Building Bridges in IBD

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Abstracts
Poster Abstracts
Symposium 216

BUILDING BRIDGES IN IBD

Brussels, Belgium
September 13 – 14, 2019

Scientific Organization:
S. Vermeire, Leuven (Belgium)

Scientific Co-Organization:
I. Dotan, Petah Tikva (Israel)
M. Ferrante, Leuven (Belgium)
E. Louis, Liège (Belgium)
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CONTENTS

Session I

Building bridges with other disciplines: Most important tips for interdisciplinary decision making

Chair:
I. Dotan, Petah Tikva
S. Vermeire, Leuven

The gastro-surgical tandem:
A stepwise protocol for joint patient care (no abstract)
M. Ferrante, A. D’Hoore, Leuven

The gastro-rheumatology tandem:
The therapeutic approach to IBD patients with rheumatologic manifestations
G.J. Mantzaris, D. Vassilopoulos, Athens

The gastro-dermatology tandem:
Addressing the most frequent questions
A. Van Laethem, Leuven; H. Yanai, Petah Tikva

The gastro-gynecology tandem:
IBD and pregnancy: A two pipe problem – A multidisciplinary joint venture
A. Shitrit, S. Grisaru-Granovsky, Jerusalem

Session II

The multidisciplinary team from A to Z:
Building bridges with non-medical disciplines

Chair:
D. Schwartz, Be’er Sheva
P. Van Hootegem, Brugge

Patient-centered care & EHealth: How to take PROs into account (no abstract)
P. Munkholm, Frederikssund

Work with your nutritionist!
J.D. Lewis, Philadelphia; T. Pfeffer Gik, Petah Tikva
Management of high output ileostomy (no abstract)
S. Gabe, London

Psycho-socio-economic aspects in IBD: Facts and possible interventions
Y. Inspector, London

Session III

Building bridges in Europe

Chair:
F. Baert, Roeselare
G.J. Mantzaris, Athens

Importance of registries, population-based and other interesting cohorts to unravel causes of IBD
J.-F. Colombel, M. Agrawal, New York

Telemedicine: The way forward to unite patients in Europe?
M.J. Pierik, Maastricht

The role of EFCCA and national patient associations in promoting IBD care
L. Avedano, Brussels

Value for money, affordability and willingness to pay for innovative interventions in IBD (no abstract)
D. Greenberg, Be’er Sheva

Session IV

Building bridges between the lab and the clinic: Translational IBD care

Chair:
E. Louis, Liège
D. McGovern, Los Angeles

Biomarkers at diagnosis: What is absolutely needed for diagnosis and prognosis in 2019?
S. Vermeire, Leuven

The best way to monitor your patient: Fecal calprotectin or immune cell characterization? (no abstract)
M. Allez, Paris
Predicting response to drugs in 2020
Y. Chowers, Haifa

State-of-the-Art Lecture:
Will understanding of fibrosis help to treat Crohn's disease?
F. Rieder, Cleveland

Session V

Building therapeutic bridges

Chair:
Y. Chowers, Haifa
B. Siegmund, Berlin

Do patients need the same treatment over the course of their disease? (no abstract)
K. Gecse, Amsterdam

Moderate to severe ulcerative colitis: The next step after 5-ASA and steroids is...?
P.L. Lakatos, Montreal

Mild ileal Crohn's disease: Do nothing or prescribe biologicals?
B. Siegmund, Berlin

Combination of biological therapy: Dream or reality?
E. Louis, Liège

BIO-MDT: The future of IBD patient care
I. Dotan, Petah Tikva

Session VI

Let's visualize!

Chair:
P. Dewint, Gent
K. Gecse, Amsterdam

Poster Award Presentation
I. Dotan, Petah Tikva; S. Vermeire, Leuven

New opportunities for intestinal ultrasound
K. Novak, Calgary
Capsule endoscopy – The best tool for diagnosis and follow-up of patients with Crohn’s disease
A. Bourreille, Nantes  

New techniques for endoscopic surveillance in UC: From chromoendoscopy to image acquisition?
H. Neumann, Mainz  

State-of-the-Art Lecture:
Reengineering the microbiome in prevention and therapy of IBD
J. Braun, Los Angeles  

List of Chairpersons, Speakers and Scientific Organizers  

50 51 52 53 – 56
1. The impact of anti-TNF therapy on intestinal mucosal gene expression of molecules involved in inflammatory response and autoimmunity in patients with inflammatory bowel disease
   N. Andreou, G. Michalopoulos, M. Gazouli (Athens, Piraeus, GR)

2.* Microscopic ileitis in clinically suspected inflammatory bowel disease patients – Can it predict the future?
   F. Abu Baker, S. Nafrin, A. Mari, M. Suki, B. Ovadia, A. Bishara, O. Gal, Y. Kopelman (Hadera, Nazarith, IL)

3. Ulcerative colitis in association with diverticular disease of the colon: Case report
   A. Antonenko, M. Gschwantler, M. Ouhadi (Kiev, UA; Vienna, AT)

4.* Organoids derived of inflammatory intestinal biopsies in ulcerative colitis patients lose their inflammatory transcriptional signature during ex vivo culture
   K. Arnauts (Leuven, BE)

5. Investigation of anaemic syndrome in inflammatory bowel diseases
   D. Badea, A. Genunche-Dumitrescu, M. Badea, S. Mitran, G. Tartea, A. Badea (Craiova, RO)

6. Essential thrombocythemia or thrombocytosis secondary to inflammatory bowel disease? (case study)
   M. Badea, D. Badea, A. Genunche-Dumitrescu, G. Tartea, A. Badea (Craiova, RO)

7. An old man with Crohn's disease presented by subileus clinic and diagnosed by double balloon enteroscopy
   M. Basaranoglu, M. Kapsigay (Istanbul, TR)

8. Patients with Crohn's disease had an increased NET development on long-term follow-up
   M. Basaranoglu (Istanbul, TR)

9. Testing the availability of fecal calprotectin (instead of colonoscopy) in the remission/activation evaluation in patients with inflammatory bowel diseases at an outpatient IBD clinic
   M. Basaranoglu (Istanbul, TR)

10. Ascites in a young woman: A rare presentation of eosinophilic gastroenteritis
    E. Belhadj Mabrouk, M. Ayari, Y. Zaimi, S. Ayadi, L. Mouelhi, R. Dabbèche (Tunis, TN)

11. Predictive factors for extraintestinal manifestations associated with Crohn's disease
    A. Benkhemmar, O. Daboussi, M. Luwawu, A. Herber (Le Coudray, FR)
12.* Inflammatory stricturing Crohn’s diseases: Results of medical treatment
(Tunis, TN)

13. First onset of colitis after Helicobacter pylori eradication therapy
P. Cacic, M. Živković, M. Nikolić, I. Budićmir, N. Ljubičić, D. Hrabar (Zagreb, HR)

14. The predictive role of gut microbiota in treatment response to vedolizumab and
ustekinumab in inflammatory bowel disease
C. Caenepeel, S. Vieira-Silva, J. Vázquez-Castellanos, B. Verstockt,
M. Ferrante, J. Raes, S. Vermeire (Leuven, BE)

15. Hematological scales in ulcerative colitis patients treated with infliximab –
A single-centre experience
H. Cichoż-Lach, A. Michalak, K. Laskowska, P. Radwan,
B. Kasztelan-Szczerbińska (Lublin, PL)

16. Is red blood cell distribution width an essential parameter in Crohn’s disease
patients? A single-centre observation
H. Cichoż-Lach, A. Michalak, K. Laskowska, P. Radwan,
B. Kasztelan-Szczerbińska (Lublin, PL)

17. Compliance to vaccination guidelines in patients with immune-mediated
inflammatory diseases: A single-center, cross-sectional study
S. Coenen, D. Bertrand, T. Vanhoutvin, P. Verschueren, P. De Haes,
P. De Munter, S. Vermeire, M. Ferrante (Leuven, BE)

18. Biological therapy increases NCR+ ILC3 levels in IBD patients
B. Creyns, B. Verstockt, J. Cremer, M. Ferrante, S. Vermeire, J. Ceuppens,
G. Van Assche, C. Breynaert (Leuven, BE)

19. Predictive factors for an aggressive clinical course in ulcerative colitis
O. Daboussi, M. Luwawu, A. Herber (Le Coudray, FR)

20. Inflammatory bowel diseases patient profiles are related to specific information
needs – A nationwide survey
S. Daher, T. Khoury, A. Benson, J. Walker, O. Hammerman, R. Kedem,
T. Naftali, R. Eliakim, O. Ben-Bassat, C. Bernstein, E. Israeli
(Jerusalem, Nahariya, Ramat Gan, Kfar Saba, Petah Tikva, IL; Winnipeg, CA)

21. Evaluation of cardiac and pulmonary manifestation in patients with Crohn’s
disease
I. Deliu, O. Diaconu, N. Deliu, A. Genuanche, D. Neagoe (Bals, Craiova, RO)

22. Sacroiliitis an “undiagnosed” extraintestinal manifestation in patients with
inflammatory bowel disease
I. Deliu, N. Deliu, O. Diaconu, A. Genuanche, D. Neagoe (Bals, Craiova, RO)
23. Diagnosis of complications in intestinal inflammatory diseases
   O. Diaconu, I. Diaconu, A. Genunche-Dumitrescu, D. Neagoe, I. Deliu
   (Craiova, Bals, RO)

24. The role of blood and fecal markers in intestinal inflammatory diseases
   O. Diaconu, I. Diaconu, I. Deliu, A. Genunche-Dumitrescu, D. Neagoe
   (Craiova, Bals, RO)

25. Treatment of Crohn’s disease depending to localization and clinical forms
   O. Diaconu, I. Diaconu, I. Deliu, A. Genunche-Dumitrescu, D. Neagoe
   (Craiova, Bals, RO)

26. The changing face of IBD epidemiology
   H. Dix, L. Walla, J. Fyall, M. Ross, S. Walsh, J. Todd, M. Groome, J. Paterson,
   C. Mowat (Dundee, GB)

27. Gene expression profiling study: TLR9-IL23-IL17 axis in inflammatory bowel
   disease development
   S. Dragasevic, B. Stankovic, A. Milutinovic Sokic, T. Milovanovic, S. Lukic,
   T. Milosavljevic, M. Lalosevic Stojkovic, S. Drazilov Srzentic, K. Klaassen,
   N. Kotur, S. Pavlovic, D. Popovic (Belgrade, RS)

28. Cyclospora cayetanensis parasite infection with Crohn's disease-like symptoms
    (case report)
    L. Erne (Liepāja, LV)

29. The modulation of the gut microbiota as a factor in improvement of the efficacy
    of combined therapy with oral mesalazine and budesonide in patients with
    moderate ulcerative colitis
    A. Genunche-Dumitrescu, D. Badea, M. Badea, P. Mitrut, C. Deliu, O. Diaconu
    (Craiova, Bals, RO)

30. The relationship between bone mineral density, disease activity and remission
    maintenance therapy in inflammatory bowel disease with rheumatic
    manifestation
    A. Genunche-Dumitrescu, D. Badea, M. Badea, D. Neagoe, O. Diaconu,
    C. Deliu, A. Badea (Craiova, Bals, RO)

31. IBD and malignancy as treatment dilemma – Case report
    (Banjaluka, BA)

32. Thromboembolic events among patients with inflammatory bowel disease
    C. Gorincioi, R. Nemteanu, A. Clim, A. Plesa, B. Mazilu, C. Sfrijan (Iasi, RO)

33. Deficits in health-literacy of inpatients – A cross-sectional study
    F. Gundling, P. Parasiris, T. Mühling (Munich, Würzburg, DE)
34. Are severe endoscopic lesions in steroid-refractory ulcerative colitis associated to the response to cyclosporine therapy?
   A. Hammami, A. Ben Slama, N. Elleuch, H. Jaziri, A. Braham, S. Ajmi,
   M. Ksiaa, A. Jmaa (Riadh City, Sahloul, TN)

35. Long-term efficacy and safety of azathioprine maintenance therapy in Crohn’s disease
   A. Hammami, M. Moalla, A. Ben Slama, N. Elleuch, A. Braham, S. Ajmi,
   M. Ksiaa, A. Jmaa (Riadh City, Sahloul, TN)

36. Radiation exposure in patients with Crohn’s disease: Separating fact from fantasy
   A. Hammami, N. Elleuch, A. Ben Slama, H. Jaziri, A. Braham, S. Ajmi,
   M. Ksiaa, A. Jmaa (Riadh City, Sahloul, TN)

37. High incidence of hyperglycaemia in steroid-treated hospitalised inflammatory bowel disease (IBD) patients and its risk factors identified by machine learning methods
   R. Harris, M. McDonnell, T. Mills, L. Downey, S. Dharmasiri, R. Felwick,
   F. Borca, H. Phan, J. Cummings, M. Gwiggner (Southampton, GB)

38. Inflammatory bowel disease: A side effect of anti-IL-17A inhibitor (secukinumab)
   P. Hodges, J. Saunders, R. Sengupta, W. Tillet, D. Walker (Bath, GB)

39. Combined intestinal diseases in patient with chromosome disorder
   D. Janelidze (Kiev, UA)

40. The association of diabetes mellitus with inflammatory bowel disease in a tertiary referral center
   M. Jurcau, M. Mihai, O. Petrea, C. Muzica, G. Frunzuc, S. Zenovia, A. Trifan
   (Iasi, RO)

41. Biologic treatment persistence in Greek patients with IBD: 15-year real-life data from a single center
   C. Kapizioni, P. Kourkoulis, G. Koutoufaris, P. Giannelis, A. Mellos, K. Milioni,
   K. Makris, G. Michalopoulos, S. Vrakas, V. Xourgias (Athens, GR)

42. A fistula between sigmoid colon and left colonic vein as a symptom of Crohn’s disease
   M. Karin, E. Babić, M. Volarić (Mostar, BA)

43.* Granulocyte-monocyte apheresis in the treatment of ulcerative colitis (GRACULA) interim analysis of a sham-controlled study
   C. Kölbl, M. Lehmann, S. Weber, R. Schmid, W. Huber (Grafing, Munich, DE)
44.* Long-term outcomes of paediatric patients admitted with acute severe colitis – A multicenter study from the paediatric IBD Porto Group of ESPGHAN

45. Molecular changes in the non-inflamed terminal ileum in patients with ulcerative colitis

46. Serological markers associated with development of pouchitis after ileal pouch-anal anastomosis

47. Hematological indices as potential markers in the monitoring of patients with Crohn's disease
A. Michalak, H. Cichoż-Lach, K. Laskowska, P. Radwan (Lublin, PL)

48. Red blood cell distribution width and its derivatives in ulcerative colitis patients treated with infliximab
A. Michalak, H. Cichoż-Lach, K. Laskowska, P. Radwan, B. Kasztelan-Szczerbińska (Lublin, PL)

49. Hepatic steatosis and cholesterol levels in patients with inflammatory bowel disease in a tertiary referral center
M. Mihai, M. Jurcau, O. Petrea, C. Sfarti, A. Trifan (Iasi, RO)

50. South Asian ethnicity drives differences in microbial and metabolic profiling in a newly diagnosed ulcerative colitis cohort
R. Misra (Hendon, GB)

51.* Pregnancy outcomes in inflammatory bowel disease patients treated with vedolizumab, anti-TNF or conventional therapy: Results of the European CONCEIVE study
A. Moens (Leuven, BE)

52. Intestinal microbiota metabolic activity in inflammatory bowel diseases in children
N. Narinskaya (Moscow, RU)
53. A retrospective study on risk factors for infections in adult patients with inflammatory bowel disease
R. Nemteanu, A. Clim, C. Gorincioi, B. Mazilu, A. Plesa (Iasi, RO)

54. Predicting Outcomes For Crohn’s disease using a molecular biomarker: PROFILE trial recruitment update

55. Crohn’s case: Recurrent ‘gloves and socks’ distribution with bullous eruptions after adalimumab and infliximab treatment
E. Ozkan, M. Basaranoglu (Istanbul, TR)

56. Rectal non-Hodgkin’s lymphoma presented as ulcerative proctitis: A case report
E. Ozkan, M. Basaranoglu (Istanbul, TR)

57. Pharmacy technician in the IBD team maintains patient safety whilst freeing up pharmacists and physicians
A. Packham (Haywards Heath, GB)

58. Long-term efficacy and safety of CT-P13, a biosimilar of infliximab, in patients with inflammatory bowel disease: A retrospective multicenter study
D. Park, N. Kim (Seoul, KR)

59. Can fatigue in inflammatory bowel disease be classified as a separate entity?
J. Paterson (Dundee GB)

60. Oral manifestations of Crohn’s disease
B. Perše, O. Žaja (Zagreb, HR)

61. Ways of adjusting nutrition in the inflammatory bowel diseases
O. Petrascu (Sibiu, RO)

62. Effect of biological therapy on the grade of inflammatory bowel disease activity and values of inflammatory parameters
A. Pilav, N. Zubčević (Sarajevo, BA)

63. The study of colonic resistance as a background for microbiome engineering in IBD

64. Rare extraintestinal manifestations in a Crohn’s disease patient
65. Factors associated with non-adherence to medication for inflammatory bowel disease: A monocentric Tunisian study
H. Romdhane, B. Bouchabou, A. Nakhli, N. Hemdani, H. Ben Nejma, R. Ennaifer (Tunis, TN)

H. Romdhane, B. Bouchabou, H. Ben Nejma, R. Ennaifer (Tunis, TN)

67. Risk factors for decreased bone mineral density in inflammatory bowel disease in a Tunisian cohort
H. Romdhane, B. Bouchabou, A. Nakhli, N. Hamdeni, H. Ben Nejma (Tunis, TN)

68. Colonic amyloidosis
C. Sfrijan, R. Nemteanu, C. Gorincioi, B. Mazilu, A. Plesa, A. Clim (Iasi, RO)

69. Chronic diarrhea due to Capillaria philippinensis: A case report
M. Sharaf-Eldin (Tanta, EG)

70. Helicobacter pylori may be an initiating factor in newly diagnosed ulcerative colitis patients

71. Fecal calprotectin in the diagnosis of ulcerative colitis (UC) among Egyptian patients
S. Shoman, I. Amer, I. Saber (Desouk, Kafr El-Shiekh, Tanta, EG)

72. IBD case report presented only by jaundice: It is rare among Egyptians
S. Shoman, I. Hussien (Desouk, Tanta, EG)

73. A rare case of ascites (retroperitoneal fibrosis)
S. Shwana (Merthyr Tydfil, GB)

74. Trace elements status in patients with inflammatory bowel disease

75.* Embedding pharmaceutical care into the IBD multidisciplinary team
A. St. Clair Jones (Brighton, GB)

76.* Multi-omic data integration assisted identification of molecular features contributing to disease heterogeneity in Crohn’s disease
P. Sudhakar (Norwich, GB)
77. Pathogenetic associations of kidney impairment, endothelial and intestinal inflammation  
A. Sydorchuk, L. Sydorchuk, V. Dzhuryak, I. Sydorchuk, I. Sydorchuk, O. Plehutsa, R. Sydorchuk, A. Vakarchuk, M. Plehutsa, N. Plehutsa (Chernivtsi, Storozhynets, UA; Frankfurt, DE)

78. Bridging microbiome modeling with 5-ASA use in IBD  
L. Sydorchuk, N. Plehutsa, I. Sydorchuk, A. Sydorchuk, O. Plehutsa, I. Sydorchuk, A. Sydorchuk, A. Vakarchuk, R. Sydorchuk (Chernivtsi, Storozhynets, UA; Frankfurt, DE)

79. Use of polarized confocal microscopy of colon for improving colonoscopy diagnostic value and accuracy in IBD  
R. Sydorchuk, P. Fomin, L. Sydorchuk, O. Plehutsa, A. Sydorchuk, I. Sydorchuk, A. Vakarchuk, M. Plehutsa (Chernivtsi, Kiev, Storozhynets, UA; Frankfurt, DE)

80. Presentation and treatment of spontaneous bacterial peritonitis in a local district hospital  
D. Taha (Cardiff, GB)

81. Significant cost savings utilising a regional prescribing approach to mesalazine therapy in inflammatory bowel disease  
J. Tham (Glasgow, GB)

82. Long-term outcome of immunomodulator use in pediatric patients with inflammatory bowel disease  

83.* The role of Oncostatin M in diagnosis, prognosis and therapy response of IBD  
S. Verstockt, B. Verstockt, K. Machiels, M. Vancamelbeke, M. Ferrante, I. Cleynen, S. Vermeire (Leuven, BE)

84. Gastrointestinal manifestations in HIV-infected people. From diarrhoea to AIDS  
A. Veshapidze (Tbilisi, GE)

85. High rates of clinical response are maintained after switching from originator to biosimilar infliximab  
K. Waddell, R. Haggarty, J. Veryan, J. Seenan, J. Macdonald (Glasgow, GB)

86. Therapeutic drug monitoring supports clinical decision making when employed before and after biosimilar infliximab switching  
K. Waddell, R. Haggarty, J. Veryan, J. Seenan, J. Macdonald (Glasgow, GB)

87. Malnutrition risk screening in hospitalized patients with IBD  
P. Zalizko, T. Hermine Roshofa, L. Meija, A. Pukitis (Riga, LV)
88. Association between use of azathioprine and non-Hodgkin lymphoma in patient with IBD
M. Zivkovic, M. Nikolić, P. Ćaćić, I. Budimir, N. Ljubičić, D. Hrabar (Zagreb, HR)

* = Posters of Distinction
Session I

Building bridges with other disciplines: Most important tips for interdisciplinary decision making
The gastro-rheumatology tandem: The therapeutic approach to IBD patients with rheumatologic manifestations

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Depending on definition, up to 50% of IBD patients experience at least one extra-intestinal manifestation (EIM), more commonly from the joints, eyes, and skin. Musculoskeletal involvement (MI) in IBD ranges between 15–39% and includes peripheral or axial spondyloarthritis (SpA), arthralgias, enthesitis and dactylitis. Axial SpA (spondylitis and/or sacroiliitis) can be found in up to 25% of IBD patients but progression to ankylosis occurs in ~10% of patients. Peripheral SpA is typically a non-destructive, seronegative arthropathy which is categorized traditionally into type I and type II. Type I involves 1–4 joints (mono or oligo-articular involvement of large joints of the lower extremities) and runs in parallel with the intestinal activity. Type II involves ≥ 5 joints (symmetric involvement of small joints of the upper extremities resembling rheumatoid arthritis) and runs independently from the intestinal activity. Arthralgias are non-specific and can be due to different etiologies including IBD itself or drug-related (rapid withdrawal of corticosteroids, azathioprine, anti-TNF induced lupus erythematosus-like syndrome, paradoxical inflammation to vedolizumab or ustekinumab).

MI in IBD impacts remarkably upon patients’ quality of life and causes various degrees of disability. Timely diagnosis and early treatment are essential to avoid long-term sequelae. These should be done in the context of a Multi-Disciplinary Team (MDT) with dedicated Rheumatologists because Gastroenterologists tend to underestimate MI or MI are overshadowed by treatments targeted to the intestinal disease.

MI diagnosis is based on careful evaluation of patient’s symptoms and local signs of inflammation, exclusion of other types of articular involvement, and careful selection of the appropriate imaging modality. MRI is more sensitive than plain x-rays for the diagnosis of axial SpA while for peripheral SpA (enthesitis, synovitis, dactylitis) ultrasonography is a useful imaging tool due to its wide availability, low cost, and sensitivity to detect joint and tendon involvement even in the absence of symptoms.

Treatment aims to relieve intestinal and articular inflammation in order to prevent permanent damage and disability. Peripheral SpA usually responds to pharmacological or surgical treatment of the underlying IBD. Depending on the severity and activity of IBD and peripheral SpA, non-biologic (sulphasalazine, methotrexate for CD-associated peripheral arthritis) and biologic (anti-TNF: infliximab, adalimumab and golimumab either alone or in combination with methotrexate, anti-IL12/IL-23: ustekinumab) agents have shown efficacy.

Symptomatic axial SpA responds only to anti-TNF agents since neither other medical nor surgical treatment of IBD can halt the inexorable progression to ankylosis. Response to other biologics such as ustekinumab or vedolizumab is poor.
Arthralgias, dactylitis and enthesitis require rest, physical therapy and local injections of corticosteroids. The use of NSADs is controversial as it may trigger flares of IBD, especially colitis. Short courses (1–2 weeks) of COX-2 inhibitors or steroids and/or pulse steroid therapy may be alternatives. In resistant cases, anti-TNFs or anti-IL12/IL-23 agents can be used.

Anti-TNF-, vedolizumab-, or ustekinumab-induced arthralgias usually respond to drug discontinuation or switching to another class of biologics, appropriate for the treatment of IBD. A short course of steroids may be needed to bridge the time interval to the new biologic.
The gastro-dermatology tandem: 
Addressing the most frequent questions

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The skin is commonly affected with extraintestinal manifestations in inflammatory bowel disease (IBD) patients. These manifestations may occur before or after diagnosis of the IBD and different categories are recognized based on their pathophysiological interrelation with the underlying intestinal disease.

Specific or metastatic skin manifestations share the same histopathological features as the underlying intestinal disease and are therefore not considered “true” cutaneous disorders.

Reactive skin diseases, however, manifest as a reactive process to the intestinal inflammation, characterized by common pathogenic and immunologic mechanisms with the underlying bowel disease. Neutrophilic dermatoses such as pyoderma gangrenosum, Sweet’s and BADAS syndrome fit this category of reactive disorders involving neutrophilic driven (auto)inflammatory skin manifestations.

When a common pathogenic link seems absent, but the skin disease is more frequently observed in IBD patients, the condition is called an associated skin disease. Erythema nodosum is most frequently associated, but also the concomitant occurrence of hidradenitis suppurativa gained more interest recently.

Cutaneous manifestations can arise secondary to IBD treatment. With anti-TNF treatment becoming widely used, a new type of treatment associated skin lesions were recognized. Psoriasiform lesions, that are distinct from classical psoriasis, are most frequently encountered in anti-TNF treated IBD patients.

Knowledge of the diagnostic criteria of these extraintestinal manifestations and their clinical course should assist in finding the best therapeutic strategy: treatment of the underlying bowel disease will often parallel control of the cutaneous condition. Anti-TNF treatment associated skin lesions will necessitate prompt dermatological measures.

In turn, a treatment scheme for a particular dermatological condition should be redesigned implying the restrictions of dealing with an IBD patient. This is also illustrated by the recent introduction of IL-17 inhibitors for the management of psoriasis causing exacerbations or even new onset of IBD and underscores the importance of a good liaison between the gastroenterologist and the dermatologist.
The gastro-gynecology tandem:
IBD and pregnancy: A two pipe problem – A multidisciplinary joint venture

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Inflammatory bowel disease (IBD) usually affects women during their reproductive years and many concerns arise among these young patients. Pre, during and post pregnancy consultation with a multi-disciplinary team is crucial; smoking cessation, achieve a good nutritional status and ensure that conception occurs during a period of disease remission; conception during an IBD flare-up results in disease activity or even exacerbates disease in two-thirds of women. Exacerbation of the disease is associated with increased frequency of maternal and fetal complications. Drug therapy constitutes a considerable source of patient anxiety but most drugs used for treating IBD are considered safe. Therefore, continuing pharmacological therapy during pregnancy is necessary to maintain disease control. Optimization of pre-conception nutritional status and smoking cessation are also emphasized. The general guideline for most patients, except for active perianal disease patients, is to aim for vaginal delivery in the absence of obstetric contraindications. Based on this concept we established the IBD MOM (2011) a “sit together” (dedicated gastroenterologist, fetal-maternal medicine specialist, IBD nurse coordinator, dietitian and psychologist), nonprofit, multidisciplinary, single-center clinic aimed to benefit women with IBD and their neonates. Our preliminary experience (2011–2015) regarding the IBD MOM clinic patients compared to patients who attended antenatal and gastrointestinal disease community clinics (IBD CC) included 90 women in the IBD MOM clinic and 206 in the IBD CC. Maternal age, smoking habits, pregnancy complications, and type of IBD (CD/UC) were similar between groups. Rates of labor induction and birth weight were also similar between IBD MOM and IBD CC. The IBD MOM overall preterm delivery (PTD) rate (< 37 weeks) was significantly higher 18.9 versus 9.7% (p = 0.028). The IBD MOM group had a significantly higher disease severity score that correlated with a higher rate of PTD; however, the overall IBD MOM score and scores > 3 were significantly associated with PTD risk in both groups (p = 0.013 and p = 0.004, respectively).

Consistent, ongoing follow-up, as will detailed in our presentation, should allay the anxieties and fears surrounding pregnancy in those patients, including continuing immunosuppressive drugs during pregnancy, allowing each patient to attain the optimal conditions for achieving her goal of holding a healthy baby.
Session II

The multidisciplinary team from A to Z: Building bridges with non-medical disciplines
**Work with your nutritionist!**

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The goals of inflammatory bowel disease therapy include controlling inflammation and managing side effects of the disease and its treatment. Malnutrition can complicate both Crohn’s disease and ulcerative colitis. There are many easy to use tools to assess for malnutrition, such as the Malnutrition Universal Screening Tool (MUST), a validated 5 step tool to identify adults who are malnourished or at risk of malnourishment. Importantly, a low body mass index is not required to qualify as malnourished or at risk of malnourishment. Once identified, incorporating a registered dietitian into the management of patients can help in correcting nutritional deficiencies.

Gastroenterologists and dietitians are increasingly partnering in the use of nutrition as a primary or adjunctive treatment for inflammatory bowel diseases, particularly Crohn’s disease. There are a number of diets that are used to attempt to control inflammation and/or manage symptoms for those with persistent symptoms despite resolution of inflammation. The strongest evidence available for dietary therapy is the use of exclusive enteral nutrition in which > 90% of the patient’s calories are provided in the form of liquid dietary formulas. Remission rates with exclusive enteral nutrition are often greater than 60%, are comparable with fully hydrolyzed proteins and other formulas, and are generally more effective in children than adults, possibly due to greater adherence. Implementation of exclusive enteral nutrition when planned for longer than a few weeks is likely best implemented when there is collaboration between dietitians and gastroenterologists.

The latest advances in the field of nutrition as treatment for Crohn’s disease is the use of modern diets that incorporate whole foods with or without partial enteral nutrition. An example is the Crohn’s Disease Exclusion Diet. Because of the complexity of implementing such diets, it is almost impossible for the gastroenterologist to provide sufficient counseling and partnering with a dietitian is essential.
Psycho-socio-economic aspects in IBD: Facts and possible interventions

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Inflammatory bowel disease (IBD) and its medical and surgical treatment does not affect only the body, it can influence all domains of the patients’ life: Their mood, anxiety and stress levels, self and body image, their capacity to socialize, their family life and their intimate relationships as well as their capacity to be employed, maintain work and study consistently.

After providing the statistics regarding these issues I will focus on the necessity to address and meet the unique individual IBD patient and the challenge of individually tailoring her/his treatment and support to her/his specific holistic needs. IBD in comparison to other chronic diseases has its own unique aspects and I will explore especially shame and embarrassment as the core experiences which accompany this condition.

