA Clinical Practice Update on Management of Inflammatory Bowel Disease During the COVID-19 Pandemic: Expert Commentary

David T. Rubin,[1] Joseph D. Feuerstein,[2] Andrew Y. Wang,[3] and Russell D. Cohen[1]

Patients with IBD are not at increased risk

Patients who DO NOT have the infection should continue their medications

If the patient has a known infection w/o symptoms, hold thiopurines, methotrexate and tofacitinib and delay biologics by 2 weeks

If symptomatic, hold medications until symptoms resolution or negative testing

Gastroenterology 7/2020

Conclusions

With any GI symptoms, you must always think of COVID-19

Consider imaging when patients present with abdominal discomfort or unexplained sepsis

Very likely that fecal shedding can be infectious

Famotidine appears to be an effective treatment and prospective trials are on the way

Consider changing PPIs to H_2 blockers in your outpatients

Questions?


Thank You for
Attending the
Annual Dinner and
Business Meeting
6

Einstein Montefiore | Center for Continuing Professional Development

YOU HAVE 48 HOURS TO REGISTER AND COMPLETE EVALUATION FORM FOR THIS ACTIVITY

PASSCODE for this RSS Activity Event is:

15VACS

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Physians: Albert Einstein College of Medicine-Montefiore Medical Center designates this live activity for a maximum of 1.0 *AMA PRA Category 1 Credits*™. Physicians should claim only credit commensurate with the extent of their participation in the activity.

This activity was planned by and for the healthcare team, and learners will receive 1 credits Interprofessional Continuing Education (IPCE) credit for learning and change.