I will share what I have learned from my nine years of experience of working intensively together with IBD suffers in the field that can be defined as “Psycho-Gastroenterology” at the Psychological Medicine Unit of St. Mark’s Hospital. I will present the treatments and the support that our team has been offering and reflect on the possible future interventions that can help patients to cope better with the adversities of IBD and improve their quality of life. Finally, it will be also important to mention the support the clinicians who are serving at the frontline of the battle with IBD need, and what we can try to do about it.
Session III

Building bridges in Europe
Importance of registries, population-based and other interesting cohorts to unravel causes of IBD

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The inflammatory bowel diseases, which include Crohn’s disease (CD) and ulcerative colitis (UC), are immunologically-mediated gastrointestinal diseases associated with substantial morbidity, complications, low mortality, and exorbitant direct and indirect costs. Their pathogenesis implicates complex, and as yet poorly-delineated, interactions among genetic, non-genetic and microbiome risk determinants. Identifying these determinants, especially ones that are modifiable, is a critical first step toward unravelling the pathogenesis of IBD, changing its natural history and ultimately, preventing it. Such data are difficult, if not impossible, to procure from small-sample or short-term studies, with additional noise from confounders and biases. In this regard, well-designed, long-term registries and population-based studies are highly informative and provide tremendous opportunities to characterize IBD risk and protective factors, phenotype and natural history. Assimilating what we have learned from such data will help harness the full potential of such resources to determine the cause(s) of IBD, especially those that are preventable and modifiable.

Through data from population-based cohorts, we know that IBD was until recently, a disease of Caucasians, and appeared in Europe and North America in parallel with industrialization. Rare in developing and recently-developed countries until the 1990s, IBD is now rising rapidly in these countries in the context of Westernization. Among immigrants from low- to high-incidence countries, IBD incidence changes over subsequent generations, with UC incidence changing before CD incidence. Early age at immigration, longer duration of stay and acculturation are associated with higher risk. The rapidity of evolution of IBD incidence is highly informative, and implicates environmental factors and genetic-non-genetic interactions, mediated, at least in part, by dysbiosis. UC occurs in context of exposure to risk factors at any age, with a short lag between exposure and disease onset, while CD is associated with prenatal and early-life exposures and a longer lag. Urbanization, dietary factors and oral contraceptive are implicated as risk factors, while breastfeeding and Helicobacter pylori are considered protective.

Registries and population-based studies that capture accurate and granular long-term data on non-genetic factors in well-defined cohorts will be extremely informative. Understanding differences in risk determinants, phenotype and natural history in developing versus developed countries, and in UC versus CD will be critical. Immigrants from low- to high-incidence countries provide a unique opportunity to study the impact of changing environment and its assimilation on IBD risk. These pathways will lead us closer to understanding IBD pathogenesis and the ultimate goal of IBD prevention.
Telemedicine: The way forward to unite patients in Europe?

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Inflammatory bowel disease (IBD) is a lifelong inflammatory disorder of the gut with a complex background resulting in a heterogeneous clinical presentation and treatment response. The economic burden for IBD is high and increasing due to the attenuating incidence, expensive medical treatment, the need for tight monitoring and work productivity losses. Disease management based on treating symptoms and a ‘step-up trial and error’ drug introduction did not improve the long-term outcome sufficiently. Guidelines therefore advice long term stringent monitoring of mucosal inflammation. Interventions that address psychosocial and life style factors that influence disease activity, such as non-adherence to treatment, smoking, nutritional status and psychological factors can prevent disease relapse, decrease health-care utilization and work absenteeism. To improve the long-term outcome of IBD thight control in combination with monitoring of all disease related aspects is therefore warranted. To improve the quality of care systematic registration of outcomes that matter most to patients is necessary and registration of patient reported outcome (PROs) and experiences (PREs) should be implemented in every day care. From a patient perspective integral communication, shared decision making, duration of a consultation, personalized information and speed of advice are strongly associated with better quality of care. Tight control, systematic registration of PROs, PREs and lifestyle and psychosocial determinants of disease are at present not implemented in every day care, because acquiring all the necessary information at the right moment for every patient during a standard outpatient clinic visit is not feasible. Increasing the number of visits or the duration will further strain the health care system. Therefore, reorganisation of care for patients with chronic inflammatory disease like IBD is warranted.

Telemedicine allows for the strict and instantaneous follow-up of health parameters and PROs amd timely, personalised interventions. Moreover, these systems can provide tailored information based on each patient's needs and increase speed of communication with the health care professionals. This lecture summarises available data of telemedicine interventions to improve outcome, reduce costs or improve quality of care for inflammatory bowel diseases.
The role of EFCCA and national patient associations in promoting IBD care

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EFCCA is an international association representing 40 national IBD patient associations in Europe and beyond. It was founded in 1990 and it is recognized as an international not for profit organization by the Belgian law.

Mission: to improve the overall well-being of people affected by Crohn’s Disease and Colitis, collectively referred to as Inflammatory Bowel Disease (IBD).

EFCCA Strategy Plan 2019–2023 identified “IBD and quality of care” as its 2020 priority area and its activities will prioritize on discrimination in accessing adequate care, doctor-patient communication and relationship, personalized medicine.

4 are the foreseen areas of intervention
- Networking: encouraging and facilitating collaboration, exchange of information, knowledge and practices, and the promotion of international activities. To reinforce its partnership with stakeholders a joint conference with relevant medical societies has been planned.
- Awareness-raising: organizing various initiatives, delivering education and tackling taboos and stigmas around IBD. The main activity will remain World IBD Day (19 May) a global campaign that involves over 50 countries every year. Medical societies and other stakeholders are also active part of it.
- Advocacy: with EU institutions and international organizations such as WHO to move from a therapy-focused approach to a more patient/person-focused approach, ensuring that concerns, needs and priorities of people living with IBD are included in the decision-making process for policies and other related health initiatives.
- Empowerment: supporting its members in their work and mission at national level through the exchange of best practices and capacity building activities such as educational seminars, thematic workshops, policy initiatives and helping to establish new associations in countries where they do not yet exist. EFCCA wants to invest creating sustainable resources, training independent, self-confident patient, and increasing the collaboration with members. The EFCCA Academy will be the main instrument for this purpose
Session IV

Building bridges between the lab and the clinic: Translational IBD care
Biomarkers at diagnosis: What is absolutely needed for diagnosis and prognosis in 2019?

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The incidence of inflammatory bowel disease (IBD) is still rising. At the same time the therapeutic options available have been continuously increasing over the last decades. Thus, one could conclude that more options are available for treatment of IBD resulting in no need for further development. However, one has to appreciate several clinical problems that clearly emphasize the “needs” in the field. First, and in fact challenging, is the time point of diagnosis. Clinically we see a patient not knowing whether over time this will be a rather mild course, and hence no aggressive medical treatment is required or on the opposite, whether this will be a complicated disease course that might demand for an early intense treatment. Current management is mostly based on the phenotypic appearance and more or less simple biomarkers. An initial study by Lee and colleagues could demonstrate that CD8+ T cell transcriptional signatures was sufficient to divide patients into two otherwise indistinguishable subgroups [1]. Following up on this approach patients with active IBD were recruited before treatment and the two subgroups were identified by consensus clustering of CD8+ T cell transcriptomes. The data indicated that a 17-gene qPCR-based classifier stratified patients into two distinct subgroups and might in fact be the next step towards personalized therapy [2]. Second, it is well described that independent from the medical therapy chosen, the response to a first biological is better than to the second- or third-line treatment. This raises the key question how to choose the right drug for the right patient and which biomarkers or phenotypic disease characteristics are currently supporting these clinical decisions. Some markers will be addressed here, a future perspective will be provided in a later talk of this session. Last, a particular focus should be on patients diagnosed early in life or in the case of a “remarkable” phenotype later on, in those selected cases the search for a monogenetic disease (“very early onset IBD”) is justified, since it might open additional therapeutic options.

In summary, the current biomarkers (including disease phenotype) have a very limited informative power. However, the novel data discussed above hold promise that there will be significant changes in the near future.

References:

Predicting response to drugs in 2020

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Inflammatory bowel diseases (IBDs) are heterogeneous in their clinical presentation with major differences noted between Crohn's disease (CD) and ulcerative colitis (UC). These differences are based upon involved bowel segments and pathologic characteristics as well as some of the associated complications. However, detailed analysis supports the possibility that both are in fact syndromes rather than two distinct entities and that a continuum of genetic and other pathogenic factors exists in both. Furthermore, clinical, endoscopic, pathological, genetic and transcriptional data reveal both differences and overlaps between them. These observations, combined with the shared treatment efficacy on the one hand, and incomplete response rates of the different drug classes on the other, suggest that a change in the paradigm by which treatments are tested in trials and selected for therapy is needed.

The variability of disease characteristics reflects only partially on treatment choice. Current practice involves trial and error drug selection based on results of double blind placebo controlled trials demonstrating efficacy in a selected “average” patient population, the characteristics of which may not overlap with an individual patient at all. This approach leaves a sizable proportion of IBD patients with relentless inflammation leading to significant morbidity and accumulating tissue damage.

Because the understanding of IBD pathogenesis did not reach a level which allows tackling basic disease mechanisms, to date, treatments are aimed at abrogating the immune response which is responsible for tissue damage. This approach, which is not gut selective, leads to side effects associated with the various modes of immune suppression, some of which can be life threatening including infections and malignancy. Therefore, the decision to embark on treatment should take into account prediction of disease course, such that patients with propensity for a complicated course will be those who undertake the significant risks. To date, little is known regarding disease course prediction, although studies have suggested CD8 cells gene expression, serology and microbial signatures as potential predictors. Furthermore, the immune milieu which is the target of therapy may be dynamic, affected by the immune-modifying treatment itself, and necessitate continuous adaptation during disease course.

Drug efficacy depends on drug availability and an effective target. Thus, PK/PD considerations are relevant to achieve beneficial outcomes. In the case of biologics, drug availability should also take immunogenicity into consideration. Furthermore, accumulating evidence suggests that molecular characterization of pretreatment drug target availability and understanding mechanism of action (MOA) using unbiased systems approach, may serve to identify biomarkers for response before treatment. This, combined with therapeutic drug monitoring, will predictably allow to effectively predict treatment efficacy and sustain its effect. In the future, a systematic approach may be adapted from oncology wherein some drug combinations may be calculated in advance based on known disease mechanisms and complementary drug effects. The challenge of balancing efficacy with side effects and effectively predicting their occurrence remains to be solved. However, a more personalized approach to treatment balancing between these factors offers improved future outcomes.
State-of-the-Art Lecture:

Will understanding of fibrosis help to treat Crohn’s disease?

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The inflammatory bowel disease (IBD) course is highly heterogenous. Intestinal fibrosis causing clinically apparent stricture formation is a common feature of both entities of IBD, Crohn’s disease and ulcerative colitis. In its most pronounced form it can cause intestinal obstruction as well as need for surgical intervention. This constitutes a major treatment challenge. Despite the emergence of stronger immunosuppressive medications, we can only minimally reduce the incidence and prevalence of fibrostenosing IBD. No specific antifibrotic therapy is available. Fibrosis results from the response of gut tissue to the insult inflicted by chronic inflammation. The underlying fibrogenic mechanisms are complex and dynamic, involving multiple cell types, interrelated cellular events, and a large number of soluble factors. This includes luminal bacterial products or fat wrapping around the bowel wall, the so-called ‘creeping fat’. Clinical and experimental evidence indicates that once fibrosis is established it can progress independently of inflammation. The composition of the intestinal extracellular matrix, its mechanoproperties and matrix bound factors are dramatically altered in chronic gut inflammation and can actively promote fibrosis. The conventional view that intestinal fibrosis is an inevitable and irreversible process in patients with IBD is gradually changing in light of an improved understanding of the cellular and molecular mechanisms that underline the pathogenesis of fibrosis. Novel animal models assist in the discovery and investigation of novel anti-fibrotics. Clinical initiatives are under way to build a pathway to test anti-fibrotics in IBD by developing clinical trial endpoints. We provide a roadmap for the translation of novel anti-fibrotic compounds in patients with IBD.
Session V

Building therapeutic bridges
Moderate to severe ulcerative colitis: The next step after 5-ASA and steroids is...?

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The past decade has brought substantial advances in the management of inflammatory bowel diseases (IBD). The therapeutic armamentarium has changed significantly including the advent of tumor necrosis factor (TNF) antagonists, combination therapy, the introduction of agents targeting lymphocyte trafficking and activation, and the need for early treatment of high-risk patients. As a consequence there has been a repositioning of the “conventional therapies”. 5-aminosalicylate (5-ASA) agents remain the mainstay initial treatment in mild to moderate ulcerative colitis (UC), while corticosteroids remain the initial treatment of choice in patients with moderately severe or severe UC. Anti-TNFs, anti-integrins and JAK inhibitors has become the first choice in moderate-to-severe UC refractory to conventional therapies, with recent concerns on the cardiovascular safety of the higher dose of tofacitinib in elderly patients with high baseline cardiovascular risk. In addition, the first head-to-head clinical trial has shown the superiority of vedolizumab compared to adalimumab in inducing clinical remission and mucosal healing. In contrast, recent studies have shown that methotrexate is not effective in inducing or maintaining remission in steroid dependent UC (Meteor and Merit trials) after the failure of 5-ASAs or steroids, similar to data published on azathioprine with limited evidence for a steroid sparing effect, in steroid dependent UC patients. In addition, the use of immunosuppressives is further limited due to concerns regarding infections and malignancy risks (lymphoma and non-melanoma skin cancer for AZA). Studies have suggested the value of concomitant immunomodulatory therapy in treatment-naïve patients starting anti-TNF-α therapy to enhance the effectiveness and prevent antibody formation to anti-TNF-α agents. Little is known about the role of immunomodulators in combination with other classes of biologic therapies. Finally, infliximab and cyclosporin has shown a comparable efficacy signal in acute severe colitis, yet most centers in the Western world use infliximab as initial therapy in the real life setting. In summary, biological therapies are increasingly used in moderate-to-severe UC patients after the failure to 5-ASA and steroids, while the use of immunosuppressives is limited to selected patients with steroid dependent phenotype considering also the risk/benefit profile.
Mild ileal Crohn’s disease: Do nothing or prescribe biologicals?

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The management of mild ileal Crohn’s disease remains a challenge since studies on prevalence and disease course of this particular disease subgroup are entirely lacking. The following question is how do we define mild ileal Crohn’s disease. The diagnosis of mild ileal Crohn’s disease excludes strictures, penetrating disease and ulcerations. Then, what is leading to the diagnosis and what are the symptoms. Part of this patient group undergo screening colonoscopy for colorectal cancer and get diagnosed with mild ileitis without any relevant symptoms. The other subgroup might suffer from diarrhea due to bile-acid malabsorption in the terminal ileum. But do we need to treat these patients and if yes, would we use a biological? One study did in fact focus on patients with ileal and right-sided Crohn’s disease [1]. The disease activity, determined by CDAI at inclusion had to be more than 200 and less than 400. Thus, one can argue whether or not this still counts as mild disease. The study compared 9 mg budesonide/day with 4.5 g mesalamine/day with a primary endpoint of clinical remission (CDAI ≤ 150) at week 8. This endpoint was met by 69.5% of patients given budesonide and 62.1% of patients with mesalamine. Thus, both strategies resulted in a high rate of clinical remission which would clearly argue against the use of biologics with this disease phenotype. However, endoscopic data are lacking from this study. Probably the best data we have are from the post-surgical setting after ileocecal resection. Here, we have follow-up data of mild versus more severe recurrence. From this scenario we know that a mild disease (Rutgeerts i0/i1) will have an excellent disease course without the need of medication [2]. Finally, there is increasing evidence that ileal Crohn’s disease differs from an immunological point of view significantly from colonic Crohn’s disease and might consequently require own, yet underexplored therapeutic strategies [3–5].

In summary, the current data do not allow for arguing in favor of treatment with biologics in truly mild ileal Crohn’s disease. But we should reconsider the different underlying immunology in ileal versus colonic Crohn’s disease. This might ultimately lead to “ileum-specific” treatment regimens.

References:


Combination of biological therapy: Dream or reality?

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Every biological therapy used in immune-mediated inflammatory disorders (IMID) has its own limitations. Particularly in inflammatory bowel disease (IBD) the remission rate at one year after starting biological therapy ranges between 20% and 40% depending on the drugs and situations. On the top of this, primary non responders to a first biological may respond to another biological therapy, emphasizing that some immune-inflammatory pathways may be more prominent or more relevant in some individual patients. Hence it makes sense to contemplate combination of biological therapies in IMID, including IBD. The first hurdle in most of the countries may be the cost and the absence of reimbursement by insurance companies or public health system of several biologicals at the same time. However with biosimilars, the costs have dramatically diminished and this hurdle may no longer be as high as it was. The second more consistent hurdle is safety as already combining biological therapies with conventional therapies like steroids or immunomodulators was associated with increased risk of infections. Beyond this, the favourable and unfavourable consequences of interfering at the same time with different inflammatory pathways are most often unknown and are difficult to figure out.

In rheumatologic diseases and in psoriasis there is already quite an extensive experience with such combinations, while it is much more limited in IBD. In rheumatologic conditions, the study of efficacy of combined biological therapies has given mixed results, but most of the randomized controlled trials were negative, including combination of anti-TNF with abatacept and anti-TNF with rituximab. Mixed results were also observed as far as safety in these individual trials or case series. A recent systematic review and meta-analysis revealed a significantly higher risk of adverse events and serious adverse events on combined biological therapies than on monotherapies. There was also a trend (but not reaching statistical significance) for an increased rate of serious infections.

More specifically in IBD only one exploratory randomized control trial and a few case reports or series were published. The exploratory trial randomized patients having active disease under infliximab to combined therapy with natalizumab or placebo. In this study there was no significant difference in treatment-emergent adverse events or infections. Albeit not powered for efficacy assessment, no significant difference was observed in this study over 10 weeks. Since then, case reports or series concern combination of vedolizumab and anti-TNF, vedolizumab and ustekinumab, and ustekinumab and anti-TNF. It is very difficult to draw any conclusion from this limited experience.

In conclusion, combining biological therapies may seem very attractive in theory, and the cost may seem at the first glance the main hurdle. However, experience in rheumatologic conditions has highlighted a significant increase in the risk of serious adverse events, and so far the evidence for an improved outcome has not been strong. More trials are definitely needed but a better knowledge of the impact of combining biological therapies and of the dominant immune-inflammatory pathways in the treated patients could help to better delineate the best indications for such combinations.
BIO-MDT: The future of IBD patient care

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The format of care provided to patients with inflammatory bowel diseases (IBD) depends on multiple factors. Patients may be seen by family physicians, community gastroenterologists, hospital-based gastroenterologists and those in referral centers. Some hospital-based services and large clinics evolved into multi-disciplinary IBD centers with additional health-care providers, including IBD nurses, dieticians, colorectal surgeons, psychologists, social workers, stoma nurses and additional allied professionals. Each format of care provision has inherent advantages and disadvantages. There is no data to suggest which format of care is more beneficial for patients, and no controlled cost effectiveness analysis compared outcomes of patients treated by any of this formats. We suggest a new format of patient care, a biomarker-based MDT (bio-MDT). In this format professional health care givers provide advice and care based on patients biomarkers, analyzed in real time, using clinic, laboratory based and point-of-care evaluations of data and biomaterial. The features of the various models of care, as well as of the bio-MDT, will be presented, as well as the possibility to adopt only parts of the model. The measures that may be used to evaluate the various formats of care will be discussed.
Session VI

Let’s visualize!
New opportunities for intestinal ultrasound

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Cross-sectional imaging in inflammatory bowel disease (IBD) is recognized as imperative to comprehensive staging at diagnosis, as reflected in recently updated ECCO guidelines (2018). Transmural response and healing is also an important predictor of improved outcome. Therefore, imaging is increasingly used as an accurate, objective adjunct in monitoring strategies, beyond assessment of clinical symptoms and surrogates of inflammation such as C-reactive protein and fecal calprotectin to guide a ‘treat to target’ strategy. There are a number of available imaging options, but safety and cost are important factors limiting their repeatability and accessibility. Mounting evidence demonstrates accuracy of intestinal ultrasound (IUS) in the detection of disease activity, presence of complications and extent of disease for Crohn’s disease and importantly, with high patient acceptance and tolerability. Published data for use of IUS in monitoring ulcerative colitis (UC) has been fairly limited; however, increasing evidence suggests IUS also accurately reflects the extent and severity of inflammation in UC. Thus, IUS is gaining prominence in routine clinical care for IBD patients, as it can be easily repeated in clinic by trained gastroenterologists during intermittent IBD patient follow up. International collaborative efforts are underway to standardize the interpretation of activity on IUS, reduce inter-observer variability and improve consistency in interpretation through established of a central reading platform. The goal of this presentation is to outline the extant evidence reflecting therapeutic response and healing on cross-sectional imaging with specific focus on IUS and highlight where the gaps in the current literature exist; secondly to discuss how the use of a monitoring tool such as IUS may enhance treat to target strategies and improve outcome for patients with IBD and finally, how multidisciplinary care (MDT) includes Diagnostic Imaging in the core team of providers.
Capsule endoscopy – The best tool for diagnosis and follow-up of patients with Crohn’s disease

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In contrast to ulcerative colitis in which lesions are strictly limited to the colon, Crohn’s disease (CD) is more heterogeneous and can affect the entire gastrointestinal tract. The Montreal classification distinguishes anatomical disease location in the ileum (L1), colon (L2), and both ileum and colon (L3), each accounting for approximately one-third of patients diagnosed with CD. About 10–15% of patients have associated upper gastrointestinal lesions (L4). It has been demonstrated that jejunal disease is a significantly greater risk factor for stricture disease and multiple abdominal surgeries than either esophagogastrroduodenal or ileal (without proximal) disease. The assessment of small bowel (SB) in patients with suspected or diagnosed CD is therefore necessary, as it may have a significant impact on prognosis with potential therapeutic implications.

Since its first approval by the Food and Drug Administration (FDA), small bowel capsule endoscopy (SBCE) has become an important tool for assessing the SB. Its diagnostic potential is significantly higher than all of the radiologic methodologies used to visualize mucosal lesions especially, those located in the proximal part.

Until recently, therapeutic strategies relied on a progressive and step-wise approach based solely on IBD-related symptoms. However, there is now accumulating evidence demonstrating the poor correlation that exists between symptoms and endoscopic disease activity. In this regard, the “treat-to-target” paradigm has been developed in 2015, based on regular and objective assessment of disease activity, and subsequent adjustment of treatment. The treatment goal has evolved to the achievement and maintenance of deep remission, combining both clinical and endoscopic remission.

In this context, mucosal healing can be assessed by SBCE to monitor the effect of medical treatment in patients with CD. However, the definition of endoscopic remission as assessed by SBCE remains unknown, as there is currently no consensus on the therapeutic objective to reach in luminal SB CD (normalization of SBCE or absence of deep or superficial ulcerations).

Similarly, endoscopic re-assessment should be timely in the post-operative setting, in order to detect post-operative recurrence at an early stage. SBCE could detect post-operative recurrence to a similar extent as ileocolonoscopy, and is able to detect proximal SB lesions beyond the reach of the colonoscope in more than half of patients. SBCE could be used to detect very early post-operative recurrence especially in patients without any risk factor who do not necessarily require pharmacological prophylaxis immediately after surgery.

The advent of pan-enteric capsule offers the possibility to monitor both the SB and the colon in a one-time ambulatory exam. Preliminary data suggest that, its diagnostic yield is similar to conventional endoscopy into the colon with the add-on value of the detection of SB lesions. However, the place of this new technology in the surveillance strategies remains to be defined.
New techniques for endoscopic surveillance in UC: From chromoendoscopy to image acquisition?

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Patients with long-standing or extensive ulcerative colitis or Crohn’s disease are at an increased risk of developing colorectal cancer (CRC) compared to the average risk population. Accordingly, regular and extensive surveillance colonoscopies are recommended. In this context, advanced endoscopic imaging may be of benefit by (I) increasing the detection rate of neoplasia, (II) improving the differentiation of lesions (colitis-associated neoplasia, sporadic neoplasia, and non-neoplastic lesions), and (III) reducing the number of unnecessary biopsies. Guidelines recommend the routine use of dye-based pancolonic chromoendoscopy or virtual chromoendoscopy with targeted biopsies for neoplasia surveillance in patients with long-standing colitis. However, there is still limited proof that better detection of neoplasia by chromoendoscopy also translates into reduced CRC mortality or decreased risk of interval CRC. In the era of high-definition and virtual chromoendoscopy, the value of random biopsies is controversially been discussed. In general, most neoplasia in IBD is macroscopically visible. Therefore, targeted biopsies are mostly recommended for surveillance and in the situation of quiescent disease activity and adequate bowel preparation, non-targeted four-quadrant biopsies should be abandoned. Training seems to be of paramount importance to achieve the skills for an adequate surveillance in IBD. Most recently, the ESGE proposed a new training curriculum to address this important topic. Finally, advanced endoscopic imaging is recommended to assess the borders of a lesion in previously colitic mucosa, to assess resectability. Data on advanced endoscopic imaging for characterization of IBD-related lesions is so far not convincing and therefore, standard histology can still not be replaced.
Reengineering the microbiome in prevention and therapy of IBD

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After so much work around the globe, we’ve reached the consensus first draft of the microbiome in IBD. What does this draft look like? What are the current microbiome therapies now under study? And, what where will be 10 years hence?

There are two features of the consensus draft. First, compared to unaffected individuals, a distinct set of both bacteria and fungi are selectively deficient or over-abundant in patients with active IBD. This set is largely overlapping between Crohn’s disease and ulcerative colitis, although there are distinguishing taxa associated with these IBD subsets. These ecologic changes are correlated with metabolomic changes in the intestinal lumen or feces, many of which are bioinformatically or functionally linked to likely-source microbial organisms. These may be termed “disease activity dysbiosis”. Curiously, the extreme form of such dysbiosis occurs all individuals (CD > UC > healthy), with a characteristic 6 week half-life and uncertain etiology.

Second, most of these compositional and metabolomic features of the microbiome are also observed in patients during remission, and in a substantial number of healthy subjects without IBD. This may be termed “predisease dysbiosis”, and is related to the enterotype structure of the urban human microbiome ecology. Notably, while human genetics has a minimal effect on overall microbial composition, it has a substantial impact on the deficiency of health-associated (presumably beneficial) microbiota, indicating that IBD genetics may be a significant factor in the deficiency part of this microbiome state.

Microbiome-targeted therapy today centers on ecologic restoration, with efforts of some promise using elimination diets, fecal microbial transplantation, and administration of defined bacteria consortia chosen to benefit predicted immunologic endpoints. Ten years hence, a critical advance will be the appreciation of a small number of critical bacterial and fungal taxa and their key bioactive metabolites, which will be assessed and monitored by index metabolites detected in the blood or saliva. Microbiome therapy will separately target disease activity and pre-disease microbial features, akin to induction and maintenance immunotherapy. These will include first generation phage-like agents and drug inhibitors targeting deleterious microbial functions of disease activity dysbiosis; and, integrated diet and targeted microbial replenishment for predisase dysbiosis.
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POSTER ABSTRACTS

Poster Numbers 1 – 88

Author Index to Poster Abstracts
The impact of anti-TNF therapy on intestinal mucosal gene expression of molecules involved in inflammatory response and autoimmunity in patients with inflammatory bowel disease

Nikolaos-Panagiotis Andreou (Athens, GR), George Michalopoulos (Piraeus, GR), Maria Gazouli (Athens, GR)

Introduction: The pathogenesis of Crohn's disease (CD) and ulcerative colitis (UC), the two main entities of inflammatory bowel disease (IBD), is still unclear, but both inflammatory and autoimmune phenomena are involved. Despite proven efficacy of anti-TNF therapy, subgroups of patients have no therapeutic benefit. This study investigated the impact of anti-TNF therapy on the intestinal mucosal gene expression of molecules involved in inflammatory response and autoimmunity in IBD patients.

Methods: In total 43 mucosal biopsy samples were obtained from the rectum during colonoscopy from 29 individuals (14 CD patients, 6 UC patients, and 9 controls) before anti-TNF therapy. The gene expression of 84 genes involved in inflammatory response and autoimmunity was analyzed.

Results: In colonic IBD (UC and CD taken together) of responders to anti-TNF before therapy, the mRNA expression of CCL5, CCL24, CCR3, CD40LG and KNG1 was significantly increased compared to non-responders, while the mRNA expression of IL23R, CCL23, CXCR4, CXCL1, IFNG, TLR2, TLR9, CXCL3, IL1R1, IL1RN, TNF, FOS, CCL16, LY96, CCL4, IL23A, was significantly increased in non-responders as compared to responders to anti-TNF therapy. Most of these dysregulations at baseline in IBD was restored by anti-TNF therapy at responders mainly. No genes remained dysregulated after therapy in IBD responders as compared to controls.

Discussion/Conclusion: Our results demonstrate that many genes involved in inflammatory response and autoimmunity are dysregulated in IBD mucosa. Intestinal expression of these genes may represent a biomarker that predicts therapeutic response to subsequent anti-TNF treatment.
Microscopic ileitis in clinically suspected inflammatory bowel disease patients – Can it predict the future?

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Introduction: Several studies have shown a low yield of biopsies in normally appearing terminal ileum (TI) during ileocolonoscopy for different indications. However, the role of TI biopsies in the setting of patients referred for ileocolonoscopy for clinically suspected inflammatory bowel disease (IBD) is still not well defined and its diagnostic yield is unknown. Moreover, the significance of microscopic ileitis (MI) finding in this setting and the correlation of histological findings with long term clinical outcome has not been fully studied. The current study aims to determine the prognostic yield of biopsies from a normally appearing TI in patients undergoing ileocolonoscopy as part of their evaluation of a suspected IBD, and to evaluate the correlation of histological findings with long term clinical outcome.

Methods: Endoscopic reports of patients referred to the gastroenterology department at the Hillel-Yaffe medical center for ileocolonoscopy in the years 2006–2016, as part of a diagnostic work-up for a suspected IBD were revised. Patients were included if they have normal appearing colon and terminal ileum mucosa by endoscopy, provided that TI biopsies were performed. According to the biopsy results, patients were divided into normal and MI groups. Normal group included patients with normal biopsy or reactive and non-specific changes, while MI group included patients with inflammation or ileitis of any severity. In order to determine the long term clinical outcome, patients in both groups were followed prospectively by tracking gastroenterology and primary care physicians’ reports and when data is missing or equivocal, by direct contact with patients.

Results: Overall 439 patients were considered suitable and were included. Of these 64 (14.6%) had evidence of inflammation of any severity on biopsy and were included in the MI group. Average age (30.8 ± 15.6 vs. 33.2 ± 16.6; p = 0.25) and male gender (48.5% vs. 50%; p = 0.89) didn't differ significantly between groups. Follow-up period was 5.5 ± 2.3 and 6.7 ± 2.3 years for the MI and normal group, respectively. Patients in the MI group were significantly associated with IBD diagnosis during follow-up period as compared to normal biopsy group (19% vs. 2%; p < 0.01). In multivariate analysis, finding of MI was highly associated with development of IBD as compared to normal (OR = 11.98, 95% CI: 4.48–32.01; p < 0.01). Moreover, patients with granuloma or more severe ileitis on biopsy specimen were significantly associated with IBD development (100% vs. 11%; p < 0.01) compared to mild or non-specific inflammation.

Discussion/Conclusion: Microscopic ileitis finding in clinically suspected IBD is associated with increased risk of future diagnosis of IBD.
Ulcerative colitis in association with diverticular disease of the colon: Case report

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Introduction: Ulcerative colitis (UC) is now recognized as a disease involving all age groups. In older patients it may start de novo, or it may exist for a long time in the chronic stage with periodic exacerbations. The incidence of colonic diverticulosis increases with age, with a 45% prevalence in the population > 70 years of age.

Methods: We present the case of a 80-year-old female admitted to our clinic in 2016 due to lower digestive tract hemorrhage and abdominal pain within the last 10 days, associated with fever 1 day prior to admission, nausea and vomiting. Infectious enterocolitis was excluded based on the negative result of the stool culture, which ruled out infections with Escherichia coli spp., Salmonella spp., Shigella spp., Klebsiella spp., and Clostridium difficile. The anamnesis revealed the presence of diverticular disease since 2010. The laboratory tests performed on the first day of admission revealed leukocytosis with neutrophilia (Leu 14,900/μl; Neu 12,710/μl), thrombocytosis (Plt 338,000/μl), anemia (Hb 10.1 g/dl; Hct 30.8%), elevated inflammatory biomarkers (CRP 114 mg/l; ESR 39 mm/h), and low serum urea levels (17.21 mg/dl). The abdominal ultrasound examination was normal. Lower digestive endoscopy pointed out multiple ulcerations, hemorrhage, and edema of the sigmoid colon, thus suggesting a possible IBD and multiple diverticula of the colon. Histopathological examination of the colonic biopsy specimens showed active inflammation associated with architectural changes of the colonic mucosa and crypt abscesses, which highly suggested a chronic inflammatory process, most likely UC.

Results: Therapy with corticosteroids (prednisone 1 mg/kg/day, orally) and 5-aminosalicylate derivatives (mesalazine 50 mg/kg/day, orally), as well supportive treatment (antibiotics – ciprofloxacin 20 mg/kg/day orally, glucose, electrolytes, and analgesics). On the control colonoscopy in 2019 multiple diverticula are observed, no signs of bleeding, level of calprotectin 3298 μg/g.

Discussion/Conclusion: As a few reports have described, diverticular colitis can progress to typical ulcerative colitis, suggesting a possible pathogenic similarity between the two diseases and association between colorectal surgery and disease progression. The diverticula may perforate; localized abscesses or peritonitis may develop; or other complications inherent in either disease may appear. The association of the two diseases results in greater morbidity and mortality.
Organoids derived of inflammatory intestinal biopsies in ulcerative colitis patients lose their inflammatory transcriptional signature during ex vivo culture

Kaline Arnauts (Leuven, BE)

Introduction: Patient derived intestinal organoids provide an excellent tool to unravel the multifactorial mechanisms underlying ulcerative colitis (UC). Organoids develop from stem cell containing intestinal crypts and recapitulate many features of the source tissue. However, it remains unclear if ex vivo organoids retain the inflammatory character of their origin. To address this, we isolated crypts from both inflamed and non-inflamed regions of the colon, created organoids and compared the transcriptome of whole biopsies, crypts and ex vivo cultured organoids.

Methods: Fresh biopsies from both inflamed and non-inflamed segments were obtained during endoscopy from 8 patients with active UC (endoscopic Mayo subscore of ≥ 2) and an accessible border of inflammation. Crypts were isolated and cultured as organoids for 4 weeks with weekly mechanical splitting. RNA was extracted from biopsies, crypts and 1- and 4-week old organoids. RNA sequencing was performed by Lexogen QuantSeq for Illumina. Differential gene expression and pathways were studied through DESeq2 and Ingenuity Pathway Analysis (FDR < 0.05).

Results: Biopsies and crypts from inflamed regions showed separate clustering on principal component analysis (PCA) and significantly higher activation of inflammatory pathways including antigen presentation (p < 0.01 and p < 0.001), interferon signalling (p < 0.05 and p < 0.001) and granulocyte adhesion (both p < 0.001) compared to non-inflamed biopsies and crypts. However, organoids derived from inflamed crypts lost part of their inflammatory character after 1 week in culture. Several inflammatory markers (IFNγ [p = 0.01], IL1β [p < 0.001], JAK1 [p < 0.001]) and pathways involved in antigen presentation (p < 0.005) and interferon signalling (p < 0.001) were significantly decreased after 1 week ex vivo culture compared to inflamed crypts. After 4 weeks in culture, organoids derived from inflamed and non-inflamed regions were indistinguishable in PCA clustering, and expression levels of inflammatory signalling pathways were not significant.

Discussion/Conclusion: We conclude that ex vivo organoids lose their inflammatory transcriptional signature in culture. After 4 weeks in culture, organoids derived from inflamed and non-inflamed biopsies were no longer distinguishable. Therefore, it is not essential to obtain biopsies from inflamed regions to culture organoids from UC patients. We hypothesize that to mimic the inflammatory phenotype and create a physiological representative model, inflammatory components and/or immune cells should be added to the ex vivo culture system.
Investigation of anaemic syndrome in inflammatory bowel diseases

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Introduction: Patients with inflammatory bowel diseases (IBD) are commonly found to have iron deficiency anaemia (IDA) secondary to chronic blood loss and impaired iron absorption due to tissue inflammation. Pathogenesis of the anaemic syndrome is complex and it can be generated by chronic inflammation, repeated blood loss, malabsorption of the folic acid and vitamin B12, etc. Chronic inflammation by TNF-alpha and other cytokines induce increased levels of the iron-regulatory hormone hepcidin, which sequesters iron in macrophages, shunting iron away from erythropoiesis. The formation and release of hepcidin are induced by iron loading and inflammatory stimuli, such as IL-1 or IL-6, whereas its synthesis is blocked by iron deficiency, hypoxia and anemia.

Methods: We evaluated 42 patients with IBD during 5 years, 26 with ulcerative colitis (UC) and 16 with the Crohn’s disease (CD). It was determined hematocrit (Ht) value, hemoglobin (Hb), erythrocytes indices, reticulocyte count, total iron binding capacity (TIBC), latent iron binding capacity (LIBC), serum ferritin, transferrin saturation (TS), fibrinogen, sedimentation rate erythrocytes, C-reactive protein (CRP) – useful to estimate the level of inflammation, serum protein electrophoresis.

Results: 18 of the patients with IBD presented anaemia. In 61.11% (11 patients), intestinal disease was active. The Hb value was 8.3 ± 1.6 g/dl and Ht value was 28 ± 3.5%. The median value of erythrocytes indices was: VEM 87 ± 13 fl, CHEM 29.45 ± 5.3 g/dl, HEM 30.14 ± 4.65 pg, reticulocyte count 0.9 ± 0.5%. In patients with anaemia, CRP, used as surrogate for serum IL-6 is frequently elevated above (8.5 mg/dl), versus CRP level in patients without anaemia. Serum iron concentration was 40 ± 7.2 µg/dl and TIBC = 250 ± 82 mg/dl, both low in this lot.

Discussion/Conclusion: Anaemia is associated with IBD in 42.85% of patients and is thought to be secondary to active inflammation, so that effective IBD therapy could achieve both disease remission and iron status normalization because mucosal healing could stop intestinal bleeding.
Essential thrombocythemia or thrombocytosis secondary to inflammatory bowel disease? (case study)

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Introduction: We reported the case of a 22-year-old woman with persistent stool modifications, thrombocytosis over 600,000/mm³, VSH 20/35 mm, fibrinogen 520 mg/dl, PCR 4.6 µg/ml. It was evaluated by endoscopy, the diagnosis was inflammatory bowel disease (IBD) and received only symptomatic therapy and intermittent sulfasalazine.

Results: Bone marrow aspirate is normocellular without significant changes in the erythroid and granulocyte series, moderate increase in megakaryotic cells. Thrombocytosis is considered secondary to IBD and no specific therapy is initiated.

At the age of 28 she presented a migraine that is resistant to aspirin, considered to be due to hormonal dysfunction and gallbladder lithiasis, thrombocytosis is maintained at 600,000–800,000/mm³.

At the age of 32, the patient has diffuse abdominal pain, changes of transit and fecal materials, abdominal distension; the thrombocytosis is 850,000/mm³. Abdominal ultrasound reveals splenomegaly 13 cm and significant thrombosis of portal vein in Doppler ECHO. Bone marrow aspiration show no increased cellularity, only an increased number of large, sometimes gigantic megakaryocytes, with hyperlobulated nucleus and mature cytoplasm. It is initiated treatment with Hydrea 1 g/day, low dose aspirin (75 mg/day) plus endovenous and per os anticoagulant therapy. Clinical symptoms have improved, but portal venous thrombosis persists. Later, it is administrated INF 3 MU every 2 days with the stabilization of the platelets number, about 400,000/mm³.

At the age of 40, patient presented a stable hematological disease negative for mutation in JAK2, CALR, or MPL, but bone marrow biopsy shows normocellularity with prominent large to giant megakaryocytes with abundant mature cytoplasm and deeply lobulated and hyperlobulated nuclei. She has portal hypertension and presence of esophageal varices of II degree secondary to venous portal thrombosis. She needs continuous myelo-suppressive therapy.

Discussion/Conclusion: Essential thrombocythemia is a non-reactive, autonomous disease that is part of chronic myeloproliferative disease and the diagnosis should exclude secondary and/or other thrombocytosis.
An old man with Crohn's disease presented by subileus clinic and diagnosed by double balloon enteroscopy

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Introduction: Crohn’s disease (CD) is a disease that causes inflammation or swelling of any part of the gastrointestinal (GI) tract. The part most commonly affected is the end part of the small intestine, called the ileum. We, here, presented a case with CD diagnosed by taken specimens during the double balloon enteroscopy and enteroscopy findings.

Methods: A 60-year-old male was admitted to the clinic with abdominal pain and vomiting. His medical history includes diabetes and hypertension, besides cholesistectomy and inguinal hernia operation. He was an ex-smoker.

Results: Labarotory examination showed nothing. Abdominal tomography showed that the wall of the jejunum and ileum were thickened. Small bowel contrast examination revealed thickened wall in the ileum with ulceration and nodularity. Colonoscopy showed no abnormality in the colon and 15 cm of the distal part of the ileum. Oral double balloon enteroscopy first performed and showed multiple xantomas in the jejunum and proximal ileum segments. Then, double balloon enteroscopy performed by anal route and showed semisircular ulcers and narrowing in the ileum, approximately 100 cm far from the ileocecal region. Multiple biopsies performed and specimens showed ulceration with active inflammation. Quantiferon was positive as PCR-tuberculosis of the specimens from the ileum was negative. Chest examination was normal. Crohn’s disease was diagnosed in this elderly patient.

Discussion/Conclusion: Crohn’s disease affects men and women equally and seems to run in some families. Crohn’s disease occurs in people of all ages, but it most commonly starts in people between the ages of 13 and 30. Men and women who smoke are more likely than non-smokers to develop Crohn’s disease. People of Jewish heritage have an increased risk of developing Crohn’s disease, and African Americans have a decreased risk. The most common symptoms of Crohn’s disease are abdominal pain, often in the lower right area, and diarrhea. In our presented case, suspected radiological findings confirmed by double balloon enteroscopy with histologic examination. Tuberculosis should be carefully excluded in patients with ileum ulcers and positive blood quantiferon test results, particularly in developing countries which tuberculosis still is endemic.
Patients with Crohn's disease had an increased NET development on long-term follow-up

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**Introduction:** The incidence of colorectal (adeno)cancer is increased in patients with inflammatory bowel diseases (IBD) and mainly due to the long duration of IBD. However, neuroendocrine tumor (NET) risk was not fully evaluated in IBD, particularly Crohn's disease (CD). We aimed to determine whether there is an increased risk for the development of NET in CD. We also questioned whether the incidence of any cancer in patients with IBD is increased.

**Methods:** We studied on patients with ileocecal resection at the Surgical Clinic of Bezmialem Vakif University Medicine Faculty Hospital between 2011-2017. Of the 246 patients performed ileocecal resection for any reason (15 to 98 and average 59 years), 56 were due to CD with or without fistula and stricture.

**Results:** Of the 246 patients, 16 with NET, 6 with carcinoid tumour, 164 had adenocancer and 60 were non-malignant reason. In subgroup analysis, of the 56 patients with CD, 2 had NET, 4 had carcinoid tumour, 4 showed adenocancer. Of the 190 non-IBD patients, 14 had adenocancer with NET differentiation, 2 had carcinoid tumour, 160 with adenocancer and 14 with non-malignant reason.

**Discussion/Conclusion:** Our study showed that patients with CD had an increased NET development risk.
Testing the availability of fecal calprotectin (instead of colonoscopy) in the remission/activation evaluation in patients with inflammatory bowel diseases at an outpatient IBD clinic

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**Introduction:** The diagnosis and the activation and remission of IBD is classically made by the mucosal changes during the lower GI evaluation with colonoscopy. Colonoscopy is an invasive procedure that is wanted to be avoided from time to time due to both it is invasive and takes time for both the physician and patient and sometimes requires hospitalization. Therefore, non-invasive tools are needed to evaluate the activation of inflammatory bowel diseases instead of the colonoscopy. The CRP, leucocyte, ESR and Platelet values measured in blood have been used because of this. However, as seen in the clinical practice, in addition to all patients with activation, one or more of these parameters are measured high in patients with very little actually active disease. Fecal calprotectin levels are the new non-invasive tools used in inflammatory bowel diseases and indicate inflammatory activation in the bowel. In this study, the fecal/calprotectin sensitivity was tested and compared with the classical blood tests such as CRP, leucocyte, ESR, Platelet count.

**Methods:** A total of 21 patients were included in this study. The data of 3 patients were lacking, so they were excluded from the study. The study was designed prospectively (30.01.2018–30.07.2018). The follow-up time was at least 6 months for each patient. In this study, the diagnoses of the patients were made with the CT (abdominal oral iv contrast), clinical and laboratory (primary the CRP, WBC, ESR, Platelet, and fecal calprotectin) parameters. The mesalazine and immunosuppressive therapies (azathioprine ± biological agent) were used for the patients with Crohn’s disease. The ulcerative colitis patients were also managed similarly. The colonoscopy and laboratory parameters taken at the beginning and after a treatment period of at least 6 months were compared.

**Results:** The data and colonoscopy and laboratory (CRP, ESR, Platelet, WBC, stool/calprotectin) parameters of 18 patients were complete. When examined individually, in 6 of 18 patients, at least one of the CRP, WBC, ESR, Platelet, the classical activation parameters, measured during the activation period was high and became normal when the disease was in remission. On the other hand, in all 18 patients, the fecal calprotectin levels were measured as very high or too high to be measured at the beginning of the disease. In colonoscopic complete or partial remission, sometimes depending on the severity of the disease, partial but significant recoveries were seen in the complete remission calprotectin.

**Discussion/Conclusion:** The fecal calprotectin levels were found to be closely correlated with the severity of the inflammatory bowel disease. When the classical 4 were evaluated individually, the CRP value was found to be more sensitive to the severity of the disease compared to the other three. However, it was seen that it was a useful tool only in 1/3 of the patients. In 2/3 of the remaining patients, it was not possible to report any sensitivity
for the CRP. The calprotectin levels showed colonoscopic changes, namely the changes related to the endoscopic mucosal remission and remission level. In conclusion, the fecal calprotectin levels rise to prominence, when it is considered at least on the patient basis, as a useful, as well as cheap, non-invasive tool, which does not take up much time of both the physician and patient, for ensuring the reduction of the number of invasive, expensive and time-consuming colonoscopies done throughout the life in patients with chronic inflammatory bowel disease.
Ascites in a young woman: A rare presentation of eosinophilic gastroenteritis

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Introduction: Primary eosinophilic gastrointestinal disorders are characterized by abnormal accumulation of eosinophils in the gastrointestinal tract in the absence of secondary causes of eosinophilia and mainly include eosinophilic esophagitis and eosinophilic gastroenteritis (EGE). Eosinophilic ascites (EA) represent an unusual presentation of EGE, occurring when there is serosal involvement of the affected section of the bowel.

Results: We report the case of a 29-year-old white woman, without any medical history. She came to emergency department with a 2 weeks history of abdominal distention and vomiting without fever or abdominal pain. She denied dysphagia, difficulty eating or food impaction. She presented distended abdomen with active bowel sounds and ascites. Hepatomegaly, splenomegaly, and abdominal mass were ruled out. Urgent abdominal ultrasonography confirmed these clinical signs but ruled out portal hypertension. A complete blood count revealed an increase in the white cell count (13,650 m/l with 6380 m/l eosinophils), elevated C reactive protein (25.8 mg/l), and normal results in the liver and renal function tests. Tumor markers, celiac serology, and digestive parasites were normal during admission. Serology for human immunodeficiency virus, hepatitis B and C viruses was negative. Serum IgE was elevated (> 500 UI/ml). A thoracic-abdominal pelvic computed tomography scan showed a high abundance pelvic free fluid, which was identified as moderate ascites without lymphadenopathies. Paracentesis revealed hematic fluid (total protein, 5.60 g/dl) with abundant count of eosinophils. No cytological signs of malignancy were detected. Upper gastrointestinal endoscopy up to the second part of duodenum did not reveal macroscopic anomalies. Histopathology showed heavy infiltration of eosinophils corresponding to esophageal epithelium (35 cells/HPF). Stomach and duodenum biopsies were normal. With a high suspicion of EA, we started the patient on oral prednisone (60 mg/day). Symptoms resolved rapidly after a few days, the blood eosinophil count (1800 m/l) decreased, and the abdominal fluid gradually disappeared (confirmed by ultrasonography). Oral corticosteroids were maintained for 2 weeks and then tapered. The patient presented 3 similar episodes that were resolved after corticosteroid treatment. After 2 years follow-up, the patient was clinically asymptomatic without medication, and her abdominal scan was normal.

Discussion/Conclusion: Eosinophilic gastroenteritis is a rare condition with a non-specific and highly variable clinical presentation, which requires a high level of clinical suspicion. It is a diagnosis of exclusion. Secondary causes of eosinophilia such as intestinal tuberculosis, parasitosis, and malignant neoplasms should be excluded.
Predictive factors for extraintestinal manifestations associated with Crohn’s disease

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Introduction: Inflammatory bowel diseases (IBD) are frequently accompanied by extraintestinal manifestations (EIM). In the course of Crohn's disease, their frequency varies from 24 to 40%. They often complicate an active disease but they can reveal this latter. The purpose of this work was to precise the epidemiological profile and risk factors associated with these events in our Crohn's disease patients.

Methods: A retrospective study including 95 patients hospitalized in our department for Crohn's disease. All patients benefited from dermatological and ophthalmological examination, liver function assessment, radiography of sacroiliac joints and bone density test.

Results: The EIM were present in 45 patients (47.3%). There were 33 men and 12 women with a sex ratio of 2.75 and an average age of 36.8 years (23–72 years). The median follow-up was 31 months (4–108 months). The most frequent EIM were osteoarticular (53.3%), followed by hepatobiliary involvement (22.2%) followed by cutaneous (17.7%) and ocular (15.5%) lesions. Two types of EIM were found in 8.9% of cases. Osteoarticular EIM corresponded to low bone mineral density in 12 patients, peripheral joint manifestations in 7 cases, axial joint manifestations in 6 cases. It involved both peripheral and axial joints in one case. Seven patients had fatty liver disease and three had impaired hepatic status in relation to primary sclerosing cholangitis. Cutaneous EIM were dominated by erythema nodosum in 5 patients, followed by oral aphthosis (1 case), Sweet's syndrome (1 case) and pyoderma gangrenosum (1 case). All patients with ocular EIM had anterior uveitis. Compared to other patients with Crohn's disease, patients with EIM were more frequently male (73% vs. 54%, p < 0.05) and smokers (42% vs. 34%, p < 0.05). They had more frequently anoperineal lesions (37% vs. 20%, p < 0.05). In multivariate studies, the independent predictor of EIM was the presence of anoperineal lesions.

Discussion/Conclusion: Extraintestinal manifestations associated with Crohn's disease were found in 47.3% of our patients. These were more frequently associated to anoperineal lesions.
Inflammatory stricturing Crohn’s diseases: Results of medical treatment

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Introduction: Stricture is the most common complication of Crohn’s disease (CD). Treatment of stricturing CD depends on the inflammatory or fibrotic character of the stricture. However, therapeutic management of stricturing CD remains a complex situation as it has been shown that inflammatory and fibrosis are two overlapping entities. The aim of our study was to assess the short- and long-term impacts of medical treatment in inflammation stricturing CD and to identify predictors of therapeutic failure and lead to surgery.

Methods: A retrospective study over a period of 15 years (2001–2016) including all patients with CD receiving medical treatment for symptomatic inflammatory stricture was performed. The inflammatory nature of stricture was mainly identified by cross-sectional imaging examinations showing signs of active inflammation. Therapeutic failure was defined as symptomatic recurrence leading to hospitalisation or endoscopic dilation or surgery. Short and long-term medical therapy failure were defined by occurrence of cited above events within respectively 6 and 24 months after initiation of medical therapy.

Results: Fifty-one inflammatory strictures were collected in 43 CD patients who received medical treatment. Medical therapy was based on a full-dose of oral corticosteroids in 37 cases (73%) and anti-TNF agents in 14 cases (27%). Azathioprine was prescribed in maintenance for patients who received corticosteroids in 21 cases (63%) and in combination with anti-TNF (combotherapy) in 12 patients (85%). The short-term therapeutic failure rate was 22% (n = 11) and the long-term therapeutic failure rate was 45% (n = 23). Nineteen patients (37%) needed surgery within an average of 11 months (7–18 months).

In multi-variate analysis, only the presence of fistulas was associated with short-term medical therapy failure (p = 0.014). Active smoking (HR = 3.46, 95% CI: 1.129–10.821, p = 0.009), age at diagnosis (A1 according to the Montreal classification) (HR = 2.02, 95% CI: 0.613–6.715, p = 0.036) and presence of enteroenteric fistulas (HR = 7.188, 95% CI: 1.804–28.634, p = 0.001) were independent predictors of long-term medical therapy failure and surgery requirement.

Discussion/Conclusion: Despite the identification of inflammatory nature of intestinal stricture, medical treatment fails in half of the cases and nearly 40% of patients are operated on after 2 years. This emphasises the fact that the two entities, inflammation and fibrosis, cannot be dissociated. Identify predictors of therapeutic failure, may allow us to select from the outset patients at high risk of surgery.
First onset of colitis after Helicobacter pylori eradication therapy

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Introduction: While most researches shows significantly lower incidence of Helicobacter pylori infection in patient with inflammatory bowel disease (IBD), suggesting its protective role in development of aforementioned [1, 2], there are some indicators that eradication therapy may precede to development of IBD.

Methods: Case report.

Results: A 70-year-old female, with history of postmenopausal osteoporosis and thyroidectomy due to autoimmune hyperthyreosis, presented to our outpatient clinic with symptoms of dyspepsia. Upper endoscopy was performed and H. pylori-positive chronic gastritis with partial metaplasia was diagnosed. 7th day of eradication therapy with clarithromycin, metronidazole, rabeprazole and probiotic, patient developed severe urticaria with acute oedema of the tongue and triple therapy was discontinued. Clarithromycin was introduced as a first line therapy while patient had vague symptoms after penicillin administration in childhood. Meanwhile she underwent excision of vocal fold leucoplakia and therefore stopped smoking. Before second line therapy with amoxicillin, levofloxacin, esomeprazole, bismuth oxide and probiotics was introduced penicillin allergy was excluded by allergy testing. A few days after finishing with second line therapy patient presented to emergency department with haematochezia and mild abdominal pain. Endoscopic and histologic findings verified pancolitis (Mayo score 2). Extended microbial testing was performed and large number of Candida spp. was revealed. Initial calprotectin value was 1542.2 mg/kg so oral and topical therapy with mesalazine was initiated. In consultation with clinical pharmacologist systemic antifungal therapy was also encountered. Control colonoscopy, performed 4 months later, showed mild active disease in proctosigmoid (Mayo score 1) and calprotectin value of 220.9 mg/kg. At that time patient reported only occasional abdominal discomfort. Mesalazine therapy was continued and high potency microbiotic food supplement was added.

Discussion/Conclusion: Gut microbiota plays an important role in nowadays perception of IBD pathogenesis, and impact of double antibiotic therapy in combination with proton pump inhibitor certainly impact microbiota tremendously [3]. Whether studies till know have not shown significant connection between eradication therapy and new onset of IBD in general population, further subgroup analyses are warranted [4].
The predictive role of gut microbiota in treatment response to vedolizumab and ustekinumab in inflammatory bowel disease

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Introduction: The past decade has highlighted the central role of the gut microbiota in inflammatory bowel disease (IBD). The fecal microbiota is evolving as a useful predictive and diagnostic biomarker in the development of personalized medicine. We here investigated if the fecal microbiota aids in predicting therapeutic response to vedolizumab (VDZ) or ustekinumab (UST) in Crohn’s disease (CD) and ulcerative colitis (UC).

Methods: Fecal samples of 116 patients with IBD, treated with UST (n = 68 CD) or VDZ (n = 30 for CD and 18 for UC) with endoscopic active disease were collected prior to biological therapy. Quantitative microbiota phylogenetic profiling was conducted by combining 16S rRNA gene sequencing and microbial loads determination using flow cytometry. Endoscopic response in the UST cohort was defined as a 50% decrease in SES-CD score at week 24. Remission in the VDZ cohort was defined as an endoscopic Mayo-subscore of 0–1 at week 14 in UC and absence of endoscopic ulcerations endoscopy at week 24 in CD. Multivariate hyperbolic tangent neural network models (JMP) were trained to predict treatment response based on features describing the baseline fecal microbiota, clinical data (age, sex, BMI, diagnosis, disease duration and smoking) and biomarkers (C-reactive protein, albumin, hemoglobin and fecal calprotectin) or the combination. The cohorts were split in a training (2/3) and validation set (1/3). Fecal microbiota features comprised the enterotypes and quantitative abundance of taxa significantly (p < 0.1) correlated with outcome.

Results: Ten (14.7%) UST and 27 (56.2%) VDZ patients showed endoscopic response (UST) or remission (VDZ). 13 genera correlated with treatment outcome in the VDZ cohort and 14 in the UST cohort, with 3 genera overlapping. Neural networks were trained to predict treatment response in VDZ and UST on 2/3 of the cohorts, based on baseline clinical features and biomarkers, baseline microbiota features, or both. For VDZ treatment response prediction, all models had reliable training (training: AUC = 0.71–0.87; sensitivity = 0.62–0.88, specificity = 0.55–0.85), but the combined model had the best validation performance (n = 17; misclassification rate = 31%). UST response prediction was not very reliably trained on microbiota features alone (AUC < 0.70) and was best predicted by the combined features (training AUC = 0.86; sensitivity = 0.88, specificity = 0.33, with a validation misclassification rate of 4% (compared to 13% for the clinical + biomarkers model).
**Discussion/Conclusion:** Our analyses do show that quantitative fecal microbiota profiling is helpful in predicting therapeutic outcome and provides valuable additional information beyond clinical features and biomarkers. Nevertheless, these predictive models were trained on still relatively small cohorts, and therefore further validation in preferably large prospective randomized cohorts is needed.
Hematological scales in ulcerative colitis patients treated with infliximab – A single-centre experience

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Introduction: There is a growing body of evidence that new routinely obtained non-invasive blood indices could become markers of inflammation in UC patients. We aimed in our survey to look for relationships between hematological parameters in UC patients treated with infliximab (IFX).

Methods: One hundred twelve participants were enrolled to the study: 56 patients with active UC and 56 persons in control group. UC patients were treated with IFX (3 doses of standard induction therapy). Neutrophil-to-platelet ratio (NLR), platelet-to-lymphocyte ratio (PLR), mean platelet volume-to platelet ratio (MPR) and their correlations with red blood cell and platelet indices were measured in the blood of UC patients at 0, 2, and 6 weeks of induction regimen and in follow-up six weeks later. Results were compared with control group.

Results: NLR and PLR levels in UC patients prior to the first dose of IFX were higher in comparison to controls; MPR value was lower (p < 0.001). NLR value decreased after finished IFX induction therapy (p < 0.001). PLR level became lower too, however not significantly. MPR value became higher (p < 0.001). Several correlations were noticed in UC patients. PLR correlated positively with mean platelet volume (MPV) and red blood cell distribution width (RDW) before the introduction of IFX (p < 0.01); there were also positive correlations between MPR and both – platelet distribution width (PDW) and plateletcrit (PCT) (p < 0.001). In follow-up after finished induction regimen PLR correlated positively with NLR and PCT (p < 0.001); negative correlations were noticed between PLR and both MPR and PDW (p < 0.01).

Discussion/Conclusion: Deviations in white blood cell, red blood cell and platelet indices seem to be closely linked to each other in UC patients and affected by IFX therapy. NLR, PLR and MPR are potential diagnostic tools in the monitoring of UC patients.
Is red blood cell distribution width an essential parameter in Crohn’s disease patients? A single-centre observation

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Introduction: The role of red blood cell distribution width (RDW) as a potential marker of inflammation or mortality in the course of various disorders has been highlighted recently. The aim of our study was to analyze levels of RDW and its derivatives – red blood cell distribution width-to-platelet ratio (RPR) and red cell distribution width-to-lymphocyte ratio (RLR) – in patients with Crohn’s disease (CD) qualified to the treatment with infliximab (IFX).

Methods: Study group consisted of 40 patients with active CD; control group was represented by 40 healthy volunteers. CD patients were treated with IFX (five doses of standard therapy). RDW, RPR, RLR and their relationships with CRP, platelet indices – mean platelet volume (MPV), plateletcrit (PCT) and platelet distribution width (PDW) – were assessed in the blood of CD patients at 0, 2, 6, 14 and 22 weeks. Results were compared with controls.

Results: Baseline RDW and RLR levels in CD group were higher in comparison to control group (p < 0.001); RPR value was lower (p > 0.05). After five doses of IFX the increase in RPR level was noticed in CD patients (p = 0.05); values of RLR and RDW decreased (p < 0.001 and p > 0.05, respectively). We also observed significant correlations at baseline and after five doses of IFX. RPR correlated negatively with CRP and PCT (p < 0.01); positive correlations between RPR and both MPV and PDW were noticed, too (p < 0.01). Additionally, RLR correlated positively with RPR after IFX treatment.

Discussion/Conclusion: Collected data suggest that indices containing RDW should be explored and potentially included to the parameters routinely monitored in CD patients.
Compliance to vaccination guidelines in patients with immune-mediated inflammatory diseases: A single-center, cross-sectional study

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Introduction: Despite the existence of (inter)national guidelines, vaccination in patients with immune-mediated inflammatory diseases (IMID) has not yet been optimally integrated in routine clinical practice. In 2015, we reported that only 32% of our patients with inflammatory bowel disease (IBD) were completely vaccinated according to guidelines. We evaluated the evolution of vaccination coverage between 2015 and 2018 in IBD patients, and compared the current coverage with other IMID patients.

Methods: Between August 2018 and October 2018, the vaccination status of 1488 consecutive IMID patients (45% male, median age 51 years) was collected at the outpatient clinics of a tertiary referral center (55% gastroenterology, 43% rheumatology, 3% dermatology). A one-page vaccination questionnaire was completed by the treating physician and reasons for non-vaccination were recorded. Missing data were added after contact with the general practitioner or by consulting the national web-based system ‘Vaccinnet’.

Results: Among IBD patients, vaccination rates had increased significantly from 2015 to 2018, namely 62% vs. 73% for pneumococci \( p < 0.001 \), 53% vs. 66% for hepatitis B \( p < 0.001 \), and 32% vs. 42% for all vaccines \( p < 0.001 \). One hundred and seventy-seven patients were included in both IBD cohorts. One hundred and three were not completely vaccinated according to guidelines in 2015 and 37 of them (36%) changed vaccination behavior in the last 3 years. In 2018, vaccination rates were significantly greater in IMID patients followed at the gastroenterology department vs. patients followed at rheumatology, namely 76% vs. 70% for influenza \( p < 0.05 \), 73% vs. 34% for pneumococci \( p < 0.001 \), 66% vs. 32% for hepatitis B \( p < 0.001 \), 80% vs. 60% for tetanus \( p < 0.001 \), and 42% vs. 22% for complete vaccination according to guidelines \( p < 0.001 \). Regarding dermatology patients, IBD patients more frequently received a hepatitis B vaccination (66% vs. 47%, \( p < 0.05 \)). Non-awareness (46% for pneumococcus) and no specific reason (39% for influenza, 55% for hepatitis B and 51% for tetanus booster) were the most commonly reported reasons for non-vaccination.

Discussion/Conclusion: Thirty-four percent of all IMID patients were vaccinated according to guidelines. Although recent efforts on vaccination education in IBD patients have significantly improved vaccination rates, there is still need for awareness in both patients and health care professionals.
Biological therapy increases NCR+ ILC3 levels in IBD patients

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Introduction: Innate lymphoid cells (ILCs) reside at mucosal barriers where they exhibit high cytokine producing capacity to maintain homeostasis and control infections. Natural cytotoxicity receptor (NCR) positive ILC3s, an important source of intestinal IL-22, have been shown to be decreased in the mucosa of patients with Crohn’s disease (CD) and ulcerative colitis (UC) in favour of pro-inflammatory ILC1s. To study whether current biological anti-TNF, ustekinumab (UST) or vedolizumab (VDZ) therapy can restore the intestinal ILC balance, ILC frequencies were determined in serial blood and biopsies samples.

Methods: We included 26 CD patients initiating UST, 14 patients initiating VDZ (9 CD, 5 UC), 14 CD patients initiating anti-TNF (8 infliximab, 6 adalimumab) and 10 healthy controls (HC) without endoscopic abnormalities. All cohorts were matched for age, gender and age at diagnosis. Colonic biopsies and blood were taken at baseline and during endoscopic assessment (week 8–14 UC, 24 CD). Peripheral blood and lamina propria mononuclear cells were stained for flow cytometric analysis. Pairwise comparisons were performed on ILC numbers determined as frequency of total ILC or total leukocyte population.

Results: Intestinal NCR+ ILC3 levels before initiation of biological treatment were significantly decreased in anti-TNF and VDZ cohort (42.0, 37.5 vs. 86.8% of total ILC, both p < 0.001) while ILC1 levels were increased (15.7, 7.7 vs. 2.7, both p < 0.01) as compared to HC. In contrast, ILC subgroup levels were not different in the UST cohort (NCR+ ILC3: 74.8, ILC1:2.4, p = 0.9). In the anti-TNF and VDZ cohort, recovery of NCR+ ILC3s compared to start (p = 0.04, p = 0.03) was observed after first endoscopic evaluation independent of treatment response. Mucosal ILC levels could not be correlated to peripheral ILC levels (r = 0.39, p = 0.27), however an increase of peripheral NCR+ ILC3s in the total ILC (Fig. 1) and leukocyte population could be observed in both the anti-TNF (p = 0.01) and UST (p = 0.001) cohort as compared to the start of therapy. In contrast, no effect of VDZ (p = 0.47) was observed on peripheral ILC levels.

Discussion/Conclusion: Biological therapy can restore the intestinal ILC levels towards homeostatic proportions even in absence of endoscopic response. Anti-TNF and UST treatment increased NCR+ ILC3s levels in the circulation, which are not described in physiological conditions. In contrast no increased NCR+ ILC3s levels were not observed in VDZ-treated patients. NCR+ ILC3 level will be correlated to cytokine levels in future.
Predictive factors for an aggressive clinical course in ulcerative colitis

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Introduction: The natural course of ulcerative colitis can range from an indolent course with prolonged periods of remission to aggressive, incapacitating disease. Predicting which patients are more susceptible to developing severe disease is important, especially when choosing therapeutic agents and treatment strategies. We considered UC to be aggressive when patients had a high relapse rate (> 2), need for surgery, development of colon cancer, or extraintestinal manifestations. The purpose of our study was to assess the risk factors associated with an aggressive UC.

Methods: A retrospective study that included 70 patients with UC divided into 2 groups: the first group with aggressive UC compared to a second group of patients with UC who did not meet the criteria.

Results: The average age of patients with aggressive UC was 32 years (17–59 years) with a sex ratio of 0.5. The average BMI was 21.83 kg/m². Sixty-six percent of these patients had an extensive involvement of the colon and 21% had deep ulcerations at the onset of the disease. Forty-eight percent of these patients had extraintestinal manifestations. Fifty-five percent of the patients were on immunosuppressive drugs. Patients with aggressive UC were more often younger at the onset of the disease (32.7 vs. 37.48 years, p < 0.05), with a higher incidence of pancolitis (66% vs. 33%, p = 0.03). There was no significant difference between the 2 groups regarding sex (44% males vs. 36%, p = 0.56), BMI (21.83 kg/m² vs. 22.63 kg/m², p = 0.54) and the disease duration (8.5 years vs. 11.9 years, p = 0.76).
Patients with aggressive UC needed more frequently steroids (100% vs. 33%, p = 0.0001) and immunomodulaters (55% vs. 10%, p = 0.0001).

Discussion/Conclusion: In our study aggressive UC was significantly associated with young age at diagnosis and an extensive involvement of the colon.
Inflammatory bowel diseases patient profiles are related to specific information needs – A nationwide survey

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Introduction: IBD is a heterogeneous, lifelong disease, with an unpredictable and potentially progressive course, that may impose a negative psychosocial impact on patients. While informed patients with chronic illness have improved adherence and outcomes, previous research showed that the majority of IBD patients receive insufficient information regarding their disease. The large heterogeneity of IBD and the wide range of information topics makes a one-size fits all knowledge resource overwhelming and cumbersome. We hypothesized that different patient profiles may have different and specific information needs, the identification of which will allow building personalized computer-based information resources in the future.

Methods: We conducted a nationwide survey addressing hospital-based IBD clinics. A total of 571 patients completed a 28-item questionnaire, rating the amount of information received at the time of diagnosis and the importance of information, as perceived by participants, for a newly diagnosed patient, and for the participants themselves, at the current time. We performed an exploratory factor analysis of the crude responses aiming to create a number of representative knowledge domains (factors) and analyzed the responses of a set of 15 real-life patient profiles generated by the study team.

Results: Participants gave low ratings for the amount of information received at disease onset (averaging 0.9/5) and high ratings for importance, both for the newly diagnosed patients (mean 4.2/5) and for the participants themselves at the current time (mean 3.5/5). Factor analysis grouped responses into six information-domains. The responses of selected profiles, compared with the rest of the participants, yielded significant associations (defined as a difference in rating of > 0.5 points with a p < 0.05). Patients with active disease showed a higher interest in work & disability, stress & coping, and therapy & complications. Patients newly diagnosed at age > 50, and patients with long-standing disease (> 10 years) showed less interest in work & disability. Patients in remission with mesalamine or no therapy showed less interest in all domains except for nutrition and long-term complications.

Discussion/Conclusion: We demonstrate unmet patient information needs. Analysis of various patient profiles revealed associations with specific information topics, paving the way for building patient-tailored information resources.
Evaluation of cardiac and pulmonary manifestation in patients with Crohn’s disease

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Introduction: Pulmonary and cardiovascular manifestations of inflammatory bowel disease may be incidental findings that cause no symptoms, but could be a source of considerable morbidity and mortality. The purpose of this study was to evaluate the pulmonary function and cardiac involvement at patients Crohn’s disease.

Methods: In the study was enrolled 48 patients diagnosed with Crohn’s disease (in remission, with median age 38 years, range 18–48; 62.5% males) without cardiovascular and pulmonary diseases. They were compared with 24 healthy subjects matched for age and sex. All patients underwent hert ultrasound and pulmonary function tests: forced expiratory volume in 1 s (FEV1), forced vital capacity (FVC), Tiffeneau value (FEV1/FVC).

Results: The cardiac involvement at patients with Crohn’s disease had higher pulmonary artery systolic pressure (45 ± 6 vs. 40 ± 3 mm), larger left atrial antero-posterior dimension (31 ± 6 vs. 28 ± 6 mm) and reduced left ventricular ejection fraction (57 ± 4 vs. 61 ± 8 mm) than healthy subjects. Pulmonary function tests was abnormal in 14 (29.1%) patients and 1 (4.1%) control (p < 0.0005). Of the 14 patients with abnormal pulmonary function tests, obstructive and restrictive defects are detected in 6 (42.8%) and 1 (14.1%). No relation of pulmonary function tests abnormalities was found with sex, age and duration of disease.

Discussion/Conclusion: Our study suggests that patients with Crohn’s disease have abnormal pulmonary functions with predominant involvement of restrictive defects and also heart disease is common in these patients.
Sacroiliitis an “undiagnosed” extraintestinal manifestation in patients with inflammatory bowel disease

Ionela-Cristina Deliu (Bals, RO), Nicusor Deliu (Bals, RO), Oana Diaconu (Craiova, RO), Amelia Genunche (Craiova, RO), Daniela Neagoe (Craiova, RO)

Introduction: Extraintestinal manifestations in inflammatory bowel disease are frequently observed and involve the joints. An inflammatory arthropathy associated with ankylosing spondylitis is found in patients with inflammatory bowel disease but may go undiagnosed. The purpose of this study was to determine the prevalence of sacroiliitis in inflammatory bowel disease and to determine association between clinical characteristics of inflammatory bowel disease and sacroiliitis.

Methods: In the study was enrolled 68 patients diagnosed with inflammatory bowel disease and 67 controls. All patients and controls underwent a gastroenterological and a rheumatological clinical examination. Sacroiliitis was confirmed using IRM examinations. Two blinded readers used a standardised model where presence of ankylosis or erosion score > 3 indicated sacroiliitis. Inflammatory bowel disease scoring was blinded to the presence of sacroiliitis. The inflammatory articular disease was defined as persistent or recurrent joint pain with an inflammatory pattern (night pain, progressive relief during the day, morning stiffness lasting at least 30 minutes).

Results: A total of 68 patients with inflammatory bowel disease, 42 with Crohn's disease and 50% male were included. 41.1% patients fulfilled the criteria for inflammatory articular disease, whereas 19.1% presented with other extraintestinal manifestations. IRM examination identified 12 (17.6%) with sacroiliitis. Radiologists had reported sacroiliitis in 41.6% of these. Three patients had been to a spondylitis clinic. More than 5 sacroiliac erosions were associated with radiologist-reported sacroiliitis (p < 0.0001). There was no difference in prevalence between Crohn’s disease and ulcerative colitis. Sacroiliitis was associated with male sex, known arthritis, pain as an inflammatory bowel disease symptom.

Discussion/Conclusion: Patients with inflammatory bowel disease have a high prevalence with inflammatory articular disease. Sacroiliitis is underdiagnosed in inflammatory bowel disease and is associated with male sex, arthritis, and inflammatory Crohn's disease.
Diagnosis of complications in intestinal inflammatory diseases

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Introduction: Inflammatory bowel diseases are idiopathic inflammatory diseases that have a chronic evolution, with remission periods and disease activity. In case of Crohn’s disease and ulcerative colitis there will be a difference between the extradigestive manifestations and the complications of the disease or the treatment. The objective of the study was to evaluate the occurrence of complications in intestinal inflammatory diseases. Complications can be located locally, ileo-cecally, at any segment of the digestive tract, but also at the extraintestinal level (bones, joints, eyes, skin, liver, kidneys).

Methods: The study included 140 patients diagnosed with Crohn’s disease and ulcerative colitis between May 2013 and December 2108 based on clinical criteria (rectangles, diarrheal stools, abdominal pain with sub-obesity localization and right iliac fossa) and paraclinical (inflammatory markers: sedimentation of red blood cells, C-reactive protein, fibrinogen, fecal calprotectin, radiological, imaging-CT/MRI and endoscopic methods).

Results: 140 patients were diagnosed with inflammatory bowel diseases, 80 with Crohn’s disease and 60 with ulcerative colitis. 35 patients experienced local complications, 20 had abscesses located at the terminal portion of the ileum, and 15 patients developed fistulas and strictures. 85 patients had extraintestinal complications. 60 of them presented osteo-articular complications diagnosed with radiological and imaging examinations, 40 patients were diagnosed with axial and peripheral arthropathies, 20 with osteoporosis and osteopenia. 15 patients had ocular complications (episcleritis, uveitis and blindness) diagnosed with the slit lamp. Skin complications have been seen in 20 patients diagnosed with histopathological examinations, skin biopsy (determined by malnutrition, malabsorption, adverse drug reactions: 5-ASA, azathioprine, corticosteroid and anti-TNF-alpha agents).

Discussion/Conclusion: The extraintestinal complications of intestinal inflammatory diseases require early diagnosis and treatment. Local complications are diagnosed by MRI and CT. The prognosis of intestinal inflammatory diseases varies depending to the extent of the inflammatory process, complications, treatment followed as well as patient compliance.
The role of blood and fecal markers in intestinal inflammatory diseases

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Introduction: Biological and fecal markers are used to highlight inflammation, evaluate disease activity and the appearance of recurrence. Markers have increased sensitivity and specificity, are non-invasive and reproducible. The objective of the study was to demonstrate the role of serum, genetic, serological and fecal markers in the diagnosis of the disease, in the identification of inflammatory bowel diseases (Crohn’s disease and ulcerative colitis), in the prognosis of the disease and for adjustment of the treatment.

Methods: I have done a study on a lot of 123 patients diagnosed with inflammatory bowel diseases from October 2013 to December 2018 based on investigation of serum markers (hemoleucogram, the rate of sedimentation of the red blood cells, the C-reactive protein), genetics (interleukins, anti-TNF-α), serologic (ASCA – anti-Saccharomyces cerevisiae antibodies type IgA and IgG) and fecal markers (calprotectin, lactoferrin).

Results: 123 patients were diagnosed with inflammatory bowel diseases, 70 with Crohn’s disease and 53 patients with ulcerative colitis. Of these, 91 patients had elevated C-reactive protein and rate of sedimentation of the red blood cells associated with a moderate-severity disease, 76 patients developed changes in the blood count, 50 had anemia, 55 thrombocytosis and 68 patients had leukocytosis. Fecal calprotectin was found in 112 patients.

Discussion/Conclusion: The serologic and fecal markers used attest to the inflammatory process as well as the disease activity. Fecal calprotectin has higher sensitivity and specificity than C-reactive protein, is used in differential diagnosis between inflammatory bowel diseases and irritable bowel syndrome and is a marker of relapses.
Introduction: Crohn’s disease is a chronic inflammatory disease of the gastrointestinal tract that has a variable evolution, with periods of induction and maintenance of remission of the disease, as well as prevention of relapse. Treatment takes place in stages, starts with monotherapy, followed by combination therapy and finally biological therapy. The objective of the study was to obtain the period of induction and maintenance of remission of clinical manifestations (decrease in the number of chairs, amelioration/disappearance of fever, colic abdominal pain, tenesms) and paraclinical elements (decrease in C-reactive protein values, sedimentation rate of red blood cells and calprotectin feces).

Methods: The study included 123 patients diagnosed with inflammatory bowel diseases (Crohn’s disease and ulcerative colitis) from October 2013 to December 2108 who received 5-ASA (mesalazine, salazopyrine), corticosteroid treatment (prednisone, prednisolone), immunomodulators (azathioprine, 6-mercaptopurine, cyclosporine) and biological therapeutic agents (infliximab, adalimumab).

Results: 123 patients were diagnosed with inflammatory bowel diseases, of which 70 with Crohn’s disease and 53 with ulcerative colitis. 9 patients presented mild and moderate form of Crohn’s disease, located at the ileocecal level, and received budesonide and prednisolone treatment. 5 patients had severe ileocecal form and received corticosteroid therapy and biological therapy (infliximab) combined with azathioprine. Colonic form was found in 18 patients and enlarged form in the intestine was present in 21 patients, who received combination therapy (anti-TNF-alpha and azathioprine or 6-mercaptopurine). 3 patients had Crohn’s disease located in the upper gastrointestinal tract and benefited from early treatment with anti-TNF-alpha agents and proton pump inhibitors.

Discussion/Conclusion: Crohn’s disease is a chronic condition, where the treatment depends on the location, clinical form, severity of the disease and the age of patient. Treatment in Crohn’s disease can be individualized and long-lasting.
The changing face of IBD epidemiology

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Introduction: The most recent Inflammatory Bowel Disease (IBD) incidence data in Northern European cities was collected 25 years ago [1]. with the incidence of ulcerative colitis (UC) and Crohn’s disease (CD) quoted as 11.8/100,000 and 7/100,000 respectively. Historically, incidence data has been variable, likely reflecting the multifactorial aetiology of the disease, but all studies agree that incidence is increasing, with Northern Europe and the United Kingdom having the highest incidence and prevalence rates [2]. Epidemiological data collected between 1940 and 1993 looking at age and sex suggests median age of diagnosis is 29.5 years in CD, with a slight female preponderance and 5–10 years later in UC, with a slight male preponderance [3]. We wished to gather up to date data on incidence in our region.

Methods: Over a one year period from 19/10/16 to 19/10/17, we prospectively gathered data on all patients with a new endoscopic diagnosis of IBD throughout NHS Tayside. Confirmation of diagnosis was made via histological and radiological investigation and all patients classified via the Montreal system.

Results: 129 patients were thought to have a new diagnosis of IBD at endoscopy. Histological and radiological confirmation of diagnosis was made in 119; of these 64% (76 patients) had UC and 36% (43 patients) had CD. With NHS Tayside serving a population of 415,470 people [4], incidence of UC and CD in NHS Tayside can be calculated at 18.3/100,000 and 10.3/100,000, respectively.

Of those diagnosed with UC, the most common phenotype was proctitis E1 (38%), followed by pancolitis E3 (36%) and distal colitis E2 (20%); Median age 41 years (IQ range 31.5–51.5) and M:F ratio of 1:1.24.

Of those diagnosed with CD, 63% were diagnosed between the age of 17 and 40 and 37% above the age of 40. There were no diagnoses made in patients below the age of 16. The most common site affected was the colon L2 (40%) followed by ileocolonic L3 (35%), ileal L1 (23%) and isolated upper gastrointestinal tract Crohn’s disease L4 (2%). The most common phenotype was non-stricturing, non-penetrating disease (58%), followed by penetrating disease (35%) and stricturing (7%). Only 1 patient had evidence of perianal disease at diagnosis. Median age was 36 years (IQ range 26–51) and female to male ratio of 1:1.15.

Discussion/Conclusion: These data show a high incidence of both UC and CD. Although CD presents at a younger age, our patients are on average 6.5 years older at diagnosis than previous studies, and we see a switch in male: female ratio with slight preponderance to females in UC and males in CD. Colonic CD is the now most common phenotype. Having up to date epidemiological data and a better understanding of patterns of disease in the area NHS Tayside serves is valuable.
Gene expression profiling study: TLR9-IL23-IL17 axis in inflammatory bowel disease development

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Introduction: Mucosal gene expression has not been fully enlightened in inflammatory bowel disease (IBD). Aim of this study was to define IL23A, IL17A, IL17F and TLR9 expression in different IBD phenotypes.

Methods: Evaluation of mRNA levels was performed in paired non-inflamed and inflamed mucosal biopsies of newly diagnosed 104 IBD (50 Crohn's disease [CD] and 54 ulcerative colitis [UC]) patients by quantitative real-time PCR analysis.

Results: IL17A and IL17F expression levels were significantly increased in inflamed IBD mucosa. Inflamed CD ileal and UC mucosa showed increased IL23A, while only inflamed CD ileal samples showed increased TLR9 mRNA level. Correlation between analysed mRNAs levels and endoscopic and clinical disease activity were found in UC, but only with clinical activity in CD.

Discussion/Conclusion: Both CD and UC presented expression of Th17-associated genes. Nevertheless, expression profiles between different disease forms varies which should be taken into account for future research and therapeutics strategies.
Cyclospora cayetanensis parasite infection with Crohn's disease-like symptoms (case report)

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Introduction: Cyclospora cayetanensis is a coccidian protozoan. Humans appear to be the only major host for C. cayetanensis. Occasionally, cysts are recovered from animal feces, but it is likely that this represents spurious passage following coprophagy. Cyclosporiasis has been reported in many countries, but is most common in tropical and subtropical areas. After an average incubation period of one week, symptomatic infections typically manifest as watery diarrhea of varying severity. Other manifestations include complications of dysentery, further abdominal symptoms, and sometimes non-specific systemic symptoms (e.g. headache, low-grade fever). When freshly passed in stools, the oocyst is not infective (thus, direct fecal-oral transmission can not occur; this differentiates Cyclospora from another important coccidian parasite, Cryptosporidium). In the environment sporulation occurs after days or weeks at temperatures between 22 °C to 32 °C, resulting in division of the sporont into two sporocysts, each containing two elongate sporozoites. The sporulated oocysts can contaminate fresh produce and water, which are then ingested. The oocysts excyst in the gastrointestinal tract, freeing the sporozoites, which invade the epithelial cells of the small intestine. Inside the cells they undergo asexual multiplication into type I and type II meronts. Merozoites from type I meronts likely remain in the asexual cycle, while merozoites from type II meronts undergo sexual development into macrogametocytes and microgametocytes upon invasion of another host cell. Fertilization occurs, and the zygote develops to an oocyst which is released from the host cell and shed in the stool. Several aspects of intracellular replication and development are still unknown, and the potential mechanisms of contamination of food and water are still under investigation [1].

Methods: Case report: Patient A.S., 45-year-old, acutely ill, complaints about ileocecal pain, diarrhea with blood and pain in large joints. At the time of illness, he worked on the Costa-Rican ship, consuming fresh fruit in food. Blood tests, infusion therapy, ultrasonography and the patient were sent back for further treatment on the homeland – Latvia, where CT abdominal organs were performed. With diagnosis: mesenteric lymphadenopathy (lymph nodes up to 9 mm), the patient sent to the oncologist, but the pathology was excluded. For further treatment, the patient was sent to a gastroenterologist with suspicion of Crohn's disease. Calprotectin 275 mg/g, but no pathology is found in the colonoscopy. The patient underwent endoscopy, HIV, B, C hepatitis test, ANA, ANCA, MR abdominal organs, but no pathology. The patient has also had bacterial and viral fecal passages confirming the diagnosis: in the patient in the feces Cyclospora cayetanensis oocyst. The patient lost 7 kg during the test. The patient has been advised by an infectologist, since the parasite is encapsulated, treatment is currently not possible. The patient receives symptomatic treatment.
Results:
1. The clinical picture of Cyclospora cayetanensis is similar to Crohn's disease, HIV infection and abdominal oncology process.
2. The patient should have both endoscopic and laboratory tests for diagnosis.
3. Important travel history.

Discussion/Conclusion: Cyclospora cayetanensis is an emerging protozoan pathogen that causes an acute or chronic diarrheal disease known as cyclosporiasis, which can affect immunocompetent and immunocompromised (infected with human immunodeficiency virus) humans. Cyclosporiasis was firstly described and related to a coccidian in feces of patients with diarrhea in 1979 by Ashford [2].

Stomach pain in the right flank with bloody liquid abdominal cavity is also characteristic of Crohn’s disease and oncological process in the intestine, but in the colonoscopy examination the patient did not see any changes in the ileocecal region. The patient also had other symptoms that may be characteristic of both Crohn's disease and oncological processes: weight loss, fatigue, abdominal pain, mesentery lymphadenopathy, increased calprotectin – 275 mg/g. At a later stage of the disease, the patient also noted pain in the large joints, which might also be characteristic of other diseases mentioned above. The diagnosis of the correct diagnosis was helped by the history of the patient's laboratory analysis of feces in the Costa Rico, where fresh fruit was eaten, where Cyclospora cayetanensis oocysts were found whose clinic coincided with the patient's complaints. Diagnosis was made difficult by statistically rare morbidity in Latvia with this parasite and lack of information.

The patient was in the endemic region of Costa Rica at the time of illness. This case report draws attention to all health professionals to consider C. cayetanensis as potential etiologic cause of persistent human enteritis. Although it was described more than a decade ago, cyclosporiasis is still rarely reported in private or public health laboratories. Unawareness of this disease might often lead to misdiagnosis and incorrect treatments. The possible explanation for this problem is lack of information among clinicians and laboratory workers about this protozoan parasite and its impact on public health [2].

In recent years, several studies have shown that Cyclospora cayetanensis is a worldwide intestinal pathogen, and it has been implicated in a number of sporadic cases and epidemic outbreaks of diarrheal illness in several endemic areas. The parasite is associated with prolonged and relapsing watery diarrhea in immunocompetent persons, as well as in AIDS patients. Most reports of Cyclospora infection concern travelers visiting endemic countries. In European countries, a few cases of Cyclospora cayetanensis infection have been reported, and almost all of them were observed in persons after foreign travel [3].

References:
1. CDC – Cyclosporiasis: https://www.cdc.gov/parasites/cyclosporiasis/index.html
The modulation of the gut microbiota as a factor in improvement of the efficacy of combined therapy with oral mesalazine and budesonide in patients with moderate ulcerative colitis

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Introduction: The aim of this study was to assess the efficacy and safety of mesalazine-budesonide combined therapy in association with probiotics in inducing remission in moderate UC.

Methods: We included in our study 42 patients with mild-moderate forms of UC who was divided in two groups. The A group composed of 24 patients received combined therapy with oral mesalazine (Salofalk® 2–3 g/day) and oral budesonide (3 mg x 3 times/day), for 6–8 weeks in association with probiotics: Lepicol (L. plantarum, L. deslbrueckii, L. acidophilus, L. rhamnosus and B. bifidum) or Eubiotic (L. rhamnosus, Bifidobacterium). The B group consist of 18 patients who received oral budesonide monotherapy (3 mg x 3 times/day) or combined therapy with oral mesalazine and oral budesonide. We evaluated the Powell-Tuck index and endoscopic classification at baseline, after 1, 3, 6 and 12 months.

Results: In the A group most of the patients (14 cases) presented left-sided UC, 7 patients had proctitis and 3 patients had extensive colitis. In the B group the localization was: left-sided UC in 11 cases and proctitis in 7 cases. At 3 months, the rate of clinical and colonoscopically confirmed remission was: 62.50% in the A group and 50.00% in B group. Also, a significant decrease of Powell-Tuck index from 1.9 ± 0.5 at baseline to 1.1 ± 0.4 at 2 month was observed in the A group. In the A group rapid response was observed in the young patients. Relapse was reported in 20.84% of patients in the A group compared to 33.34% in B group. There was no significant difference in the incidence of adverse events comparative in the A and B groups. In both groups, the adverse events include: diarrhea, abdominal pain, nausea and vomiting.

Discussion/Conclusion: The modulation of the gut microbiota can assure a significantly improvement of the efficacy of combined therapy with oral mesalazine and oral budesonide in UC patients. The beneficial effect of probiotics in the treatment of UC was associated with decreased rate of recurrences.
The relationship between bone mineral density, disease activity and remission maintenance therapy in inflammatory bowel disease with rheumatic manifestation

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Introduction: We studied the types of rheumatic manifestation (RM) in IBD and identified possible relationships between the bone mineral density (BMD) and the localization and activity of disease, the long term therapy with steroids drugs or therapeutic options for maintenance of the remission of the IBD.

Methods: We investigated 32 patients with IBD: 22 patients with ulcerative colitis (UC) and 10 patients with Crohn’s disease (CD). The therapy for induction of remission consist of mesalazine (Salofalk® 2–3 g/day) associated with budesonide (3 x 3 mg/day). Patients with UC received mesalazine (Salofalk® 2–3 g/day) or immunosuppressant therapy for maintenance of remission. In CD patients maintenance therapy consist in azathioprine (1–2 mg/kg BW/day) or anti-TNF-alpha antibodies.

Results: The rheumatic manifestations of UC patients were: pauciarticular peripheral arthropaties (7 cases), polyarticular peripheral arthropaties (3 cases) and only one patient was diagnose with ankylosing spondylitis. CD patients present polyarticular peripheral arthropaties in 2 cases (20%) and ankylosing spondylitis in one case. We identified 5 cases with cutaneo-mucosal lessions (3 cases with oral apthosis and 2 cases with erythema nodosum), 4 patients with ophtalmologic involvement (uveitis in 2 case and scleritis in 2 cases) and only one cases with primary sclerosing cholangitis. The incidence of osteoporosis was significant higher in UC patients (36.36%) comparative with CD patients (20%). Young age at first diagnosis as well as acute flare of disease were identified as risk factors for the development of RM in CD patients. We have not found a correlation between BMD and ages, gender or severity of IBD activity, but T-score was correlated with C-reactive protein and hypocalcemia. History of long term treatment with corticosteroids (in the last 3 years) was associated with less than minus-2.5 values of T-score. The localization of IBD and values of clinical disease activity index (CDAI in CD and Powell Tuck Index in UC) were not significantly correlated with T-score, but osteoporosis was present more frequent in patients with CDAI > 220 or large extension of disease. The types of RM and evolution of the extraintestinal symptoms was not correlated with therapy for maintenance of remission of IBD, but improvement of the rheumatic symptoms was observed in therapy with anti-TNF-alpha antibodies.

Discussion/Conclusion: The low BMD, common in both CD and UC patients, uncorrelated with the localization, duration and severity of disease, remain one important problem in IBD management. The therapy for maintenance of remission of IBD can improve of the rheumatic symptoms.
IBD and malignancy as treatment dilemma – Case report

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Introduction: Treatment of patients with ulcerative colitis who previously had melanoma skin cancer is till now unclearly defined with limited literature data and because of that, this topic, presents a challenge for clinicians. Patients with inflammatory bowel disease (IBD) are at increased risk to develop melanoma and this risk may increase with use of biological therapy. Sometimes clinicians, due to the possibility of recurrence of cancer as a consequence of the treatment of active IBD, decide for surgical treatment.

Methods: We present a case of 44-year-old patient who has been suffering from ulcerative colitis for last 4 years. He has been visiting his gastroenterologist because of blood and mucus in stools since 2015. His previous treatment included 5-ASA and corticosteroids intermittently, but he did not perform recommended periodic screenings. In 2014, he was diagnosed skin cancer, melanoma, which was localized, without signs of metastatic disease. Excision was done and sentinel lymph node biopsy was negative. Till now, five years after, there are no signs of melanoma recurrence. During his current hospitalization, patient was clinically and biochemically evaluated, including colonoscopy with biopsy and pathological finding of an acute proctosigmoiditis with pseudopolyposis. First-line therapy were systemic and topical corticosteroids with aminosalicylates, but with no success. Second-line therapy considered either biological therapy – vedolizumab or colectomy. He was introduced with possible side effects of biologics and the treatment with vedolizumab was started.

Discussion/Conclusion: Patients with active form of IBD and previously diagnosed malignancy are complex patient population and treatment of them is individual and interdisciplinary. It requires strict monitoring and good collaboration between gastroenterologist, dermatologist and surgeon.
Introduction: Inflammatory bowel disease (IBD) patients have a 2- to 3-fold increased risk of developing deep venous thrombosis (DVT) and pulmonary embolism compared with the general population. The pathogenic mechanism that lead to the increased thrombotic risk in IBD is not clear. 

Methods: We present the case of a 30-year-old female patient previously diagnosed with extensive ulcerative colitis, admitted for rectal bleeding, diarrhea, recurrent abdominal pain and cramping. The patient was in symptomatic remission for two years, compliant with prescribed 5-ASA oral therapy. She was diagnosed and treated on two separate occasions for infectious colitis (Salmonella spp. Clostridium difficile), and subsequently presented clinical manifestations suggestive for deep vein thrombosis (edema, tenderness, erythema, left leg pain). Oral anticoagulation therapy with Factor Xa inhibitor (apixaban) 5 mg twice a day was initiated with complete resolution of symptoms. One year later, the patient was readmitted for rectal bleeding after voluntary cession of anticoagulant medication. The colonoscopy report revealed active disease and hemorrhoids. Shortly after, thrombosis of the inferior superficial femoral vena was confirmed and treatment with apixaban and 5-ASA was reinitiated with favorable outcome.

Discussion/Conclusion: DVT in IBD is a multifactorial process in which acquired risk factors seem to play the most important role. Thromboprophylaxis in IBD patients, although guideline-recommended is still poorly implemented because of concerns about its safety and, over all, the lack of awareness of the magnitude of thrombotic risk in these patients. Increased awareness among clinicians of the risks and management of thromboembolic complications are of vital importance for preventable morbidity and mortality.
Deficits in health-literacy of inpatients – A cross-sectional study

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Introduction: Diagnosis and course of patients with inflammatory bowel diseases is mainly based upon evaluation of clinical symptoms. Systematic investigations of health literacy in patients are rare and mostly based on subjective self-assessment.

Methods: In a cross-sectional survey, 196 patients (female 38%, male 62%) in medical and surgical units were asked to complete a questionnaire that we had developed for this purpose. This questionnaire contained 43 questions about common medical terms. We investigated whether patients were familiar with these terms and could name the meaning according to correct definition. Furthermore, the association with the patients’ socio-economic and demographic parameters (e. g. education, insurance status, utilization of media) was analyzed.

Results: Among all questions of the questionnaire, more patients claimed to know their meaning than this was the case by objective testing. Association of medical knowledge with demographic and socio-economic data revealed that correct answers were more frequent among women compared to men (51.1% vs. 47.2%; p = 0.12). Patients’ age was negatively correlated with medical knowledge (p < 0.001). Higher educational level was associated with a higher percentage of correct answers (p < 0.001). Private insurance status had significant an influence on medical knowledge (p = 0.002). In contrast, male patients working intellectually (compared to working physically) had a higher percentage of correct answers (p = 0.001). Other factors like reading newspapers, watching TV and number of consultations per year did not influence the percentage of correct answers.

Discussion/Conclusion: Physicians should make sure by active inquiries whether the patient understands them correctly. Furthermore, there is a considerable gap between subjective and objective medical knowledge that future evaluations of health literacy should be aware of.
Are severe endoscopic lesions in steroid-refractory ulcerative colitis associated to the response to cyclosporine therapy?

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Introduction: Cyclosporine (CSA) is an effective rescue therapy in steroid-refractory ulcerative colitis (UC) and may avoid immediate colectomy. Approximately 20% of patients fail to respond to intravenous CSA. The aim of this study was to determine the role of endoscopic findings in predicting response to CSA in steroid-refractory UC.

Methods: We conducted a retrospective study of all patients admitted for acute severe corticosteroid refractory UC and treated with intravenous CSA between January 2007 and December 2017.

UC severity was determined according to the modified clinical index by Truelove-Witts or presence of severe colonic lesions (SCL). The patients were divided into two groups by the presence or the absence of SCL. CSA response was compared between the two groups. A probability (p) value of less than 0.05 was considered statistically significant.

Results: Our study included 114 cases. Forty-four were males and seventy were females with a mean age of 33 years (14–73 years). Median follow-up was 34.66 months (6 months–120 months). Sixty-six patients (57.9%) were known to have UC, while 48 patients (42.1%) were experiencing the first attack of UC. All patients received intravenous CSA therapy at an initial dose of 2 mg/kg/day. Initial response to CSA was observed in 82 cases (72%). However, 32 patients failed to respond and required colectomy. Sixty-six patients (58%) had SCL: 42 responders (63.63%) and 24 non-responders (36.36%) to CSA. Among 48 patients without SCL, 36 patients (75%) were responders, while CSA failure was observed in a quarter of our cases. The difference of CSA response between the groups was statistically significant (p = 0.036).

Discussion/Conclusion: Our study shows that presence of SCL is correlated with CSA failure in steroid-refractory UC. In these cases other therapeutic alternatives have to be considered. However, a prospective study with a large number of patients is necessary to confirm our findings and research others predictors.
Long-term efficacy and safety of azathioprine maintenance therapy in Crohn’s disease

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Introduction: Azathioprine (AZA) is widely used for induction and maintenance of remission in patients with Crohn’s disease and has changed the course of patients with moderate to severe Crohn’s disease. However, the treatment must be withdrawn in 5–30% of patients due to the occurrence of adverse events. The aim of our study is to investigate its safety and performance in controlling Crohn’s disease patients.

Methods: We conducted a retrospective study, including all patients followed in our department for Crohn’s disease between 2000 and 2018, treated with AZA at the recommended dose of 2–2.5 mg/kg.

Results: One hundred seventy patients with Crohn’s disease, treated with azathioprine were included in our study. Seventy-six (44.7%) were male and ninety-four (55.3%) female. The average age was 32.38 ± 11.6 SD years, range 13–61 years. The average duration of follow-up was 10.6 ± 5.91 years (1–10 years). The average duration of azathioprine treatment was 7.44 ± 4.09 years (0.1–18 years). Treatment was interrupted due to side effects in twenty-six patients (15.3%). The more frequent adverse effects were infections, pancreatitis and digestive intolerance observed in 12 patients (7%), 10 (5.9%), 10 (5.9%), respectively. The infections noted were 6 cases of tuberculosis, 2 case of dental infection, aspergillosis and systemic candidiasis. In these cases, azathioprine was associated to biotherapy. Four patients has presented severe pancytopenia. After an average duration of 7.8 years after the institution of treatment, 118 patients (69.4%) were in steroid-free remission, 38 (22.4%) had a relapse requiring retreatment with steroids. Loss of response during follow-up was observed in 46 patients (27.1%).

Discussion/Conclusion: Azathioprine has proved its efficacy for maintaining steroid-free remission in Crohn’s disease. Drug-related side effects may occur specially when associated to TNF inhibitors and require discontinuation or dose-reduction. Careful follow-up is mandatory.
Radiation exposure in patients with Crohn’s disease: Separating fact from fantasy

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Introduction: Diagnostic imaging plays a key role in the diagnosis and management of Crohn’s disease (CD). The exposure of patients to radiation has increased as medical imaging has expanded. We aimed to quantify effective radiation exposure of patients with CD and identify factors associated with radiation exposure.

Methods: We conducted a retrospective study including all patients with CD between January 2011 and December 2016. Epidemiologic features of patients, characteristics of the disease, and types of imaging investigations that were performed during follow-up and cumulative radiation effective dose (CED) were determined. High exposure was defined as a CED > 75 mSv.

Results: A total of 148 patients with CD were included. Eighty-six patients were females (58.1%) and sixty-two were males (41.9%). The average age at diagnosis was 28.26 years (17–49 years). CD was ileocecal in 94 cases (63.51%) and ileocolic in 54 cases (36.48%). Anoperineal lesions were observed in 34 cases (23%). Median follow-up was 7.8 years (5–12 years). The median CED was 5.8 mSv/year (3.6–11.54 mSv/year) and 62.82 mSv (20–142 mSv) during the study period. Forty-two patients (28.37%) had an estimated CED of > 75 mSv. Higher exposure to radiation was associated with age at disease onset < 20 and previous surgery with Odds ratios (OR) 4.48 and 6.05 respectively.

Discussion/Conclusion: Patients with CD are at greatest risk for high cumulative radiation exposure in their lifetime. Alternative investigations which do not require radiation exposure, such as MRI, should be considered, especially in young patients and those who have undergone prior surgery.
High incidence of hyperglycaemia in steroid-treated hospitalised inflammatory bowel disease (IBD) patients and its risk factors identified by machine learning methods

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Introduction: Glucocorticoids (GC) have been first line treatment for hospitalised IBD patients for over 60 years, despite the introduction of biologic therapy. The use of steroids in IBD inpatients is common and remains prominent in international guidelines. IBD patients often have systemic inflammation complicated by malnutrition leading to metabolic stress. The frequency and specific risk factors for hyperglycaemia in hospitalised IBD patients receiving GC are unknown.

Methods: 100 consecutive IBD inpatients receiving intravenous hydrocortisone (IVH) for acute flares had capillary blood glucose (CBG) monitoring automatically triggered by the electronic prescription. CBG, biomarkers, IBD severity scores (Harvey Bradshaw, partial Mayo) and weight loss were prospectively recorded. Undiagnosed diabetes mellitus (DM) was defined as baseline HbA1c > 48 mmol/mol. Machine learning (random forest regressor, RFR) was applied to the data to evaluate risk factors of hyperglycaemia.

Results: 55% of hospitalised IVH treated IBD patients had a CBG meeting the WHO criteria of DM (>11 mmol/l), while 21% and 7% had a CBG >14 mmol/l and >20 mmol/l, respectively. Only 7 patients had pre-existing DM, which was confirmed by admission HbA1c. RFR indicated disease severity score, duration of IVH, HbA1c and electrolyte imbalances (which affected 64%) were best predictors of hyperglycaemia. 50% were started on or switched biological therapy during admissions. 59% were discharged on prednisolone, 14% on budesonide and 28% on no GC. 47 patients had HbA1c checked at 3 month follow-up of which 4 were in the diabetic range. 1 was known DM with elevated CBG during admission whose insulin had been titrated, 2 had elevated CBG as inpatients with no prior DM and was discharged on anti-diabetic medications (1 gliclazide, 1 insulin) and 1 was on long-term steroids for asthma who did not have CBG >11.0 mmol/l as inpatient. 4 patients discharged on gliclazide for steroid induced DM had documented repeat HbA1c recorded, which were all in the normal range.

Discussion/Conclusion: Our data demonstrates that hyperglycaemia is common in IVH treated inpatients, therefore CBG monitoring should be routine practice. Predictive modelling (RFR) identifies more severe disease activity, duration of IVH treatment and HbA1c as risk factors for hyperglycaemia. The importance of IVH duration suggests hyperglycaemia risk may be physician-modifiable.
Alternative treatment strategies such as earlier introduction of biologics (which were used in half of the cohort), rapid steroid taper and nutritional therapies could be used to minimise medication associated metabolic instability in high risk patients. Limited follow-up HbA1c data suggests oral hypoglycaemic medication may be effective to mitigate further hypoglycaemia.
Inflammatory bowel disease: A side effect of anti-IL-17A inhibitor (secukinumab)

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Introduction: Secukinumab is a human anti-IL-17A monoclonal antibody which is approved by NICE for use in ankylosing spondylitis, psoriatic arthritis and plaque psoriasis. Secukinumab was investigated as a therapeutic agent in Crohn’s disease; however a phase II trial assessing its efficacy was terminated early due to inefficacy and higher rates of adverse events including worsening of Crohn’s disease. A recent analysis of pooled data from 21 clinical trials has shown that incidence of IBD in this cohort appears to be low, however, IBD is an exclusion criteria in IL-17 development trials and this result may be falsely reassuring. To date there have only been a small number of case reports of inflammatory bowel disease (IBD) presenting de novo in patients receiving secukinumab for treatment of rheumatological disease. The aim of the study was to identify any patients who developed IBD since starting secukinumab in a large district general hospital cohort.

Methods: A retrospective study was performed at the Royal United Hospitals Bath NHS Foundation Trust over a 2 year period to identify all patients with a new diagnosis of IBD while taking secukinumab. The case notes of these patients were reviewed.

Results: Three cases were reported including a 33-year-old male taking secukinumab for ankylosing spondylitis, a 20-year-old male taking secukinumab for psoriasis and a 62-year-old male taking secukinumab for psoriatic arthritis. All of these patients developed symptoms of bloody diarrhoea within six months of starting this drug and went on to have endoscopic examination showing colitis with histological examination confirming IBD.

Discussion/Conclusion: This data suggests that the incidence of IBD in patients taking secukinumab is higher than previously reported. Interestingly, one of the patients outlined above had been investigated for a change in bowel habit with colonoscopy and biopsies prior to starting secukinumab and no abnormality was found, while another had a family history of inflammatory bowel disease in a second degree relative. This raises the question of whether the effect of secukinumab is to induce the condition de novo or unmask latent IBD.

These three cases add to a growing body of evidence that secukinumab is likely to be associated with a side effect of either inducing IBD or unmasking latent IBD; gastroenterologists and rheumatologists should be aware of this potential side effect. An IBD screening pathway may help to identify individuals at high risk of IBD, prior to considering treatment with secukinumab.
Combined intestinal diseases in patient with chromosome disorder

David Janelidze (Kyiv, UA)

**Introduction:** Female 23 years, non-smoker, no alcohol abuse. No family history. Complains for last several years: fatigue, sometimes soft stool – depends on meal intake, impossible weight gain. BMI = 17.5 underweight. Medical history: Chronic anemia for 5 years (uninvestigated origin). IBD indeterminate (endoscopic and morphological data for Crohn’s disease and ulcerative colitis) and infection ileitis also. Suspicious for celiac disease, no compliance to grain products (wheat and rye). Turner syndrome (45XO) from 2008. Previous treatment history: Estradiol 1 tab per day prescribed by endocrinologist from 2008. 5-ASA – 4 g 4 years ago, last 2 years – 3 g. Budesonide 3 mg per os – in previous. Methylprednisolone – decreasing dose for last 5 years, 16-12-8-4 mg per day (last 3 years 4 mg intake). No tolerance to any oral ferrum, because of AE (vomiting and abdominal pain). 3 times of blood IV transfusion. On gluten containing diet – HGB decreasing and observing acute abdominal pain and diarrhea. Last 2 year on gluten free diet (decided herself). No suggestion for immunomodulators, no suggestion for biological therapy.

**Methods:** HIV, HBV, HCV are negative, CRP – 4.77 N, WBC 9.33 N, HGB 87 ↓, HCT 30.6 N, PLT 740 ↑, ESR 25 ↑, liver enzymes – N, abdominal US – N, Helminthes test – negative, C. difficile – negative, Ig A & G Yersinia (-), IGRA-test – negative, FOBT (+), calprotectin 259 ↑, Fe 3.14 ↓, Ferritin 5.98 ↓, B12 & follic acid – N, Ig A & Ig G – TTG (-), Ig A Gliadin (-), Ig G Gliadin (31.42 ↑), Ig A – endomysial (-), DGP (-) – on gluten containing meal diet, which was possible only for 7 days. OGDS + morphological examination. Increase level of intraepithelial lymphocytes – Marsh type 1, corresponds to celiac disease. Inflamed polyp, no malignancy (no need for resection). Duodenitis (lymphocytes and plasma cells, neutrophil infiltration, focal cryptitis) corresponds to Crohn’s disease. No Hp, OLGA -0, OLGIM – 0.

Ileocolonoscopy + morphological examination.

No granuloma. Patchy chronic active inflammation with ulceration; reduced crypt numbers, multifocal crypt deformation. Active multifocal colitis; single crypts. These changes correspond to Crohn’s disease. Difficult aspects of this case are to find the true diagnosis, combined intestinal diseases on the background of chromosome disorder, and then their correct management.

**Results:** Final diagnosis – Crohn’s disease Montreal classification: A2, location L3+L4 – terminal ileitis, focal colitis (ascendant colon), with affected upper part of gut (duodenum – D2), perianal lesion (P), steroid-dependent, moderate activity, CDIA = 227. Iron deficiency anemia, moderate severity. Celiac disease. Underweight BMI = 17.5. Turner syndrome. Treatment: 6-MP 50 mg per day for a long period (10 y+), no to gluten contain products, 5-ASA 2 g per day for a long time. Methylprednisolone 4 mg per day 6–8 weeks, gradually decrease the dose (from 3-2-1 mg per day during 3 months). Than Stop! Ferrum IV
infusion – 200 mg twice per week. Repeat every 6–12 month. Dietary supplement (gluten, lactose-free). Protein intake 2 mg/kg per day. Continue administration of calcium and vitamin D 800 unit per day.

After 3 months: Symptoms were relieved, Hb increased and 4 kg gain weight was observed.

**Discussion/Conclusion:** Point to be discussed: Guidelines provide necessary tool to develop evidence-based management strategies in diagnosis and treatment of patients with combined pathology. Guidelines cannot cover all clinical problems. Every patient needs individual approach based on their data. Use of current available classification and scoring system should be implemented in routine clinical practice for better management of patients with combined diseases.
The association of diabetes mellitus with inflammatory bowel disease in a tertiary referral center

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Introduction: Diabetes mellitus (DM) is a pandemic that constitutes a major public health problem worldwide, both by the number of people affected and by the socioeconomic implications. The aim of this study was to evaluate the frequency of DM in patients with inflammatory bowel disease (IBD). There are studies that have shown that the incidence of DM in patients with IBD, and especially with Crohn’s disease (CD), was significantly higher compared with subjects in the general population. The mechanism is uncertain, but may be related to autoimmunity.

Methods: We retrospectively analyzed patients diagnosed with IBD hospitalized in a tertiary center in North-Eastern Romania between January 1, 2017 through May 31, 2019. Demographics and clinical characteristics were assessed.

Results: Ninety patients with IBD were analyzed, with a mean age of 45.2 ± 14.51 years. From these, 53 (58.88%) patients were diagnosed with ulcerative colitis (UC), predominantly males (74%), 24 (45.28%) of them with left-sided colitis and 37 (41.11%) with CD, predominantly females (64.86%). Most patients with CD had ileo-colonic form (62.16%). The frequency of DM in IBD patients included in our study was 12.22%. Among them, 10 (90.9%) had UC and only 1 CD (9.09%). During the evaluation, 6 (54.54%) of them had a persistent high blood sugar level. All the patients had type 2 diabetes mellitus and there were found only 4 (36.36%) patients with insulin-requiring type 2 diabetes mellitus.

Discussion/Conclusion: The frequency of DM in IBD patients should not be neglected and a multidisciplinary approach is often needed. In our study, the patients with DM were more commonly found in the subgroup of UC patients, probably because they are usually older than those with CD. Regular monitoring for blood sugar level is recommended, even in younger CD patients who do not use steroid medication.
Biologic treatment persistence in Greek patients with IBD: 15-year real-life data form a single center

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Introduction: The efficacy and tolerability of biologic agents in the treatment of inflammatory bowel diseases (IBD) has been extensively demonstrated. Given that clinical trials represent highly selected patient populations, it is important to demonstrate effectiveness in real-life clinical practice.

Methods: We retrospectively reviewed the IBD registry of Tzaneio General Hospital and included all patients with IBD under biologic treatment for more than 6 months from 2004 to June 2019. We recorded demographic data (age, gender), disease type, duration and characteristics (Montreal classification, perianal, and surgery), concomitant and prior medication other than biologic agents, type of biologic agent, months on biologic treatment and need for optimization. Logistic regression analysis was used to assess factors associated with persistence to biologic agents.

Results: One hundred and thirty patients with IBD under biologic therapy, 110 with Crohn’s disease (CD) and 20 with ulcerative colitis (UC) were included in the study. Mean age of our population was 42.5 years old with 60% being men. The majority of our population was receiving anti-TNF agents (112 patients, 86.15%) while the rest were receiving vedolizumab or ustekinumab. Ninety four patients (72.3%) were naïve to biologic treatment while 13.8% were under combination therapy (biologic and immunosuppressants). Half of our cohort (66 patients, 50.77%) needed treatment escalation at some point of their therapy. Mean duration of biologic treatment was 49.13 ± 41.4 months. On multivariate analysis strictureing disease (Montreal B2) in patients with CD was the only factor associated with quicker biologic treatment discontinuation (p = 0.032).

Discussion/Conclusion: Real-life data indicate that biologic treatment efficacy and tolerability are equal or better than that of clinical trials. Strictureing disease seems as a poor prognostic factor leading to loss of response and discontinuation of biologic therapy.
A fistula between sigmoid colon and left colonic vein as a symptom of Crohn’s disease

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Introduction: Crohn's disease can be manifested by the appearance of fistula as the first manifestation of the disease. Fistulae with blood vessels are extremely rare in these patients.

Methods: A forty-year-old patient is hospitalized with symptoms of abdominal pain, hyperbilirubinemia, fever, chills and shivering. The abdominal MSCT imaging showed stenosis of the sigmoid colon with a fistula between colon and left colonic vein, septic phlebitis of the lower mesenteric vein and multiple segmental inflammation of terminal ileum. Calprotectin values were elevated. Intravenous ceftriaxone and metronidazole were administered for 14 days during which period the inflammatory parameters improved and the patient was not febrile. The colonoscopy showed serpiginous ulcerations with the loss of vascular drawings of the sigmoidal colon and terminal ileum. The pathological finding indicated Crohn's disease. After having been included in corticosteroid and aminosalicylate therapy, the patient's clinical state improved and calprotectin was in regression. After four weeks, the abdominal MSCT imaging showed regressive gas dynamics in the lower mesenteric vein, a few smaller residual gas zones in the left colonic vein and a spontaneous fistula occlusion.

Discussion/Conclusion: Most GI fistulae occur as a complication of abdominal surgery. However, 15–25% of fistulae evolve spontaneously and usually result in intra-abdominal inflammation or infection, which is extremely rare in Crohn's disease.
Granulocyte-monocyte apheresis in the treatment of ulcerative colitis (GRACULA) interim analysis of a sham-controlled study

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Introduction: Antibody-therapy is less effective in ulcerative colitis (UC) than in Crohn’s disease. Therefore, treatment of severe UC is particularly challenging. Previous studies on TNF-alpha and other antibodies showed remission rates of only about 20% versus 10% in placebo group. Therefore, there is a need for other therapeutic options in severe UC. Granulocyte-monocyte apheresis (GMA) is among the most promising approaches. A pilot-study of our group (Schultheiss, Huber et al. Artif Organs. 2015) demonstrated response and remission rates of 70% and 40%, respectively. However, there is a lack of randomized controlled data. Therefore, we perform a randomized, sham-controlled trial to investigate the efficiency of GMA in UC.

Methods: Interim analysis after 24 of 51 patients with moderate to severe active UC. 2:1-randomization (GMA/sham), double blinded, sham-controlled. Both groups received 8 treatment sessions within four weeks. Four weeks after the last apheresis a follow-up took place. Endpoints: Remission: Rachmilewitz Clinical Activity Index [CAI] and/or Endoscopic Index [EAI] ≤ 4 points. Response: decrease in CAI or (CAI+EAI) from baseline to follow-up by ≥ 3 points. Changes in erythrocyte sedimentation rate [ESR] and quality of life (QoL; IBDQ-D).

Results: 24 patients (15 male/9 female; mean age 41 years, 16 GMA/8 sham. Baseline characteristics with and without GMA were comparable. 7/16 (44%) undergoing GMA patients achieved remission compared with 2/8 (25%) in control-group. 9/16 GMA-patients (56%) showed a clinical response compared with 5/8 (63%) after sham treatment. The IBDQ-D and 2-hours-ESR significantly improved in GMA-group (p = 0.026; p = 0.012), whereas there was no significant change in sham-group (p = 0.092; p = 0.279).

Discussion/Conclusion: There was a trend to higher remission rates in the GMA-group (44% vs. 25%; p = 0.371). Furthermore, ESR and QoL significantly improved under GMA, but not in sham-group. If these data will be confirmed in the final analysis, GMA might be among the most effective therapies in severe UC.
Introduction: Acute severe colitis (ASC) is associated with significant morbidity in pediatric patients with ulcerative colitis (UC). Most outcome studies in ASC since TNF antagonists became available have focused on the first year after admission. The aim of this study was to characterize the longer-term outcomes of pediatric patients admitted with ASC.

Methods: This retrospective study was conducted in 25 centers across Europe and North America. Data were collected on patients with UC aged < 18 years admitted with ASC (defined as PUCAI score ≥ 65) between 2009 and 2011 at discharge and 1, 3 and 5 years post-admission. The primary outcome was colectomy-free rates at each time point.

Results: Of the 141 patients admitted with ASC, 137 (97.1%) were treated with intravenous corticosteroids. Thirty-one (22.6%) patients were escalated to second line therapy, mainly to infliximab. Sixteen patients (11.3%) underwent colectomy prior to discharge. Long-term follow-up showed colectomy-free rates were 71.3%, 66.4% and 63.6% at 1, 3 and 5 years post-initial ASC admission, respectively, and were similar across different age groups. Sub-analysis of colectomy rates in patients with new-onset disease (42.5% of the cohort) yielded similar results. In a multivariate analysis use of oral steroids in the three months prior to admission, erythrocyte sedimentation rate > 70 mm/h and albumin < 2.5 g/dl were significantly associated with 5-year colectomy risk.

Discussion/Conclusion: High colectomy rates were demonstrated in pediatric UC patients admitted with ASC. Additional studies are required to determine whether intensification of anti-TNF treatment, close therapeutic drug monitoring and use of new drugs alter this outcome.
Molecular changes in the non-inflamed terminal ileum in patients with ulcerative colitis

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Introduction: Ulcerative colitis is a chronic inflammatory disease of the intestine and typically confined to the colon. Although the underlying mechanisms remain unknown, small bowel dysfunction has been described in ulcerative colitis. We here evaluated the molecular changes in the non-inflamed ileum of ulcerative colitis patients, and their association with the presence and extent of colonic inflammation.

Methods: Terminal ileum biopsies for mRNA expression analysis were obtained from 36 ulcerative colitis patients (7 active [Mayo endoscopic subscore ≥ 2] and 29 inactive) and 15 non-IBD controls. Subjects with endoscopic or histological ileitis were not included. Single-end RNA sequencing was performed using Illumina HiSeq4000. Gene expression differences were analysed using DESeq2, and corrected for age and gender. Weighted gene co-expression network analysis was performed to find biological networks of genes that correlate with ulcerative colitis activity. Pathways and upstream regulators were identified using IPA.

Results: Comparative analyses of gene expression levels of active ulcerative colitis patients versus controls identified 18 genes with significant different expression (p_{corrected}[FDR] < 0.05 and log2 fold-change ≥ 1). The most significant gene was DUOXA2 (log2 fold-change = 4.9, FDR = 5.58 x 10^{-03}). In inactive ulcerative colitis subjects, only two genes (CEBPD and REG1B) were dysregulated compared to controls. We further found 84 differentially expressed genes in active extensive ulcerative colitis compared to controls, and 23 in inactive extensive ulcerative colitis, with an overlap of six genes; REG1B, REG1A, MUC4, DMBT1, GRAMD2, and CASP10. Gene co-expression network analysis found 38 co-expression modules, of which 6 were significantly correlated with ulcerative colitis; 3 with active UC and 3 with inactive UC. The correlated modules in patients with active ulcerative colitis were mainly related to immune functions, and this specifically for patients with extensive ulcerative colitis. The ileal changes in the inactive ulcerative colitis subjects on the other hand converged into maintenance of the intestinal barrier through increased mitochondrial function and dampened immune functions.

Discussion/Conclusion: We found significant molecular alterations in the non-inflamed ileum of ulcerative colitis patients. These alterations were dependent on the presence of colonic inflammation and disease extent, and thus point to a cross-talk between colon and ileum in ulcerative colitis.
Serological markers associated with development of pouchitis after ileal pouch-anal anastomosis

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Introduction: Pouchitis is the most common complication in patients with ulcerative colitis (UC) requiring ileal pouch anal anastomosis (IPAA). Pouchoscopy remains the gold standard to diagnose pouchitis in the absence of other surrogate biomarkers. We performed serum proteomic profiling to identify biomarkers that could be predictive and discriminative for the development of pouchitis following IPAA.

Methods: This was a prospective cohort study in 51 patients undergoing IPAA at our center (46 UC and 5 familial adenomatous polyposis patients). Serum was collected before colectomy and at predefined clinical visits at month 1, 3, 6 and 12 after IPAA. At every clinical visit, patients had endoscopic evaluation of the pouch. Pouchitis was defined by presence of endoscopic inflammation. Serum samples from 62 age- and sex matched healthy subjects (HS) served as controls. A panel of 91 inflammation-related proteins was measured using Proximity Extension Assay (Olink). Analyses were performed in SPSS and R. False discovery rate (FDR)-corrected p-values were reported as FDR. Logistic regression and receiver operating characteristic curve analysis were used to evaluate the predictive and discriminative power of significant biomarkers and clinical variables (cutoff p < 0.1). Pathway analyses was conducted using STRING database.

Results: A total of 17 (37%) UC patients were diagnosed with pouchitis during the first year after IPAA. Younger age at colectomy (OR = 1.11, 95% CI: 1.03–1.21; p = 0.008) and backwash ileitis (OR = 8.37, 95% CI: 1.06–65.9; p = 0.04) were associated with pouchitis. When comparing the protein profiles prior to colectomy in UC patients developing pouchitis (UC-P) and UC patients with normal pouches (UC-NP), we observed respectively 42 and 45 proteins significant from the profiles in HS (FDR < 0.05). The majority (n = 35) were overlapping between UC-P and UC-NP. Ten proteins (↑OPG, MCP1, CCL4, MCP4, MMP1, CD5, 4EBP1, EN-RAGE; ↓Flt3L, CCL25) were uniquely different in UC-P (FDR < 0.05) and pathway analyses indicated an involvement of these proteins in the regulation of NK cell chemotaxis and cellular extravasation. No pathways were detected for the 7 uniquely dysregulated proteins (↑TSLP; ↓CD244, uPA, SCF, FGF5, IL12B, NT3) in the UC-NP comparison. Similarly, comparison of baseline protein profiles of UC-NP and UC-P with FAP, revealed respectively 7 and 17 significant proteins (FDR < 0.05), of which 14 solely dysregulated in the UC-P comparison. Combination of HGF, TNFRSF9 and age at colectomy was the most accurate to predict development of pouchitis within 1 year (AUC = 0.875). A panel of 4 proteins (IL17A, CXCL1, CCL25 and TRAIL) showed a good discriminative power (AUC = 0.984) to diagnose pouchitis at month 12 post-IPAA. The impact of colectomy with IPAA on the serological proteins was different in UC-NP and UC-P. UC-NP showed a significant decrease of OSM, TGFα, IL24 and FGF19.
(FDR < 0.05), which are involved in MAPK and JAK-STAT cascades, whereas CDCP1, uPA, TRANCE, IL12N, CCL25, TNFRSF9 and TNFB, of which multiple proteins are involved in response to wounding and tissue remodeling, increased post-IPAA (FDR < 0.05). In contrast, no significant temporal changes were detected in UC-P.

**Discussion/Conclusion:** Before colectomy, there is a great overlap in serum protein profiles between patients who do or do not develop pouchitis. We found that proteins involved in NK cell chemotaxis and cellular extravasation were dysregulated solely in patients developing pouchitis. HGF and TNFRSF9 in combination with age at colectomy were predictive for pouchitis and we identified a combination of 4 biomarkers with diagnostic potential. Further validation in a larger cohort is required.
Hematological indices as potential markers in the monitoring of patients with Crohn’s disease

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Introduction: Recently, neutrophil-to-platelet ratio (NLR), platelet-to-lymphocyte ratio (PLR) and mean platelet volume-to-platelet ratio (MPR) have been proposed as potential markers in various medical disorders. Our goal in this survey was to assess NLR, PLR, MPR and their relationship with platelet indices and C-reactive protein (CRP) in Crohn’s disease (CD) patients treated with infliximab (IFX).

Methods: We included 80 participants to the study: 40 patients with active CD and 40 persons in control group. CD patients were treated with IFX (five doses of standard therapy). NLR, PLR, MPR and their association with CRP, mean platelet volume (MPV), plateletcrit (PCT) and platelet distribution width (PDW) were assessed in blood of CD patients at 0, 2, 6, 14 and 22 weeks. Results were compared with controls.

Results: Baseline levels of NLR and PLR among CD patients were higher in comparison to controls (p < 0.001); MPR value was lower (p < 0.01). In CD group, after five doses of IFX, a decrease in NLR (p < 0.001) and PLR levels (p = 0.001) together with increase of MPR value (p < 0.001) were noticed. We also observed significant correlations in CD patients, present simultaneously prior to the biological treatment and after five doses of IFX. NLR correlated positively with PLR and CRP (p < 0.01). There was a negative correlation between PLR and MPR (p < 0.01), together with positive association between PLR and PCT (p < 0.001). Finally, MPR correlated positively with MPV (p < 0.01) and negatively with PCT (p = 0.001). In addition, CRP correlated negatively with MPR at baseline (p < 0.001) and positively with CRP (p = 0.004) after five doses of IFX.

Discussion/Conclusion: CD, IFX therapy, NLR, PLR and MPR are closely linked to each other. Analyzed hematological indices might be potential tools in the monitoring of CD patients.
Red blood cell distribution width and its derivatives in ulcerative colitis patients treated with infliximab

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Introduction: Red blood cell distribution width (RDW) is associated with various medical conditions. The aim of our study was to find out if there are deviations in RDW and its derivatives levels – red blood cell distribution width-to-platelet ratio (RPR) and red cell distribution width-to-lymphocyte ratio (RLR) – in the course of infliximab (IFX) induction regimen in ulcerative colitis (UC) patients. We also looked for association between mentioned parameters, platelet indices and C-reactive protein (CRP).

Methods: One hundred and twelve participants were qualified to the survey: 56 patients with active UC and 56 persons in control group. UC patients were treated with IFX (3 doses of standard induction therapy). RDW, RPR and RLR values were obtained in the blood of UC patients at 0, 2, and 6 weeks of induction regimen and in follow-up six weeks later. Results were compared with control group.

Results: RDW value in UC patients prior to the first dose of IFX was above normal range; it was also higher in comparison to control group (p < 0.001) and normalized in follow-up (p < 0.01). Baseline RLR level in study group compared to controls was higher (p < 0.001) and decreased after finished IFX induction regimen (p > 0.05). Baseline RPR value did not differ significantly; in follow up its level increased (p < 0.001). We noticed several correlations in UC patients. Prior to the treatment with IFX, RPR correlated positively with mean platelet volume (MPV) (p < 0.01) and platelet distribution width (PDW) (p < 0.001); negative correlation was observed between RPR and plateletcrit (PCT) (p < 0.001). In follow-up RPR correlated negatively with PCT (p < 0.001) and CRP (p < 0.001); positive correlation was noticed between RPR and PDW (p = 0.001).

Discussion/Conclusion: Performed study revealed that RDW, RPR and RLR values are affected by IFX therapy in UC patients.
Hepatic steatosis and cholesterol levels in patients with inflammatory bowel disease in a tertiary referral center

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Introduction: Inflammatory bowel disease (IBD) typically affects young people. It’s burden emerges from chronic intestinal and extraintestinal inflammatory status. Previously, extraintestinal manifestations (EIM) like arthritis, uveitis, psoriasis, primary sclerosing cholangitis were considered the main comorbidities, but recent studies focus on other IBD related conditions like hepatic steatosis, cardiovascular disease, renal lithiasis, neuropsychiatric conditions in order to a better understanding and management of IBD patients. The aim of this study is to assess the incidence of hepatic steatosis and cholesterol level in patients with IBD.

Methods: This was a retrospective cohort study conducted in a university-affiliated tertiary referral center from North-Eastern Romania.

Results: The study population included 90 patients (mean age 45.2 ± 14.51 years) diagnosed with ulcerative colitis (UC) and Crohn’s disease (CD) between January 2017 and May 2019. The study group involved 53 patients with UC (37 males, 69.81% and 16 females, 30.18%), predominantly with pancolitis (24 patients, 45.28%), and 37 patients with CD (13 males, 35.13% and 24 females, 64.86%), predominantly ileo-colonic form (23 patients, 62.16%). Out of 90 patients, 33 (36.66%) of them had hepatic steatosis (21 males, 63.63% and 12 females, 36.36%). 16 patients (48.48%) had normal cholesterol levels through the monitoring period while 17 patients (51.51%) had fluctuations of cholesterol level, mostly males with UC presenting high cholesterol values and ascending trend cholesterol level.

Discussion/Conclusion: In our group, more than one third of patients recently diagnosed with IBD had hepatic steatosis. While females tend to have normal cholesterol levels, males with UC presented high and/or ascending trend of cholesterol level.
South Asian ethnicity drives differences in microbial and metabolic profiling in a newly diagnosed ulcerative colitis cohort

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Introduction: The incidence of ulcerative colitis (UC) in South Asian (SA) migrants is higher than in Caucasians. Ethnicity and migration cause changes in microbial profile. We aimed to define microbial and metabolic profiles which may elucidate differing pathways in disease pathogenesis.

Methods: Demographics, disease phenotype, treatment and disease severity using simple clinical colitis index (SCCAI) were recorded. Blood, urine and faecal samples were collected at three time points over a one year period from newly diagnosed SA and Caucasian patients. We collected 102 urine, 78 serum and 85 faecal samples from 23 SA and 15 Caucasian patients and 15 healthy controls. Nuclear magnetic spectroscopy (NMRS) and liquid-chromatography mass spectroscopy with bile acid and polar molecule (HILIC) profiling of metabolites was undertaken. 16S rRNA genes were sequenced on an Illumina MiSeq platform. All patients completed a food frequency questionnaire at inclusion.

Results: There were no significant differences in median age and disease phenotype. Mean SCCAI score was higher in SA (6.6 vs. 4.3). More SA were on steroid treatment at diagnosis (26% vs. 0%). There were significant differences between the groups in microbial profiling at phylum, family and genus levels with overall lower diversity in the SA cohort by Chao 1 index. There were no significant differences in macronutrient or micronutrient dietary intake. Metabolic profiling revealed significant differences between SA and Caucasians across all biofluids and analytical platforms. The strongest models were from faecal HILIC (R2X 0.129, R2Y 0.8, Q2Y 0.596, p = 6.47 x 10^{-5}) and urine HILIC (R2X 0.164, R2Y 0.783, Q2Y 0.526, p = 7.11 x 10^{-12}). Urinary NMRS showed higher isobutyrate, lactate and alanine in the SA group whilst hippurate, 4-cresol sulphate, lysine and citrate were reduced. Secondary bile acids (5\β-cholanic acid-3\α, 6α-diol-7-one) were higher in the SA group and four secondary bile acids (3-ketocholestanic acid, lithocholic acid, isolithocholic acid, 3\α-hydroxy-12-ketolithocholic acid) were lower. There were no discriminatory features identified during time point and treatment subgroup analysis.

Discussion/Conclusion: This prospective, longitudinal inception cohort study demonstrates significant differences driven by ethnicity despite similar diet. SA had more severe disease which maybe a confounding factor. Analysis of paired samples pre- and post-remission are required. Further studies employing metagenomics techniques may define pro-inflammatory pathways specific to SA and justify different treatment approaches.
Pregnancy outcomes in inflammatory bowel disease patients treated with vedolizumab, anti-TNF or conventional therapy: Results of the European CONCEIVE study

Annick Moens (Leuven, BE)

Introduction: Women with inflammatory bowel diseases (IBD) often receive biologicals during pregnancy to maintain disease remission. Data on outcome of vedolizumab-exposed pregnancies (VDZE) are sparse.

Methods: A retrospective multicentre case-control study was performed to assess pregnancy and child outcomes of VDZE pregnancies (group A). Results were compared to anti-TNF exposed (TNFE, group B) or both immunomodulatory and biologic unexposed (CON IBD, group C) pregnancies.

Results: Group A included 79 pregnancies in 73 IBD women. Groups B and C included 186 pregnancies (162 live births) in 164 IBD women and 184 pregnancies (163 live births) in 155 IBD women, respectively. At conception, cases more often had active disease (A: 36% vs. B: 17%, p = 0.002 and A: 36% vs. C: 24%, p = 0.063). No significant difference in miscarriage rates were found between groups (A and B: 16% vs. 13%, p = 0.567; A and C: 16% vs. 10%, p = 0.216). In live-born infants, median gestational age and birth weight were similar between groups. Median Apgar score at birth was numerically equal. Prematurity was similar in the VDZE group compared to the control groups, even when correcting for disease activity during pregnancy. The frequency of congenital anomalies was comparable between groups as were the percentages of breastfed babies. During the first year of life, no malignancies were reported and infants’ infection risk did not significantly differ between groups.

Discussion/Conclusion: No new safety signal was detected in VDZE pregnancies although larger, prospective studies are required for confirmation.
Intestinal microbiota metabolic activity in inflammatory bowel diseases in children

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Background: Intestinal microbiota disorders can play an important role in the pathogenesis and natural history of inflammatory bowel disease (IBD). The aim of this study was to evaluate the metabolic activity of the intestinal microflora in children with ulcerative colitis (UC) and Crohn's disease (CD).

Patients and methods: In our study 21 children with UC and 14 children with CD were included. The diagnostics was based on the clinical data, the data of biochemical studies, endoscopic data and the results of a colon biopsies morphology. At the start of this study children with UC were E3S0 (Paris classification) with PUCA of 35–65. Children with CD corresponded to A1bL3B1G0 (Paris classification) with PCDI of 30–50. The metabolic activity of intestinal microflora (stool short-chain fatty acids [SCFA]) was assessed by gas-liquid chromatography. All children were treated according to the current protocols using 5-ASA and glucocorticoids, depending on the disease activity. The second evaluation was undertaken in disease remission (1 year after the start).

Results: Our results at the start of study (mg/l, M ± m) in UC children/in CD children (ref. value): acetic acid (C2) – 1.744 ± 0.132*/1.701 ± 0.117* (0.634 ± 0.004), butyric acid (C4) – 0.048 ± 0.016*/0.049 ± 0.023* (0.176 ± 0.004), isovaleric/valeric acid ratio (iC5/C5) – 1.744 ± 0.032**/2.645 ± 0.084* (1.471 ± 0.030). Our results at the end of study (mg/l, M ± m) in UC children/in CD children (ref. value): C2 – 0.925 ± 0.045**/1.225 ± 0.238* (0.634 ± 0.004), C4 – 0.072 ± 0.039*/0.097 ± 0.110 (0.176 ± 0.004), iC5/C5 – 1.174 ± 0.090**+/1.812 ± 0.071*+ (1.471 ± 0.030) (*p < 0.05 vs. ref. value, +p < 0.05 vs. start of study, #p < 0.05 CD vs. UC).

At the start of this study changes in the stool SCFA profile with an increase in acetate (C2) production and a decrease in butyrate (C4) production were observed. There was no significant difference between patients' groups. A predominance of iso-acids over non-isomers, a significant predominance of isovaleric acid (an increase in the ratio of iC5/C5 in 68.75% of patients with IBD) were observed. Additionally, the anaerobic index (Ai) was increased. In disease remission a decrease in acetate production and an increase in butyrate production were observed, mostly in UC patients. Full normalization of the SCFA spectrum was not observed.

Conclusions: Our data suggest a significant change in the metabolic activity of the intestinal microbiota in IBD children and support the possibility of the intestinal microflora correction in the disease remission, but further studies are needed.
A retrospective study on risk factors for infections in adult patients with inflammatory bowel disease

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Introduction: The current use of immunosuppressive agents and biological agents in patients with inflammatory bowel disease (IBD) increases the risk for opportunistic infections. Patients with IBD commonly display a significantly increased rate of morbidity and mortality. We aimed to assess the risk factors for opportunistic infections in IBD patients.

Methods: A single-center, 5-year (2013–2018) retrospective study of 278 IBD patients was conducted. The demographic characteristics of patients were collected, including age, gender, course of the disease, current smoking habits, previous bowel surgery, comorbidity, disease activity, the type of IBD, and current medications. All patients were diagnosed with UC or CD based on the previously criteria. Patients diagnosed with opportunistic infections were compared to those without, to assess the possible risk factors.

Results: A total of 89 (30.01%) patients with confirmed IBD were diagnosed with opportunistic infections. Clostridium difficile infection was found to be the most common opportunistic infection in patients with IBD, more common among older patients (aged > 45 years) with severe disease (OR = 8.12; 95% CI: 2.27–49.33), currently under treatment with immunosuppressant or immunosuppressants (OR = 2.34; 95% CI: 1.13–10.45). Mycobacterium tuberculosis infection and active tuberculosis was confirmed in 4 cases (1.43%). Furthermore, factors such as the level of C-reactive protein, hemoglobin, and fecal calprotectin were individually to a significantly increased risk of opportunistic infection. However, the use of adalimumab or 5-aminosalicylic acid alone did not increase the risk of opportunistic infection.

Discussion/Conclusion: Patients with inflammatory bowel disease (IBD) commonly display a significantly increased rate of morbidity and mortality. Factors such as severe IBD, elevated levels of fecal calprotectin, and the use of immunosuppressive medications are major risk factors for opportunistic infections in IBD patients.
Predicting Outcomes For Crohn's Disease using a Molecular biomarker: PROFILE trial recruitment update

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Introduction: The course of Crohn's disease (CD) varies substantially between individuals, but reliable prognostic markers do not exist. This hinders disease management because patients with aggressive disease are undertreated by conventional 'step-up' therapy while those with more indolent disease would be exposed to unnecessary treatment-related toxicity if a more aggressive 'top-down' approach was indiscriminately used. We have previously developed and validated a prognostic transcriptional biomarker and the PROFILE trial will assess whether this biomarker can improve clinical outcomes by appropriately matching therapy to disease course.

Methods: This biomarker-stratified trial will compare the relative efficacy of 'top-down' and 'accelerated step-up' therapy between biomarker-defined subgroups of patients with newly diagnosed CD. 400 participants from ~50 UK centres will be recruited. Subjects within each biomarker subgroup (IBDhi or IBDlo) will be randomised (1:1) to receive one of the treatment strategies until trial completion (48 weeks). The primary outcome is the incidence of sustained surgery and steroid-free remission from the completion of induction treatment through to week 48. Secondary outcomes include mucosal healing, quality-of-life assessments and surrogate measures of disease burden including number of flares, cumulative steroid exposure, number of hospital admissions and number of Crohn's-related surgeries. Analyses will compare the relative benefit of the treatment strategies in each biomarker-defined subgroup, powered as an interaction analysis.

Results: At the time of writing, 44 sites have been opened around the UK and 133 participants randomised. Recruitment is ongoing and the most up-to-date data will be available for presentation at the Falk Brussels meeting.

Discussion/Conclusion: We have developed, optimised and validated a whole-blood qPCR classifier that is able to predict disease course from diagnosis in IBD patients. This classifier is currently under investigation in the PROFILE trial. If clinical utility of a stratified treatment approach is demonstrated, this would represent a major step towards personalised therapy in IBD.
Crohn’s case: Recurrent ‘gloves and socks’ distribution with bullous eruptions after adalimumab and infliximab treatment

Esin Ozkan (Istanbul, TR), Metin Basaranoglu (Istanbul, TR)

Introduction: Crohn’s disease (CD) is a chronic inflammatory bowel disease, which can develop in any part of the gastrointestinal tract. Its underlying cause is not fully understood, yet it has a genetic ground and autoimmunity plays a role in the pathogenesis. Anti-TNF (tumor necrosis factor) drugs as biologic agents are used in severe cases or for patients, who do not respond to classic treatment. In our case a young female patient with CD was described with glove sign in her both hands and recurrent bullous skin reactions due to biologic agents.

Methods: A 18-year-old female patient attended to our hospital with diarrhea and recurrent abdominal pain. After her examination she was diagnosed with Crohn’s ileocolitis. Perianal fistula and abscess were established and treated. Adalimumab was chosen as biologic agent for active luminal disease. After the first two doses allergic reactions develop in her skin. Adalimumab was seponated and with anti-allergic drugs her skin went back to normal. The patient was not put at risk and another anti-TNF, infliximab, started immediately. The glove sign was recurred after the first dose. The adverse effects were treated again.

Discussion/Conclusion: Anti-TNF therapy has changed the paradigm of treatment in inflammatory bowel diseases, especially in Crohn’s. They promise better course of disease and more effective healing. Skin reactions are not rare in patients receiving anti-TNF drugs. However, ‘gloves and socks’ distribution with bullous eruption has not been reported before in English literature to the best of our knowledge. Here we presented a 18-year-old female patient with severe Crohn’s ileocolitis accompanied by perianal abscess and fistula. After adalimumab and infliximab treatment, recurrent glove sign with bullous eruption was described. Other than the common side effects of the skin, ‘gloves and socks’ sign must be kept in mind, if the patient uses anti-TNF drugs.
Rectal non-Hodgkin’s lymphoma presented as ulcerative proctitis: A case report

Esin Ozkan (Istanbul, TR), Metin Basaranoglu (Istanbul, TR)

Introduction: Non-Hodgkin’s lymphomas are malignant tumors of lymphatic system, characterized by extranodal involvement especially in gastrointestinal tract. Primary rectal lymphoma is a very rare condition, accounting for only 0.1–0.6% of colorectal malignancies. Here we report a case of non-Hodgkin’s extranodal marginal zone lymphoma (MALT) in rectum.

Methods: In 2015, a 25-year-old female admitted to our hospital with abdominal pain, rectal bleeding, alternating diarrhea and constipation. Colonoscopy verified the preliminary diagnosis ulcerative proctitis and it was treated. Then the biopsy specimens were examined and the patient was diagnosed with Stage 2A B cell non-Hodgkin extranodal marginal zone lymphoma (MALT). The results of immunohistochemical staining were: CD20(+), CD23(+), CD43(+), IgM(+), Bcl-2(+), CD10(-), Cyclin D1(-) and Ki67 = 20%. The patient received CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone) chemotherapy. After second session of CHOP, a repeated PET scan assessed partial metabolic progression in the rectum. Bone marrow biopsy showed no malignant infiltration, hence bone marrow transplantation was not needed. CHOP treatment was finished after 6th session. At the end of the treatment, colonoscopy was repeated and signs of recovery were found in the rectum mucosa. In the 7th year of her disease, the patient achieved a full remission. She is still taking mesalazine pills (3 g/day) and suppository (2 x 500 mg).

Discussion/Conclusion: Primary rectal lymphoma is a rare condition. It is generally seen in men older than 50 years old. The main clinical manifestations are abdominal pain, rectal bleeding and changing in bowel habits. Colonoscopy with biopsy and computerized tomography (CT) are valuable tests for diagnosis. CHOP chemotherapy is the first line therapy in disease management. In our case a 25-year-old female came to the clinic with rectal bleeding. Colonoscopy and rectal biopsy performed. The patient was diagnosed with non-Hodgkin rectal lymphoma. Remission was sustained after CHOP therapy. To conclude rare pathologies such as rectal lymphoma must be kept in mind in differential diagnosis of inflammatory bowel disease, like ulcerative proctitis.
Pharmacy technician in the IBD team maintains patient safety whilst freeing up pharmacists and physicians

Angela Packham (Haywards Heath, GB)

Introduction: We previously demonstrated that integrating pharmacy services into the IBD team releases doctors’ time and improves medicines management. A pharmacy technician providing routine drug monitoring and other duties under the supervision of the specialist pharmacist frees up clinicians’ time. We present a 3 months pilot.

Methods:
1. Provide blood monitoring service for immunosuppressant therapies (524 thiopurine patients, 419 biologics patients)
2. Manage infusion medication and infusion preparation in the pharmacy-led infusion clinic
3. Collate up-to-date patient information for the multidisciplinary virtual biologic and immunosuppressant clinic (VBIC) review
4. Manage shared care protocols (SCP)
5. Identify funds released

Results:
1. 260 patients monitored: 63 patients (24%) reminded
   48 referrals (18.4%) to the pharmacist:
   - 27 patients (10.3%) had drug levels outside therapeutic ranges or antibodies
   - 9 patients (3.5%) had deranged liver function tests
   - 5 patients (1.9%) had leucopaenia
   - 7 patients (2.6%) had either raised faecal calprotectin (FCLP) levels or anaemia
2. Biologics for 259 patients (average of 20 patients/week) dispensed and prepared, maximising vial-sharing, releasing nurses and pharmacists
3. 42 patients contacted to provide a FCLP, IBD scores and bloods 2 weeks prior to VBIC
4. 17 SCP were sent to patient GP’s
5. £3212 staffing cost released

Discussion/Conclusion: Pharmacy technicians can safely take over the majority of the drug monitoring and infusion preparation. Released funds of £13K (lower staffing cost) and cost savings £36K (vial sharing) per year are projected. This represents an increased cost saving, freeing up nursing time and releasing clinicians for advanced roles within the team (e.g. outpatient clinics, prescribing, helpline queries, counselling patients, TDM). In addition this audit has identified the on-going need for active monitoring of the medications as 1/5 of patients had abnormal results and 1/4 had to be chased up to undertake monitoring at the appropriate interval.
Long-term efficacy and safety of CT-P13, a biosimilar of infliximab, in patients with inflammatory bowel disease: A retrospective multi-center study

Dong Il Park (Seoul, KR), Nam Hee Kim (Seoul, KR)

Introduction: The biosimilar of infliximab, CT-P13 (Remsima®) has potential to reduce treatment costs and enhance access to biological therapy for inflammatory bowel disease (IBD) patients. However, long-term clinical data on its use for IBD treatment are currently sparse. We aimed to investigate the long-term efficacy and safety of CT-P13 therapy in large, real-life IBD cohort.

Methods: A total of 368 IBD patients (227 with Crohn’s disease [CD] and 141 with ulcerative colitis [UC]) treated with CT-P13 at 16 referral hospitals in Korea from July 2012 to December 2017 were retrospectively analyzed.

Results: The cumulative retention rates at year 1, 3, and 5 were 86.1%, 68.5%, and 58.7% and 69.7%, 46.0%, and 26.7% in anti-TNF-naive CD and UC patients, respectively. The clinical response and remission rates at week 14, and year 1, 3, 5 were 94.3%, 92.7%, 76.8%, and 17.6% and 78.6%, 82.4%, 72.2%, and 17.6% in anti-TNF-naive CD, and 85.6%, 80.0%, 55.2%, and 6.7% and 42.6%, 59.8%, 44.2%, and 6.7% in anti-TNF-naive UC patients, respectively. Among patients who switched from biologic originator to CT-P13, the cumulative retention rates at year 1, 3, and 5 were 88.5%, 66.1%, and 44.8% in CD, and 73.9%, 42.5%, and 42.5% in UC patients, respectively. Significant improvements in disease activity scores were accompanied by marked reductions in inflammatory markers levels, and no unexpected adverse events including death or malignancy arose during the study period.

Discussion/Conclusion: Long-term treatment with CT-P13 is effective in inducing and maintaining disease improvement, and well-tolerated in patients with IBD. CT-P13 may be a promising treatment option for IBD.
Can fatigue in inflammatory bowel disease be classified as a separate entity?

Jacqueline Paterson (Dundee, GB)

Introduction: Fatigue in IBD affects 44–86% of patients with active disease and 22–54% in remission. Patients report fatigue as a significant concern. Causes of fatigue in IBD remain unclear. Proposed mechanisms focus upon active inflammation but cannot explain the persistence in quiescent disease. Potentially fatigue could be a separate entity and that it is a consequence of myalgic encephalomyelitis (ME).

Methods: A questionnaire assessing fatigue in patients attending IBD clinics in Tayside was developed to assess whether those reporting fatigue met the diagnostic criteria for ME based upon guidance from the Centres of Disease Control (CDC), International Consensus Criteria (ICC), Institute of Medicine (IOM) and the National Institute for Health and Care Excellence (NICE). Responses were analysed to determine whether the criteria for a diagnosis of ME in the context of each of the four guidelines had been reached.

Results: Fatigue was experienced by 65% (n = 64) and was more prevalent in CD than UC (74% vs. 52%) and in females than males (77% vs. 51%). 64% of those experiencing fatigue reported fatigue persisting in the absence of gastrointestinal symptoms. Of those with fatigue, 26 patients (41%) with IBD fulfilled the NICE ME diagnostic criteria, 13 (20%) the ICC, 6 (9%) the IOM criteria and 13 (20%) the CDC criteria.

Discussion/Conclusion: Fatigue is commonly reported in IBD patients even when disease is in remission. Although confounding factors, (e.g., concurrent medication or co-morbidity), may contribute to fatigue a small proportion meet the recognised diagnostic criteria for ME and this should not be overlooked when managing fatigue in IBD.
Oral manifestations of Crohn's disease

Barbara Perše (Zagreb, HR), Orjena Žaja (Zagreb, HR)

Introduction: Crohn's disease is a chronic inflammatory bowel disease that affects the entire digestive tube. Orofacial granulomatosis describes changes in the oral cavity, without the involvement of the gastrointestinal tract. However some of the patients may have an active subclinical disease or potential for developing Crohn's disease. In patients with diagnosed Crohn's disease changes of the oral cavity are called oral Crohn's disease. In adults, the prevalence of oral Crohn's disease is 20%, in the pediatric population it is significantly higher (41.7–48%), and is often overlooked. The changes in the oral cavity can also be a side effects of pharmacological therapy (directly/indirectly), or the consequences of malabsorption and nutritional deficits which can be equally presented. Treatment is complex, it involves treatment of primary intestinal disease combined with the local therapy (corticosteroids, immunosuppressants), some authors also recommend diet without additives.

In 30% of patients, oral Crohn's disease remains present regardless of the activity of intestinal disease, and according to some studies, it is an indicator of a more severe phenotype Crohn's disease.

Methods: In this report, we describe the case of a girl whit a Crohn's disease who developed a severe chronic lesions in the oral cavity.

Results: Case report: A 17-year-old girl suffers from an extensive form of a Crohn's disease since she was 11. Initially it was presented as a pancolitis with sideropenic anemia, without other extraintestinal manifestations. She had no delay in growth or sexual development. Over the years, she had frequent relapses, pharmacotherapy was frequently modified, with whole spectrum of therapy applied (exclusive enteral nutrition, immunosuppressive therapy, biologic therapy in combination with corticosteroids during periods of acute relapses). The clinical course seemed favorable, but typical changes persisted in the ileocaecal region with the development of an intersphincteric fistula. At the age of 16, five years after diagnosis was made, she developed severe gingivitis and periodontitis with ulcer-like lesions. At first she was treated by a periodontologist, but progression of the changes arouse suspicion that it is in fact oral Crohn’s disease. Antibiotic therapy was started, with a partial effect; but significant improvement was recorded only during short periods of corticosteroid therapy (local or systemic). Histologically the changes were described as hyperplastic gingivitis with chronic inflammatory changes, without granuloma.

Discussion/Conclusion: In this case, we wanted to recall another (extraintestinal?) Crohn's disease manifestation that can significantly impair the quality of life of patients and requires special attention, knowledge and cooperation between gastroenterologists and dental specialists.
Ways of adjusting nutrition in the inflammatory bowel diseases

Ovidiu Petrascu (Sibiu, RO)

Introduction: The complementary role of a diet in enhancing the quality of life of the patients with inflammatory bowel diseases is well-known. Some foods enhance the dominant symptoms of these diseases, while others alleviate them. The adjustment of the diet must include an element related to the patient’s nutritional experience, but also the collaboration with a specialist in nutrition, whose advice can lead to a personalized diet for every individual patient.

Methods: The study included a questionnaire with twenty questions applied to a number of 45 patients, 25 of whom had ulcerative colitis and 20 of whom had Crohn’s disease. The questionnaire included a section of questions regarding the patients’ general characteristics, one regarding the impact of various foods on their clinical status and another one that targeted the ways in which their diet was patterned.

Results: Out of the 45 patients, 32 (71.1%) admitted to using a diet. The foods that were least tolerated and eventually excluded from their diet were: spicy foods (27 patients – 84%), carbonated drinks (25 patients – 78%), deep-fried foods (18 patients – 56%), processed meat (12 patients – 37.5%), milk and dairy products (10 patients – 31%), alcoholic drinks (10 patients – 31%), low-fibre bread (9 patients – 28%), coffee, cabbage and citrus fruits (9 patients – 28%). Abdominal pain generally decreased following dietary restrictions, with 23 patients (71.8%) admitting to the alleviation of the pain, while diarrhea was alleviated in only 12 patients, namely those who adopted a strict diet. All the 32 patients who stuck to a strict diet admitted that they had adopted it based on their personal experience; out of this number, only 10 patients also got advice from specialists in gastroenterology, while only 2 consulted a nutritionist as well.

Conclusion: The adjustment of the patients’ diet in the inflammatory bowel diseases influences abdominal pain in a positive manner, but it influences diarrhea to a lesser degree. In our opinion it is mandatory that the counselling of these patients with regard to the diet they adopt should be assisted by a specialist in nutrition. The nutrition plan that the nutritionist tailors to the needs of each patient may greatly improve his/her quality of life.
Effect of biological therapy on the grade of inflammatory bowel disease activity and values of inflammatory parameters

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Methods: The purpose of this study was to determine the effect of biological therapy on platelet and CRP levels in patients with IBD. The study included 30 patients with IBD who were on biological therapy from June 2016 until the end of 2017. The patients were divided into 3 groups, according to the disease activity rate, which was determined by DAI for ulcerative colitis and CDAI for Crohn's disease. 21 patient had medium disease activity, 9 had serious disease activity.

Results: The age of the patients was between 20–65 (average 38 ± 11), female 43.33%, male 56.67%. 56% had ulcerative colitis, 44% had Crohn's disease. The average platelet levels were referential at UC patients (346 ± 137 before therapy, 301 ± 101 after 6 months), while at CD, the values were above the upper limits before therapy and referential after 6 months (414.8 ± 127 vs. 273 ± 66); the difference is not statistically significant (p = 0.002). The average CRP levels were above the referential value at UC patients (26.4 before therapy [13.37–83]; 9.9 after 6 months [4.32–15.4]); the difference is statistically significant (p = 0.008). At CD, CRP levels were high before therapy – 13.2 (4.1–45.7) and referential after 6 months – 3.1 (2.2–4.6); the difference is statistically significant (p = 0.002).

Discussion/Conclusion: Analysis of the disease activity proved that biological therapy is equally effective with UC as well as CD. The differences between mean score values at UC before therapy and after 6 months of therapy were statistically significant – p = 0.002. The differences between mean score values at CD were also statistically significant – p = 0.001.
The study of colonic resistance as a background for microbiome engineering in IBD

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Introduction: The mechanisms explaining complex relationship between the commensal colonic microbiota and IBD have a common outcome, a violation of bacterial antigens exposure to effector T-cells and innate immune cells residing in the intestinal mucosa and/or alteration of the host immune response to bacteria. Application of microbiome knowledge is traditionally on treatment and prevention of dysbiosis. The discovery of dominant members of microbial communities serving beneficial functions including immunomodulation is likely to bridge gap of lacking complete understanding of microbiome engineering will widen this scope to suit preventive, therapeutic, and diagnostic needs in IBD. While the role of gut microbiota and respective immune changes has become more evident in recent years there is no sufficient database explaining the character of microbiota changes in IBD. The aim of this study is to find associations between changes of colonic microbiome and IBD.

Methods: Totally 104 individuals participate in the study. Among them 34 had clinically and endoscopically proven IBD (12 – CD, 22 – UC), others with at least three risk factors of IBD (family history, smoking, antibiotics, travel history, immune, etc). Colonic resistance studied in multiple mucosal bioplates. Standard aerobic and anaerobic microbiology techniques with nosology identification and quantity composition of microbiota were used. Diversity and microecological indices were used to assess the structures of colonic microbial populations. All isolated taxons were analyzed by antibiotic resistance analysis for each sampling event for all individuals. RT-PCR used for assessment of microbial genotypes.

Results: Major autochthonic species (14 in total) were present in all samples: among them Lactobacteria, Bifidobacteria, E. coli, several other anaerobic species were dominating. However, Lacto- and Bifidobacteria were found in significantly lower levels compared to healthy subjects (p = 0.02–0.0031). The general tendency for colonic resistance in IBD was decrease of autochthonic anaerobes (Bifido-, Lactobacteria, Bacteroides spp., Clostridia spp., Bacillae spp.) and significant growth of allochthonic aerobes and facultative anaerobes (E. coli Hly+, Pseudomonas, Serratia, Hafniae, P. mirrabilis and other conditionally pathogenic Enterobacteriaceae). Enterococci were present in 60.0% of control and 7.14–20.69% of study group. Staphylococci were present only in study group (17.24–31.58%). Group and individual biodiversity indices were significantly lower in IBD, especially in UC group.
**Discussion/Conclusion:** Our data suggest that morbid changes of colonic mucosal microbiota, e.g. abnormal ratio of autochtonic and allochtonic species, may be considered as a strong characteristic feature of IBD. Meanwhile, there is no exact IBD "pathogen" found. This study gives possible objectives for modulating therapies – restoration of microbiome's biodiversity and additional population by Bifido- and Lactobacteria with use of adjuvants or diets for creating adequate conditions for microflora development.
Rare extraintestinal manifestations in a Crohn disease patient

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Introduction: Crohn’s disease (CD) and Takayasu arteritis (TA) are chronic inflammatory granulomatous disorders of undetermined etiology. TA is a form of vasculitis that affects the aorta and its major branches. Some reports describe the presence of both diseases in the same patient. In present literature there are no clear evidences about pathophysiological mechanisms responsible for this overlap, but potential explanation could be autoimmunity or generation of the same pro-inflammatory cytokines such as tumor necrosis factor (TNF)-α in both diseases. TA may represent extraintestinal manifestation of CD. Antiphospholipid syndrome (APS) is characterized by presence of antiphospholipid antibodies (anticardiolipin antibody [aCL], lupus anticoagulant [LA], and anti-β2 glycoprotein I [aβ2GP I]), and can manifest with thrombotic complications and pregnancy loss. Antiphosphatidylserine/prothrombin antibody (aPS/PT) could be associated with APS. Some authors reported that antiphospholipid antibodies could be positive in CD patients, in patients without or with arterial thrombosis, venous thrombosis, or pregnancy loss. Bacterial translocation is one of the proposed underlying mechanisms responsible for the production of antibodies in IBD and APS. Although the relationship among CD, TA and APS is not clear, autoantibodies, the formation of granuloma, and bacterial involvement may be responsible for overlapping of the three diseases.

Methods: We report the case of a female patient diagnosed with ileo-colonic CD disease with perianal fistula at the age of 15 in 2004.

Results: The family history was positive for IBD, namely father had ulcerative colitis and brother CD. Patient was treated with steroids that were tapered and azathioprine as maintenance therapy. In 2008 she underwent cholecystectomy complicated with pulmonary thromboembolism in postoperative period. In 2009 right hemicolecction with resection of terminal ileum and ileo-colonic anastomosis was undertaken. In following few years she had CD in remission, but reported three pregnancy losses. Further investigation was done and the diagnosis of antiphospholipid antibody syndrome (APS) was established. Oral anticoagulant therapy by warfarin was started. In 2015 patient reported fatigue, headaches, occasional chest pain and shortness of breath. Physical exams showed arterial blood hypertension and systolic murmur across precordium and over both carotid arteries. Further examination (CT angiography of head and chest, color Doppler ultrasonography of carotid arteries) were performed and conclusion was the presence of arterial wall thickening and narrowing of ascending aorta and both common carotid arteries. Our patient met the 2006 EULAR/PRES consensus criteria and the diagnosis of TA was set. The therapy of methylprednisolone and then prednisone were started and the therapy with warfarin continued. Fatigue, headaches, chest pain and shortness of breath disappeared quickly. Because of the active CD complicated with active perianal fistula
and possible common mechanism of disease drive by TNF, azathioprine therapy was stopped and anti-TNF therapy with infliximab was started in our patient. In the following period there were no new thromboembolism events.

**Discussion/Conclusion:** IBD patient sometimes exhibit unusual extraintestinal manifestations or overlap syndromes that, if unrecognized can lead to prevent serious consequences or life treating conditions like thromboembolism or congestive heart failure and cerebrovascular accidents.
Factors associated with non-adherence to medication for inflammatory bowel disease: A monocentric Tunisian study

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Introduction: Adherence is generally associated with improved treatment outcomes. Risk factors for non-adherence must be understood to improve adherence. The aim of our study is to determine which variables were consistently associated with non-adherence to treatment in inflammatory bowel disease (IBD).

Methods: Retrospective study including patients with IBD receiving maintenance medication and followed in our department between 2014 and 2018. We assessed a range of adherence behaviors. Demographic, clinical, and psycho-social characteristics were also assessed by chi 2 test. Adherence was considered as a continuous variable and then categorized as high or low adherence for logistic regression analysis to determine predictors of adherence behavior.

Results: Forty-eight percent of the patients reportedly adhered to their treatment. In univariate analysis, factors associated independently with low adherence in IBD patients were age younger than 30 (odds ratio = 2.519 [95% confidence interval: 0.837–7.576]; p = 0.042), low socioeconomic condition (2.5 [0.813–8.134]; p = 0.039), active smoking (0.148 [0.045–0.489]; p = 0.001), male gender (0.148 [0.45–0.489]; p = 0.001) and patients under immunosuppression (2.7 [0.768–8.136]; p = 0.0123). In multivariate analysis, factors associated independently with low adherence in the IBD population were age under 30 (p = 0.075), low socioeconomic condition (p = 0.049), active smoking (p = 0.000) and male gender (p = 0.001).

Discussion/Conclusion: Approximately half of the IBD patients were low adherers. Predictors of low adherence were aged younger than 30 years, low socioeconomic condition, active smoking and male gender.
Management of intra-abdominal abscesses in Crohn’s disease: A monocentric Tunisian experience

Hayfa Romdhane (Tunis, TN), Bochra Bouchabou (Tunis, TN), Houda Ben Nejma (Tunis, TN), Rym Ennaifer (Tunis, TN)

Introduction: Intra-abdominal abscesses are challenging dilemma for gastroenterologists and surgeons. There are several treatment options where the role and timing of medication and surgery are conflicting.

Methods: Retrospective study including patients with Crohn’s disease admitted in our department between January 2015 and December 2018 for intra-abdominal abscess.

Results: Among 58 patients followed for Crohn’s disease, 10 had spontaneous intra-abdominal abscess. Mean age was 34 years; they were 7 men and 3 women. The abscess was associated with perforating ileocecal Crohn’s disease in all but one who had rectosigmoid fistula. The abscess was inaugural in 3 cases while Crohn’s disease was diagnosed since a mean time of 12 months (extremes: 3–36) for the others. 4 patients were on immunosuppressive therapy (corticoids, thiopurines or anti-TNF) for active luminal disease. Tomography was the initial imaging performed. It disclosed single abscess in 7 cases and multiples abscesses in 3 cases with a mean diameter of 35 mm (extremes: 10–200). Fistula was demonstrated in all cases associated with stenosis in 8 cases. All patients were started on intravenous antibiotic therapy during 21 days, alone in 8 cases and associated with percutaneous drainage in 2 cases. Total parenteral nutritional therapy was prescribed in 5 cases. Only one patient required immediate surgery. Patients with persistent fistula or stenosis after successful medical treatment underwent planned surgical resection, while patients with extensive ileal disease had anti-TNF therapy. No recurrence of the abscess was noted with a follow up ranging from 1 to 12 months.

Discussion/Conclusion: In this small case series, management was mostly non-surgical according to the characteristics of the abscess and the availability of percutaneous drainage. Following medical therapy, surgery was required only when the disease was localized with persistent fistula or obstruction. Biotherapy are now useful when the disease is extensive.
Risk factors for decreased bone mineral density in inflammatory bowel disease in a Tunisian cohort

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Introduction: Patients with inflammatory bowel disease (IBD) are at risk for metabolic bone disease. Many studies have identified various risk factors but most of them have involved Western patients. The aim of this study was to investigate the prevalence and the risk factors for metabolic bone disease in Tunisian IBD patients.

Methods: Retrospective study including patients with IBD admitted in our department between January 2015 and December 2018. Demographic and clinical characteristics of patients were analysed. Bone mineral density of the femoral neck, total femur and lumbar spine was quantified by dual-energy X-ray absorptiometry.

Results: Among 82 patients followed for IBD (70.7% with Crohn’s disease; 29.3% with ulcerative colitis), a bone densitometry was performed in 56% of cases (n = 46). 16 patients had osteopenia and 7 had osteoporosis, as assessed by T-score. Univariate analysis showed that Crohn’s disease in particular ileal disease, high steroid dose and the presence of extraintestinal manifestations were significantly associated with a low bone mineral density (for all p < 0.05). In the other hand, IBD duration since diagnosis, sex, tabagism were not associated with bone loss.

In multivariate regression analysis, risk factors for decreased bone mineral density were IBD duration since diagnosis, high steroid dose, ileal Crohn’s disease and extraintestinal manifestations.

Discussion/Conclusion: In our Tunisian cohort of IBD patients, Crohn’s disease, high steroid dose and extraintestinal manifestations were associated with increased risk for metabolic bone disease. High-risk patients should be identified and appropriate therapies should be started early to improve long term quality of life.
Colonic amyloidosis

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Introduction: Amyloidosis is a rare systemic disease characterized by the extracellular deposition of a homogenous material, the amyloid. It is a systemic disease but the most frequently involved are the kidneys, the heart, gastrointestinal tract (GI), liver, spleen and peripheral and autonomic nervous system.

Methods: A 71-year-old man with a medical history of hypertension, diabetes mellitus and an infection episode of Clostridium colitis is admitted in our hospital with edema of the legs, diffuse abdominal pain and diarrhea (10 stools/day) with a 3-month onset. Laboratory tests revealed nephrotic-range proteinuria, hypoalbuminemia and inflammatory syndrome. The presence of toxins A and B Clostridium in the stool was negative. Colonoscopy revealed congestive friable, bleeding-easily, patchy-erythematous appearing mucosa throughout the colon. The initial endoscopic impression was inconclusive but the histology revealed amyloidosis with strong birefringence with Congo red stain.

Discussion/Conclusion: Systemic amyloidosis is a complex and diverse entity with multiple etiologies and presentations that represents a significant diagnostic and treatment challenge. Within the GI tract, symptoms are often non-specific. Diagnosis depends largely on tissue biopsy and endoscopy.
Chronic diarrhea due to Capillaria philippinensis: A case report

Mohamed Sharaf-Eldin (Tanta, EG)

Introduction: Chronic diarrhea has many causes, sometimes a rare etiology is the cause.

Methods: Female patient 38 years old. Born and live in Tanta, Egypt. Complain: Frequent loose stools of 6 months duration with gradual onset and progressive course of painless watery diarrhea 6–10 motions/day awakening the patient from night sleep with significant weight loss and lastly lower limb edema. There was no mucus, blood or tenesmus. She had colonoscopy with terminal ileal biopsy done and was given treatment for two months with inadequate response. During hospital admission the patient developed yellowish discoloration of sclera, dark colored urine, normal colored stool. General and abdominal examinations: jaundice, hepatomegaly, lower limb edema. Urine, stool, and CBC were irrelevant, liver function tests showed albumin: 1.4 g/dl, Chest x-ray: normal. Hepatitis markers were negative. Abdominal ultrasound showed bright hepatomegaly. Upper GIT endoscopy showed erythematous gastritis. Barium meal follows through: Diffuse wall thickening of the ileal loops with irregular mucosal outline in the form of exaggerated mucosal folds. The radiologic finding suggests the diagnosis of malabsorption syndrome.

Results: Colonoscopic examination was done up to the terminal ileum and revealed: Hyperemic ileal mucosa, multiple biopsies were taken from the terminal ileum. Terminal ileal biopsy: chronic inflammatory reaction with eosinophils, positive for thick-shelled eggs and larva suggestive of Capillaria philippinensis. After treatment with albendazole, multivitamins, UDCA, diarrhea stopped with improvement of general condition.

Discussion/Conclusion: A case of Capillaria philippinensis.
Helicobacter pylori may be an initiating factor in newly diagnosed ulcerative colitis patients

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Introduction: Ulcerative colitis (UC) is an inflammatory bowel disease (IBD) of the colon with an unidentified cause. Genetic and environmental elements, in particular the gut bacteria appear to play a role in its development. We aimed to directly visualize Helicobacter pylori (H. pylori) by the highly sensitive and specific technique of immunohistochemical staining in colonic tissue from patients newly diagnosed with ulcerative colitis (UC).

Methods: Colonoscopic biopsies from 30 patients with newly diagnosed UC and 30 controls were stained with Giemsa stain and immunohistochemical stain for detection of H. pylori in the colonic tissue. Results were confirmed by testing H. pylori Ag in the stool then infected patients were randomized to receive either anti H. pylori treatment or placebo.

Results: Twelve/30 (40%) of the UC patients were positive for H. pylori by Giemsa, and 17/30 (56.6%) by immunohistochemistry stain. Among the control group 4/30 (13.3%) and 6/30 (20%) were positive for H. pylori by Giemsa and immunohistochemistry staining respectively. H. pylori was significantly higher in UC than in controls (p = 0.04 and 0.007). All Giemsa-positive patients and controls were positive by immunohistochemical stain. Four cases of the control group positive for H. pylori also showed microscopic features consistent with early UC.

Conclusion: H. pylori can be detected in colonic mucosa of patients with UC and patients with histological superficial ulcerations and mild infiltration consistent with early UC. There seems to be an association between UC and presence of H. pylori in the colonic tissue. Whether this is a causal relationship or not remains to be discovered.
Fecal calprotectin in the diagnosis of ulcerative colitis (UC) among Egyptian patients

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Introduction: Ulcerative colitis (UC) is characterized by recurrent episodes of inflammation limited to the mucosal layer of the colon. Fecal calprotectin (FC) has been proposed in recent studies as a sensitive, specific biomarker for the diagnosis of ulcerative colitis (UC).

Aim of the work: Is to compare fecal calprotectin in patients known to have ulcerative colitis with normal healthy controls and to investigate possible correlation of calprotectin with disease activity on clinical, laboratory and pathological bases.

Methods: Forty-two patients known to have UC were assessed, 14 males (33.3%) and 28 females (66.7%), mean age 37.5 (± 16.0) years. Ten healthy controls (8 females and 2 males), mean age 30.9 (± 16.1) years were included. Patients underwent clinical evaluation, determination of blood erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) and fecal calprotectin. Colonoscopy was done to confirm diagnosis, estimate disease extent and obtain colonoscopic biopsy specimens for histological grading of activity. An overall scoring of disease activity was done using the Mayo score.

Results: Fecal calprotectin was significantly elevated among patients (mean: 12.6 μg/g stools [± 3.2]) in comparison to controls (9.4 μg/gm stools [± 2.6], p 0.01). At a cut off 10.3 μgm/gm stools it has a sensitivity of 86%, specificity of 70%, p = 0.004, positive predictive value of 86% and a negative predictive value of 70%. No correlation was found between fecal calprotectin and ESR, histopathology and Mayo score. Calprotectin was significantly higher in cases with left-sided colitis (14.1 ± 2.7 μg/g stools) than those with pancolitis (11.8 ± 1.9 μg/g stools), p 0.02.

Discussion/Conclusion: Fecal calprotectin is a good test in differentiating Egyptian patients with ulcerative colitis from healthy controls. Thus, its use as a screening test may be helpful in the selection of cases for endoscopic examination. It lacks specific correlation with the severity of ulcerative colitis. Larger scale studies on Egyptian patients are strongly recommended with special reference to the local mucosal permeability and immune milieu of the Egyptian population.
IBD case report presented only by jaundice: It is rare among Egyptians

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Introduction: Jaundice represented about 40% of all cases attended in Desouk fever hospital. In Egypt the epidemiology of primary sclerosing cholangitis (PSC) and its association with inflammatory bowel disease (IBD) have not been studied thoroughly. Therefore, we reported this case aiming to study the association between primary sclerosing cholangitis and inflammatory bowel disease (IBD) which is rare in Egyptian people.

Case report: Egyptian male patient presented at March 18, 2019. The patient showed jaundice with normal examination of the chest, heart and abdomen, he gave history of intermittent attacks accompanied with fever and dark urine.

- No manifestations of anemia, hepatic dysfunction, epigastric pain, weight loss, diarrhea, skin lesions or bleeding per rectum.
- Investigations: Normal CBC, ESR: 70 (1st hour), 110 (2nd hour).
- Urinalysis: proteins: +, Glucose: nil, bile pigments: ++, urobilinogen: +
- Liver chemistry: Bil-T: 5.6, Bil-D: 3.5, AST: 62 (n: up to 41), ALT: 81 (n: up to 41), ALP: 640 (n: up to 104), GGT: 322 (n: up to 50), total proteins: 8.0 (n: 6.6–8.7), albumin: 3.5 (n: 3.5–5.5), creatinine: 0.72, prothrombin concentration: 78%, INR: 1.3
- Viral markers: HBsAg: -ve, HBcAb total: -ve, HBsAb: -ve, anti-HCV Ab: -ve.
- Ultrasound: Conclusion: Mild bright hepatomegaly, mild central IHBR dilatation.
- MRCP: Picture suggestive of sclerosing cholangitis.
- Liver biopsy: No evidence of specific pathological alteration was detected in the specimen received.
- Colonoscopy: Conclusion: ulcerative colitis, active phase.
- Treatment
  - We began with high dose UDCA (20–25 mg/kg)
  - Meclizine 4 g daily with improving the case.

Discussion/Conclusion: As the IBD incidence is rising in Egypt, some unusual presentations of the extra-colonic manifestations as well the associated diseases, e.g. the sclerosing cholangitis, should be put in clinical approach to cases suspected to be IBD.
A rare case of ascites (retroperitoneal fibrosis)

Shuann Shwana (Merthyr Tydfil, GB)

Introduction: A 69-year-old gentleman presented with a five week history of abdominal distension. He has a past history of diabetes and myocardial infarction, is an ex-smoker with no significant history of alcohol intake. Examination demonstrated a distended non tender abdomen with shifting dullness, no organomegaly and no signs of chronic liver disease.

Methods: Investigations included ultrasound scan of abdomen, ascitic tap, CT abdomen/ pelvis and CT guided biopsy.

Results: Ascitic tap revealed chylous ascites with high SAAG (serum ascites-albumin gradient) of > 1.1 g/dl indicating a non-peritoneal cause of ascites. Cytology revealed no evidence of malignancy. CT abdomen revealed a mildly enhancing soft tissue mass encasing the mesenteric and renal vessels and the upper abdominal aorta and also the left peritoneal space; appearances were suggestive of lympho-proliferative disorder. CT guided biopsy showed reactive changes consistent with retroperitoneal fibrosis. Immunohistochemistry done at University College of London showed no evidence of IgG4 disease. Patient was commenced on prednisolone and azathioprine. He failed to tolerate azathioprine which was then stopped. Treatment with prednisolone failed to slow the rate of reaccumulation of the ascites, and he continued to require frequent abdominal paracentesis.

Discussion/Conclusion: Chylous ascites has rarely been reported as a presenting feature of retroperitoneal fibrosis. (1) Retroperitoneal fibrosis may be a idiopathic in 70% of cases or secondary condition. The incidence of idiopathic form is 0.1 per 100,000 person-years with a prevalence of 1.4 per 100,000 population. (2) The primary modality used for diagnosis of retroperitoneal fibrosis is CT imaging, biopsies are performed in cases of unusual presentation and to exclude malignancy and IgG 4 related pathology. Treatment of retroperitoneal fibrosis in most cases depends on whether it is idiopathic or secondary. The mainstay of treatment is corticosteroids and if no response, immuno-suppressive therapy can be used. Case series data is present which has shown that high dose corticosteroids like prednisolone are effective in reducing the chronic inflammatory response caused by retroperitoneal fibrosis; however there is a high rate of recurrence once the steroids are withdrawn. Mycophenolate mofetil in addition to corticosteroids has shown reduced duration of steroid use without affecting the efficacy and reduces disease recurrence rate.
Trace elements status in patients with inflammatory bowel disease

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Introduction: The significance of trace elements (TE) status in patients with inflammatory bowel disease (IBD) is still debated. Among the most common causes of TE status alteration are malnutrition and weight loss due to enteric loss of nutrients, as well as malabsorption and reduced food intake. In recent studies, a wide range of vitamin and mineral deficiencies has been noticed in IBD patients, with varying degrees of clinical importance. Aim of our study was investigate status of TE in patients with IBD, and to investigate whether it has a correlation with disease activity.

Methods: Case-control study was performed among 30 patients with IBD as well as 30 age and sex matched healthy controls. Namely all patients undertook a total colonoscopy with polytopic colon and terminal ileum biopsies. Complete blood count was obtained after an overnight fast, in addition to inflammatory markers (CRP, erythrocyte sedimentation rate-ESR). Serum levels of zinc, copper and magnesium were measured spectrophotometrically, while serum iron was assessed with an electro-chemiluminescence immunoassay. Mayo score and CDAI respectively were calculated for each patient.

Results: Levels of iron, zinc, magnesium, selenium were significantly lower in the IBD group in comparison to control group (p < 0.05). There was no statistically significant difference in levels of copper between the two groups (p > 0.05). In the IBD group mean levels of iron (7.11 ± 8.20 μmol/l), zinc (23.62 ± 5.31 μmol/l) and magnesium (0.61 ± 0.22 mmol/l) were reduced below the reference range, while the levels of copper (28.21 ± 24.13 μmol/l) were higher. Iron and zinc levels negatively correlated with CDAI and Mayo score (p < 0.05), whereas there was no correlation in the levels of copper and magnesium with disease activity scores (p > 0.05).

Discussion/Conclusion: TE alteration is probably the result of the prolonged inflammation. Zinc and iron deficiency could be a potential indicator of the disease activity as well as increased oxidative stress in IBD, which indicates the importance of their supplementation as an additional therapy.
Embedding pharmaceutical care into the IBD multidisciplinary team

Anja St. Clair Jones (Brighton, GB)

Introduction: Pharmacists traditionally do not get involved in the long-term management of patients with chronic diseases. This service development aimed to integrate a pharmacy led medication optimisation service into the specialist Multi Disciplinary Team (MDT).
We report 4 month experience of extending our specialist pharmacists' remit.

Methods:
1. Weekly pharmacist outpatient clinics initiate immunomodulating therapies, undertake biochemical monitoring and therapy adjustments due to blood results, adverse drug reactions or concordance.
2. Pharmacists lead biologics infusion clinics strategically and operationally.
3. Pharmacist-led blood monitoring and therapeutic drug monitoring (TDM) service for immunomodulators optimises therapies and guides therapy decisions.
4. Pharmacists support rapid access service.
5. Pharmacists facilitate MDT approved pathways to initiate and review immunomodulators.
6. A workload and prescription audit was conducted, the financial benefit assessed and service anonymously peer reviewed.

Results:
1. 14 pharmacist clinics were analysed: 138 patients managed by pharmacists, 382 patients' bloods monitored ensuring clinical governance of therapies.
2. The biologics infusion clinic was expanded.
3. 65 patients had their immunosuppressants adjusted due to TDM. Pharmacist prescribers are gatekeepers for testing and responsible of therapy optimisation.
4. The advice required for the rapid access service is primarily nurse orientated with the pharmacist deputising to maximise resources.
5. The MDT reviewed 42 patients according to the developed pathways.
6. The TDM service resulted in a minimum of £60,000 savings. 6 responders returned overwhelmingly positive peer reviews.

Discussion/Conclusion: Involving the pharmacist in the long-term care of IBD patients enhances patient safety, standardises treatments and individualises medical therapies. The focus of the MDT shifted to early medicines optimisation realising considerable cost savings.
Embedding pharmaceutical skills into the multidisciplinary team influences decision making right at the initial stage, ensuring that services incorporate good medicine management and medicine optimisation principles at conception guaranteeing high-quality, compassionate care and strong governance.
Multi-omic data integration assisted identification of molecular features contributing to disease heterogeneity in Crohn’s disease

Padhmanand Sudhakar (Norwich, GB)

Introduction: The disease behaviour of Crohn’s disease (CD) is heterogeneous as evidenced by inflammatory, fibrostenotic or penetrating sub-types. Integrated molecular features that predict these sub-types at diagnosis, and biological mechanisms explaining the difference between them are lacking. Dysregulated T cell populations in CD patients have been associated with disease activity variation. We aim to identify discriminative features, from the integrative analysis of gene expression from blood-derived, sorted PBMC (CD4+ monocytes and CD14+ T-cells) and mutational profiles, which explain CD behavioural heterogeneity.

Methods: Sorted populations of circulating CD14+ and CD4+ cells were isolated from the blood of 29 patients with active CD (35% male; median [IQR] disease duration 21.5 [14.0–27.3] years; 24% inflammatory [B1], 49% stenosing [B2] and 27% penetrating disease [B3]). RNA was extracted from the CD14+/CD4+ cells and sequenced. The mutational profiles for known CD GWAS variants determined using Immunochip genotyping data was used. We integrated the three above-described -omic datasets using Multi-Omics Factor Analysis (MOFA). Features were selected from the strongest -omic layers of the explanatory Latent Factors (LFs).

Results: Fourteen Latent Factors (LFs) were identified to contribute at least 2% of the total variance. Three of the LFs explained disease behaviour (p ≤ 0.1). We identified gene expression of CD14+ and CD4+ cells as the strongest -omic layers in two of the three explanatory LFs. Post feature extraction and selection, we identified a panel of CD4+ and CD14+ genes which distinguishing the inflammatory sub-type from the fibrostenotic and penetrating sub-types. While the CD14+ discriminatory genes were enriched with various pathways such as interferon signalling, T-cell receptors, antigen presentation, interleukin signalling among others, very few pathways were over-represented in the CD4+ genes.

Discussion/Conclusion: Using multi-omic data integration, we identified gene expression signatures from CD14+ T-cells which could explain CD subtypes in terms of disease behaviour. This is expected to enhance our understanding of biological mechanisms which could further explain the heterogeneous disease behavioural patterns observed in CD.
Pathogenetic associations of kidney impairment, endothelial and intestinal inflammation

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Introduction: For many years, IBD was considered a chronic disorder, solely affecting the bowel. Nowadays, IBD is often associated with extraabdominal manifestations and complications, involving almost any organ system, including the musculoskeletal, dermatologic, hepato-pancreatobiliary, renal, and respiratory systems with prevalence that varies from 6% to 46%, and can provoke a challenge to IBD management. The most frequent renal involvements in IBD are nephrolithiasis (the hazard of nephrolithiasis is 10–100 times greater than in the general population), tubulointerstitial nephritis, glomerulonephritis and amyloidosis. Immune system has strong influence on both colonic mucosa and endothelium, and may have association with impaired kidney function through both immune and vascular pathogenetic mechanisms. However, there is lack of data connecting colonic changes including dysbiosis and inflammation, vascular-endothelial changes and kidney impairment in IBD.

Methods: Study includes 102 IBD patients with colonic dysbiosis (CD) in stable remission. Diagnosis and management provided according to ECCO Guidelines. Female – 31 (30.4%), male – 71 (69.6%), control group – 40 practically healthy individuals (female – 17 [42.5%), \( \chi^2 = 1.88, p > 0.05 \); male – 23 [57.5%], \( \chi^2 = 1.38, p > 0.05 \)). Standard aerobic and anaerobic microbiology techniques with taxon identification and quantity composition of microbiota were used. Intimae-media thickness of abdominal aorta and other flow mediated parameters of mesenteric vessels evaluated sonographically. Nitrite/nitrate plasma concentration, vascular adhesive molecule (sVCAM-1) and cytokines studied in ELISA. Level of cytokines’ production statistically calculated according to control group quartiles. 'Low' (LQ) was IL-1\( \beta \) < 23 pg/ml (lower quartile of control), TNF-\( \alpha \) < 15 pg/ml, IL-4 ≤ 4.95 pg/ml, IL-10 ≤ 15 pg/ml and IL-13 ≤ 28 pg/ml, respectively. 'High' (HQ) was TNF-\( \alpha \) > 32 pg/ml (upper quartile), IL-1\( \beta \) ≥ 60 pg/ml, IL-4 ≥ 45 pg/ml, IL-10 and IL-13 ≥ 25.96 pg/ml and ≥ 38 pg/ml, respectively. Chronic kidney disease was determined according to National Kidney Foundation Guidelines (2002, 2012) by eGFR calculations.

Results: The microbial overgrowth syndrome of II–IV degree with decreased microbial diversity detected in 95.1–95.9% of cases during the study, elimination of obligate colonic indigenous constant microorganisms and contamination by opportunistic microbiota. Ischemic changes in mesenteric blood vessels were characterized by decrease of time overage velocity, increase of peak systolic and end diastolic velocity and peripheral resistance by Gosling index (2–2.35 times, \( p < 0.05 \)). Totally, 45 (44.12%) patients presented excretory system changes, among them 26 (57.78%) were not previously diagnosed. TNF-\( \alpha \) moderately (\( r = 0.57, p < 0.04 \)) positively correlated with kidney impair-
ment. Other cytokines showed less significant correlation with kidney dysfunction but moderate to strong correlation with vascular changes ($r = 0.34–0.76$, $p < 0.05–0.001$). Abdominal manifestations as well as biopsies and SF-36, UC/CDAI showed no statistically significant differences emphasizing kidney impairment.

**Discussion/Conclusion:** Only few studies address renal function impairment in IBD. This research underlines that over half of kidney impairment cases remain underdiagnosed. In most cases, renal impairment in IBD can be characterized as moderate or asymptomatic. TNF-α is a possible proinflammatory component responsible for changes in bowel, endothelium and kidney, while the role of other cytokines remains unclear.
Bridging microbiome modelling with 5-ASA use in IBD

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Introduction: Although the exact aetiology of IBD remains limitedly understood, the most widely accepted hypothesis is that IBD is associated with abnormal immunological response to gut microbiome, where the microbial factors and the host genetic susceptibility play pivotal role. Recent studies reported a higher abundance of Firmicutes and lower Proteobacteria in the inflamed mucosae of 5-ASA treated patients compared to untreated IBD patients. Following this idea, microbiome modelling with probiotics and faecal transplant therapy has been the subject of intensive research, mainly focusing on bifidobacteria and lactobacteria. However, existing reports of probiotic therapy of IBD are unclear and even confusing. The aim of this study was to introduce novel probiotic strain with high antagonistic and immunogenic and understand whether oral probiotic therapy with P. Shermani bridged with 5-ASA has any therapeutic significance in IBD.

Methods: Specially designed strain (T73) of P. Shermani with high antagonistic potential was orally given to 12 IBD (4 CD and 8 UC) patients twice on a daily basis during 150–180 days in a form of suspension containing 10–14 lg CFU/g bacteria. Another nine (3 CD and 6 UC) patients without probiotic treatment formed control. IBD of mild and moderate severity. Both groups' patients received mesalazine 1500–3000 mg daily as a basis therapy. Treatment efficacy evaluated according to World Gastroenterology Organization Global Guidelines and included CDAI, SF-36 and IBDQ scores as well as evaluation of disease course (remissions/recurrence rates, etc.), severity, and complications.

Results: There were equally 2 (16.67%) and 2 (22.22%) recurrences in both groups respectively, requiring hospitalisation during the study period. CDAI score at the end of study was 49.37 ± 3.14 points lower in study group (p < 0.05). SF-36 score difference between groups became 11.8 ± 0.84%. Abdominal pain, stool, and drug use for symptomatic therapies improved in study group, too. However, probiotic treatment did not influence anaemia and other extra abdominal symptoms. Endoscopic picture and biopsies presented no specific differences between groups after treatment.

Discussion/Conclusion: We hypothesised that results of existing studies of probiotic use in IBD are confusing due to improper selection of probiotic agent. Moreover, mesalazine use in IBD causes changes of microbiota as well. P. Shermani T73 is comparatively rare and understudied probiotic, showing its usefulness for use in IBD. While probiotic treatment is often accepted as a “folk” therapy of IBD, our study shows underestimation of this technology as well as insufficient understanding of particular mechanisms determining both its usefulness and failure. Study limitations include low number and limited time of observations, randomisation and standardisation.
Use of polarized confocal microscopy of colon for improving colonoscopy diagnostic value and accuracy in IBD

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Introduction: Endoscopic assessment of mucosal changes in IBD is widely accepted as a measure of disease activity, therapeutic checkpoint, and the key prognostic indicator. Standard colonoscopy evaluates visual appearance of the mucosal surface and requires multiple biopsies for better diagnostic results, compared to confocal endomicroscopy (CE) that enables in vivo visualization of epithelial mucosa at up to ×1000 magnification. While CE is being introduced into clinical practice during last decade, its use is still limited due to technical difficulties and subjectivity of results assessment. In fact, visual pictures obtained during colonoscopy need to be digitized and analyzed. The fractal optical nature of the biological tissues stimulates creation and implementation of new physical methods in optical diagnostics and analysis of biological properties. In recent years, coherent polarimetric endomicroscopy (CPE) became widely used in military and space innovations as a potent diagnostic tool. The difference compared to CE is in additional use of different polarizing panes. The object of this research is to combine CPE and CE for improving colonoscopy diagnostic value and accuracy in IBD.

Methods: Fluorescein sodium based endoscopic system was used for colonoscopy examination of 19 IBD patients. The difference of CPE compared to CE is in additional use of different polarizing panes. Obtained and recorded by p-CLE device picture was digitized in MathLab® software. In addition to visual assessment, following optical parameters were calculated: S-average polarization value, Mx-mathematic expectation, STD2-average squared variation, Dx-disperse, As-asymmetry, Ex-excess, MEDx-median. Stocks-polarimetry of obtained static visual images was the final step for data analysis. The obtained statistical data was compared with 26 control group healthy volunteers and histological findings in bioptates.

Results: Data obtained at the study showed that the pathological process involving inflamed colonic mucosal structures is usually accompanied by the sufficient enlargement and disorientation of anisotropic and amorphous optical components while inner layers remain less anisotropic. CPE variables obtained in control and study groups (respectively) were as follows: S = 0.3397492 vs. 0.4314872 (p < 0.05); Dx = 0.0087377 vs. 0.0112804 (p < 0.05); As = 77.3463338 vs. -2.0407966 (p < 0.000); Ex = 2591.8348943 vs. 1231.3691156 (p < 0.000); MEDx = 0.3529412 vs. 0.4196078 (p < 0.05). STD2 did not statistically differ in study group and healthy control. Stocks-polarimetry showed 23.1–28.6% increase of Stocks vector maximal value in study group, and two-three fold evaluation of statistical distribution parameters.
Discussion/Conclusion: Endoscopic visualization of intact and pathologically changed mucosa is a major diagnostic tool for IBD, though CE improves its value. CPE is a potent development of CE introducing digitization of the visual picture and its possible standardization, possibly decreasing subjectivity of investigation due to 'human factor'. However, lack of experience and specialized diagnostic software makes this technology not fully accessible.
Presentation and treatment of spontaneous bacterial peritonitis in a local district hospital

Dlovan Taha (Cardiff, GB)

Introduction: Spontaneous bacterial peritonitis (SBP) carries high mortality. Our aim was to identify the factors that affect the mortality due to SBP in our local hospital.

Methods: A retrospective study of all cases of SBP admitted to our local district hospital over 7 year period. We excluded cases with malignant ascites, secondary peritonitis, and no clear diagnosis of SBP. Results were analysed statistically using SPSS software.

Results: Twenty-one cases with SBP were identified. The median age was 47 years for survivors and 68 years for non-survivors. Seven cases (33%) were Child Pugh grade B and 14 (67%) were Child-Pugh grade C. The median MELD score was 40. Eight cases (38%) presented with painless ascites and only 2 (10%) had abdominal pain. Seven cases (33%) only had fever and raised white cell count in blood. Eleven cases (52%) had raised neutrophils count > 250/mm³ in the ascitic fluid and ascitic fluid culture was positive in 16 (76%) cases. The in-patient mortality rate was 57%. The age was significantly higher (p < 0.05) in the non-survivor group. Creatinine level > 100 mmol/l at time of presentation with SBP and developing hepatorenal syndrome were associated with high mortality rate (p < 0.05). There was no statistical difference between the two groups with regards to sex, having albumin infusion, timing of antibiotics treatment, timing of ascetic tapping and whether SBP was hospital acquired or not.

Discussion/Conclusion: The mortality rate in our hospital was (57%). In our study, the median MELD score was > 40. Developing hepatorenal syndrome and high creatinine at SBP presentation were the main mortality predictor with mortality of 90%.
Significant cost savings utilising a regional prescribing approach to mesalazine therapy in inflammatory bowel disease

Jennifer Tham (Glasgow, GB)

Introduction: The West of Scotland (WoS) Gastroenterology Prescribing Subgroup is a clinically led multi-disciplinary group supporting the effective prescribing of GI medicines in the five health boards (HB) in the WoS with a population of 2.78 million. Group membership includes gastroenterologists, pharmacists, IBD nurses, with Regional Planning and National Services Scotland representation. The group builds regional consensus on an agent of choice in defined clinical indications where there are a number of therapeutic options. In inflammatory bowel disease (IBD) the British National Formulary states there is no difference in efficacy between different oral mesalazine brands (5-ASA).

Methods: We identified the opportunity to negotiate a preferential price of 5-ASA and to recommend this as the 1st-line agent in patients initiating 5-ASA therapy. National Procurement Scotland, undertook a price review of the different mesalazine brands on behalf of the WoS Group. For products included in consideration, the recommended 1st-line agent was the product with the lowest medicine cost to NHS Scotland in primary care, based on maintenance doses agreed by the WoS Gastro Group. In addition we recommended a switch from Asacol® to Octasa® in patients on maintenance 5-ASA therapy. Post guidance prescribing data was obtained from Information Services Directorate, Scotland.

Results: WoS guidance recommended Salofalk® preparations at 3 g/1.5 g for induction and maintenance of remission for new patients with IBD. From May 2017 the guidance was disseminated to secondary and primary care via clinical advisory channels, therapeutics committee and pharmacists. In the first year, uptake of the new guidance across the five HB was median 40% (range 17–50%) patients initiated on Salofalk® compared to other mesalazine brands. From May 2017 to September 2018 there has been a total cost avoidance of £109,618 through initiating new patients on Salofalk® increasing sequentially. With respect to cost savings with switching Asacol® to Octasa®, two HBs were excluded as they had already implemented a switch since 2016. In the three remaining HBs, switches were achieved in 71, 81 and 92% of patients respectively, incurring a saving of £291,544.84. Further savings have also been made over the period May 2017 to October 2018, due to rebates on both Pentasa® and Octasa®. This totalled £226,298.

Discussion/Conclusion: Our data shows a regional approach to cost effective prescribing of 5-ASA in IBD has been successful both in terms of implementation of the guidance and resulted in cost savings to NHS WoS of over £0.5 million.
Long-term outcome of immunomodulator use in pediatric patients with inflammatory bowel disease

Karen van Hoeve (Leuven, BE), Ilse Hoffman (Leuven, BE), André D’Hoore (Leuven, BE), Marc Ferrante (Leuven, BE), Séverine Vermeire (Leuven, BE)

Introduction: In the era where new biologicals are entering the therapeutic scene, the place of conventional immunomodulators in the treatment of paediatric inflammatory bowel disease (IBD) is more and more questioned. To further address this, we studied long-term outcomes of paediatric IBD patients receiving conventional therapy.

Methods: All children with Crohn’s disease (CD) or ulcerative colitis (UC) followed at our centre between July 2008 and July 2018 were reviewed. Only children who received conventional therapy (including mesalazine, steroids, thiopurines and methotrexate) since diagnosis were included. Patients requiring rescue therapy (either biologics or surgery) at diagnosis or children with a follow-up < 6 months were excluded. The primary outcome of interest was steroid-free clinical remission without need for rescue therapy at 6 and 12 months after diagnosis and at last follow-up visit. Cox proportional hazard modelling was performed (hazard risk [HR], 95% confidence interval [CI]) to determine variables associated with these outcomes.

Results: In total, 176 eligible IBD patients (121 CD, 55 UC) were identified with a median follow-up of 4.6 (IQR: 2.0–8.1) years. Overall, steroid-free clinical remission rates without need for rescue therapy were 80% at month 6, but decreased to 58% at month 12, and 32% at last follow-up visit. In CD patients, higher CRP (HR = 1.006, 95% CI: 1.001–1.011; p = 0.015), lower albumin (HR = 1.050, 95% CI: 1.012–1.086; p = 0.010) and growth impairment (HR = 1.214, 95% CI: 1.014–1.373; p = 0.038) at diagnosis were associated with need for rescue therapy by the end of follow-up. In UC patients, higher PUCAI score (HR = 1.038, 95% CI: 1.006–1.072; p = 0.023) and low iron (HR = 1.023, 95% CI: 1.003–1.043; p = 0.024) at diagnosis were determined as a risk factor for treatment failure. IBD patients carrying all risk factors needed rescue therapy in 100% of the cases within the first two years after diagnosis.

Discussion/Conclusion: These real-life data in paediatric IBD show that only 32% of children remain free of biologic therapies or surgery 5-years after diagnosis. Especially children with a high disease burden at diagnosis as witnessed by higher CRP, lower albumin and growth impairment for CD and higher PUCAI score and lower iron levels for UC were more likely to fail conventional therapy. This type of risk stratification algorithms will help to determine which patients will benefit from accelerated step-up therapy.
The role of Oncostatin M in diagnosis, prognosis and therapy response of IBD

Sare Verstockt (Leuven, BE), Bram Verstockt (Leuven, BE), Kathleen Machiels (Leuven, BE), Maaike Vancamelbeke (Leuven, BE), Marc Ferrante (Leuven, BE), Isabelle Cleynen (Leuven, BE), Séverine Vermeire (Leuven, BE)

Introduction: Oncostatin M (OSM) has been implicated in the pathogenesis of inflammatory bowel disease (IBD), wherein its increased mucosal expression drives intestinal stromal cell inflammation and predicts non-responsiveness to anti-TNF therapy (West et al. 2017). In this study we aimed to further unravel the potential of OSM as a diagnostic, prognostic and/or therapeutic biomarker.

Methods: We collected serum and mucosal biopsies from Crohn’s disease (CD) and ulcerative colitis (UC) patients: (1) treatment-naive newly diagnosed patients; (2) patients initiating anti-TNF or (3) vedolizumab therapy; (4) post-operative CD patients six months after ileocolonic resection with ileocolonic anastomosis; (5) multiple-affected IBD families including unaffected first-degree relatives (FDRs). For each group, matched samples from non-IBD controls were included as comparison. Serum OSM protein levels were measured using the Proseek Multiplex Inflammation panel (OLINK), and mucosal OSM expression using RNA-sequencing or microarray technology. Wilcoxon tests (R 3.5.1) were applied to assess statistical significance, defined as a p value < 0.05.

Results: In newly diagnosed CD and UC patients, we observed increased colonic OSM expression (fold change [FC] = 60.2, p = 3.7E-09) and serological protein levels (FC = 4.9, p = 1.3E-11) compared to non-IBD controls, with the strongest upregulation in extensive UC and fistulizing CD. Moreover, elevated mucosal OSM (but not serum OSM) at diagnosis was associated with the need for biological therapy within one year after diagnosis (poor- vs. good-prognosis: FC = 5.0, p = 1.5E-03). Prior to both anti-TNF and vedolizumab therapy, colonic OSM was upregulated in future non-remitters (FC = 2.5, p = 5.0E-02; FC = 2.3, p = 1.0E-02, respectively). In contrast, baseline serum OSM could not identify future anti-TNF or vedolizumab non-remitters (FC = 1.0, p = 3.0E-01; FC = 0.9, p = 4.1E-01 respectively). In CD patients with post-operative recurrence (POR) higher serum OSM levels were found at month 6, as compared to patients without POR and to controls (FC = 2.6, p = 1.9E-02; FC = 2.9, p = 4.5E-03). Furthermore, mucosal OSM in POR CD patients did not differ from CD patients without POR (FC = 1.2, p = 1.4E-01), but was significantly upregulated as compared to controls (FC = 1.5, p = 5.0E-03). In multiple-affected IBD families increased serum levels were observed in FDRs as compared to matched control families (FC = 1.7, p = 4.0E-04), and levels were similar to those of IBD patients.

Discussion/Conclusion: Colonic OSM levels are increased in CD and UC patients at the time of diagnosis, and higher levels correlate with poor prognosis. In addition, upregulation of colonic OSM is associated with future anti-TNF/vedolizumab non-remitters. Therefore, OSM at the mucosal site is a surrogate marker of biological treatment-refractoriness in IBD.
Gastrointestinal manifestations in HIV-infected people. From diarrhoea to AIDS

Ana Veshapidze (Tbilisi, GE)

**Introduction:** HIV infection still remains a global public health problem. By damaging immune system, HIV interferes body's ability to fight organisms that cause disease. That's why doctors in clinical practice often meet different manifestations of disease.

**Methods:** In our clinic where patients are treated for many different diseases, during a two month there were 3 case when patients with diarrhoea incidentally discovered that they were HIV positive. In spite of gastrointestinal manifestations aren't unusual in HIV infected patients, this cases maybe indicate that HIV with diarrhoea became more common. The theme requires more research and observation.

**Results:** All of them were treated by quinolones and local antimicrobial medications and effect was reached – diarrhoea stopped.

**Discussion/Conclusion:** Behind a common diarrhoea there maybe the most serious reasons such as HIV infection. And diagnostic AIDS on the early stage is essential for slowing the progression of disease.
High rates of clinical response are maintained after switching from originator to biosimilar infliximab

Katy Waddell (Glasgow, GB), Rebecca Haggarty (Glasgow, GB), Jennifer Veryan (Glasgow, GB), John Paul Seenan (Glasgow, GB), Jonathan Macdonald (Glasgow, GB)

Introduction: Biosimilar infliximab (BI) has been widely adopted in to clinical practice since launch in 2015. Switching patients with inflammatory bowel disease (IBD) from originator infliximab (OI) to BI was endorsed by the BSG and ECCO despite a lack of data on the long-term implications of this strategy. Infliximab discontinuation (ID) occurs in 20–40% patients per annum. It is unclear whether switching to BI affects ID rates. This study assessed long-term outcomes after a managed BI switch programme.

Methods: Individuals with Crohn’s disease (CD) and ulcerative colitis (UC) who were changed from OI to BI in a switch programme in December 2016 were reviewed via electronic patient records. Demographics and pre-switch disease characteristics were recorded. Pre-switch medications and laboratory data were collected. Changes to BI dose/frequency at switch and during follow-up were recorded along with other changes to IBD medications. Post-switch durability of clinical response was evaluated. Rates of IBD related steroid use, hospitalisation and surgery were gathered. Incidence of adverse events was determined. Potential pre-switch indicators of future ID were explored.

Results: 76 individuals considered to be clinically responding to OI were entered in to the BI switch programme. 2 patients had OI stopped prior to 1st dose BI based on clinical assessment and therapeutic drug monitoring (TDM) results. 74 people were switched from OI to BI.

Table 1 – Demographics/Disease characteristics

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<thead>
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<th>Characteristic</th>
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<tbody>
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<td>Median age</td>
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</tr>
<tr>
<td>Male</td>
<td>50</td>
</tr>
<tr>
<td>Female</td>
<td>24</td>
</tr>
<tr>
<td>Smoker</td>
<td>9</td>
</tr>
<tr>
<td>CD</td>
<td>58</td>
</tr>
<tr>
<td>UC</td>
<td>15</td>
</tr>
<tr>
<td>IBD unclassified</td>
<td>1</td>
</tr>
<tr>
<td>Disease duration &lt; 5 years</td>
<td>25</td>
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<td>Disease duration &gt; 5 years</td>
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<td>19</td>
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<tr>
<td>Disease duration &gt; 20 years</td>
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At time of switch 38 (51%) were prescribed an immunomodulator. 52/74 (70%) were on 5 mg/kg 8 weekly treatment, the rest on higher doses. 48/74 had a pre-switch FC, 32 (67%) FC < 250. 61/70 (87%), 69/73 (95%) and 65/73 (89%) had normal CRP, albumin and haemoglobin respectively < 3 months prior to switch.

2 years post switch, 54/74 (73%) remained on BI with sustained clinical response. ID was observed in 20 (27%); 11 (55%) now on another biologic, 8 (40%) biologic free. 33/54 remaining on BI had treatment escalation at time of or subsequent to switch. There was 1 non-treatment/IBD related death. 1 infusion reaction adverse event was observed. There were 6 IBD related surgeries, 4 unplanned hospital admissions and 12 required steroids for IBD flare. Evaluation of data identified no pre-switch factors associated with ID.

Discussion/Conclusion: Over 2 years of follow-up clinical response was maintained in the majority of individuals following BI switch. Rates of ID were lower than historically reported in non-switched patient cohorts. BI switching appears to be a safe and effective intervention.
Therapeutic drug monitoring supports clinical decision making when employed before and after biosimilar infliximab switching

Katy Waddell (Glasgow, GB), Rebecca Haggarty (Glasgow, GB), Jennifer Veryan (Glasgow, GB), John Paul Seenan (Glasgow, GB), Jonathan Macdonald (Glasgow, GB)

Introduction: Therapeutic drug and antibody monitoring (TDM) of infliximab (IFX) is used with increasing regularity as a tool to optimise outcomes in inflammatory bowel disease (IBD). Trough levels (TL) of 2–8 µg/ml are recommended during maintenance IFX treatment. The introduction of biosimilar infliximab (BI) in 2015 lead to widespread switching of patients from originator infliximab (OI) to BI. The value of TDM when switching to BI has not been defined. This study aimed to assess the impact of TDM testing before and after a managed switch to BI.

Methods: Individuals with IBD treated with OI and demonstrating a satisfactory response to treatment, were entered into the BI switch programme in December 2016. Pre-switch information was provided to patients, virtual or face to face clinical assessment was undertaken and it was recommended that all patients had pre-switch TDM performed. After switching patients returned to routine clinical care. Further TDM was performed at clinician discretion with recommendation to follow published TDM testing guidance (1). Virtual review of all patients was undertaken 2 years post-switch. Demographics, pre and post-switch TDM data, OI and BI dosing regimens and other IBD related medications were recorded along with clinical outcome data. Comparative analysis of pre-switch and most contemporary TDM results was performed.

Results: 76 individuals considered to be clinically responding to OI were entered into the BI switch programme. 70/76 (92%) had TDM at < 3 months pre-switch. OI was discontinued prior to switch in 2 patients. 74 people were switched from OI to BI. 52/74 (70%) were on 5 mg/kg 8 weekly OI pre-switch, 38 (51%) were on immunomodulators. Of 69/74 with pre-switch TDM, 32/69 (46%) had subtherapeutic TLs (< 2 µg/ml). Median pre-switch TL was 2.2 µg/ml (IQR 1.1–3.4 µg/ml). Pre-switch TL review lead to 37/74 (50%) receiving an increased dose of BI at switch. In total 47/74 had ≥ 1 dose escalation at the time of or subsequent to switch. 58/74 (78%) had TDM testing in the 2 years after switch (median no. tests 2; range 1–5) at which point 54/74 (73%) remained on BI with sustained clinical response. 49 out of 54 still on BI had both pre- and post-switch TDM with results demonstrating a statistically significant increase in mean TLs (2.1 vs. 6.3 µg/ml; p < 0.001); only 6% had persisting sub-therapeutic TLs.

Discussion/Conclusion: High rates of sustained clinical response were observed to occur following a BI switch supported by the use of pre and post switch TDM. TDM dose escalation resulted in a statistically significant increase in TLs, this may account for the rates of continued clinical response.
Malnutrition risk screening in hospitalized patients with IBD

Polina Zalizko (Riga, LV), Tereze Hermine Roshofa (Riga, LV), Laila Meija (Riga, LV), Aldis Pukitis (Riga, LV)

Introduction: Inflammatory bowel disease (IBD) patients are exposed to higher risk of malnutrition, especially patients with Crohn’s disease (CD) [Forbes A, et al. 2018]. Several complications are associated with malnutrition that leads to frequent and prolonged hospitalization (Rocha R, et al. 2019). Aim was to evaluate risk of malnutrition in IBD patients and possible need for nutritional support. As well as compare different screening tools.

Methods: This is a prospective plot study that was carried out from September 2018 till March 2019. We screened 50 patients ≥ 18 years old with established diagnosis IBD, using Nutritional Risk Score2002 (NRS2002) and Malnutrition screening tool (MUST). All patients were screened twice, using NRS202 and MUST, additionally for 48 of them bioelectrical impedance analysis (BIA) were done. Meanwhile control group consisting of 48 healthy adults were made. For statistical analysis IMBD SPSS22 was used.

Results: Out of 50 patients, 42% (n = 21) were female and 58% (n = 29) male; CD in 46% (n = 23) and ulcerative colitis (UC) in 54% (n = 27) patients. Median CD activity index (CDAI) was 128 (Q1–Q3 = 6.0–207.0) and Mayo score 4 (Q1–Q3 = 1.0–8.0). Screening data by NRS2002 showed that 34% (n = 17) patients were nutritionally at risk therefore in need of nutritional support, additional 24% (n = 12) were in low risk group and required observation, without necessity for additional nutritional care. By MUST score 42% (n = 21) had a high risk of malnutrition and need for nutritional care plan and 18% (n = 9) had low risk. Enteral feeding was prescribed in 34% (n = 17) patients and parenteral feeding in 10% (n = 4). Comparison between control group and IBD patient according to BIA results revealed, that median of BMI was lower for CD (Me = 21.10 [Q1–Q3 = 19.2–23.3]) than control group (Me = 23.4 [Q1–Q3 = 21.5–25.8]) (p = 0.014). Also, visceral fat mass was noticeably lower in CD (Me = -4.00 [Q1–Q3 = -12.1–5.6]) comparing to control group (Me = 7.85 [Q1–Q3 = -0.9–18.2]) (p = 0.003). Analyzing weight deviation from standard values, decreased percent body fat had 39% (n = 9) of CD patients and 19% (n = 5) of UC patients, reduced muscle mass had 48% (n = 11) of CD and 19% (n = 4) of UC patients, but reduction in BMI were observed only in 13% (n = 6) among all IBD.

Discussion/Conclusion: Both screening tools appears to show comparable applicability for nutritional screening. In both CD and UC patients malnutritional risk increases with higher disease activity. BIA shows statistical correspondence with MUST scale. More significant differences between control and patient group were found in CD patients. BIA also revealed that if patient had a BMI in its normal values, body composition can still be altered.
Association between use of azathioprine and non-Hodgkin lymphoma in patient with IBD

Mario Zivkovic (Zagreb, HR), Marko Nikolić (Zagreb, HR), Petra Čačić (Zagreb, HR), Ivan Budimir (Zagreb, HR), Neven Ljubičić (Zagreb, HR), Davor Hrabar (Zagreb, HR)

Introduction: Multiple studies have demonstrated an increased risk for lymphoproliferative disorders in inflammatory bowel disease patients, mainly from treatment modalities (thiopurines and anti-tumor necrosis factor agents). Other risk factors for lymphoproliferative disorders are: congenital and acquired immunodeficiency, viral (human T-cell leukemia virus type-I, Epstein-Barr virus – EBV, AIDS virus) and bacterial (Helicobacter pylori) infections, exposure to pesticides and organic solvents.

Methods: Case report.

Results: A 80-year-old female with history of Crohn's disease for last 30 years was operated (resection of terminal ileum) in 2007. Due to illness complications. After operation she was treated with azathioprine 2 mg/kg per day with good clinical response. Every time when we was try to interrupt therapy exacerbation of Crohn's disease occurred. In 2013 after 6 years under azathioprine monotherapy, a CT scan revealed a multiple lesions in abdomen and further medical investigation determine marginal zone B-cell non-Hodgkin lymphoma. Extra risks besides the age and therapy were positive EBV and H. pylori. Patient was treated with standard drugs protocol for non-Hodgkin lymphoma with excellence clinical response. Since non-Hodgkin lymphoma was discovered azathioprine therapy was discontinued and patient was without symptoms of Crohn's disease for 5 years. Now patient has moderate clinical and histologically active disease, with endoscopic score Rutgeerts i1. We are currently treating the patient with budesonide and mesalazine.

Discussion/Conclusion: Among adults with IBD, the use of thiopurine monotherapy was associated with a small but statistically significant increased risk of lymphoma. The risk of lymphoproliferative disorders in our patients with IBD must be considered when evaluating the risk-benefit ratios associated with our long-term therapies. It is our role to make sure our patients fully understand both the risks and benefits of therapy clearly before initiating treatment. Furthermore, it is our duty to make sure we make proper screening and prevention recommendations for lymphoproliferative disorders.
## Author Index to Poster Abstracts
*(Name - Poster Number)*

<table>
<thead>
<tr>
<th>Name</th>
<th>Poster Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abd-Elsalam, S.</td>
<td>70</td>
</tr>
<tr>
<td>Abo Ali, L.</td>
<td>70</td>
</tr>
<tr>
<td>Abu Baker, F.</td>
<td>2</td>
</tr>
<tr>
<td>Afzal, N.</td>
<td>44</td>
</tr>
<tr>
<td>Ajmi, S.</td>
<td>34, 35, 36</td>
</tr>
<tr>
<td>Aloï, M.</td>
<td>44</td>
</tr>
<tr>
<td>Amer, I.</td>
<td>70, 71</td>
</tr>
<tr>
<td>Andreou, N.</td>
<td>1</td>
</tr>
<tr>
<td>Antonenko, A.</td>
<td>3</td>
</tr>
<tr>
<td>Ardeshir Davani, N.</td>
<td>46</td>
</tr>
<tr>
<td>Arnauts, K.</td>
<td>4</td>
</tr>
<tr>
<td>Assa, A.</td>
<td>44</td>
</tr>
<tr>
<td>Ayadi, S.</td>
<td>10</td>
</tr>
<tr>
<td>Ayari, M.</td>
<td>10</td>
</tr>
<tr>
<td>Babić, E.</td>
<td>42</td>
</tr>
<tr>
<td>Badea, A.</td>
<td>5, 6, 30</td>
</tr>
<tr>
<td>Badea, D.</td>
<td>5, 6, 29, 30</td>
</tr>
<tr>
<td>Badea, M.</td>
<td>5, 6, 29, 30</td>
</tr>
<tr>
<td>Basaranoglu, M.</td>
<td>7, 8, 9, 55, 56</td>
</tr>
<tr>
<td>Belhadj Mabrouk, E.</td>
<td>10</td>
</tr>
<tr>
<td>Bellil, N.</td>
<td>12</td>
</tr>
<tr>
<td>Ben-Bassat, O.</td>
<td>20</td>
</tr>
<tr>
<td>Ben Nejma, H.</td>
<td>65, 66, 67</td>
</tr>
<tr>
<td>Ben Slama, A.</td>
<td>34, 35, 36</td>
</tr>
<tr>
<td>Benkhemmar, A.</td>
<td>11</td>
</tr>
<tr>
<td>Benson, A.</td>
<td>20</td>
</tr>
<tr>
<td>Bernstein, C.</td>
<td>20</td>
</tr>
<tr>
<td>Bertrand, D.</td>
<td>17</td>
</tr>
<tr>
<td>Bibani, N.</td>
<td>12</td>
</tr>
<tr>
<td>Bishara, A.</td>
<td>2</td>
</tr>
<tr>
<td>Bokan, G.</td>
<td>31</td>
</tr>
<tr>
<td>Bond, S.</td>
<td>54</td>
</tr>
<tr>
<td>Borca, F.</td>
<td>37</td>
</tr>
<tr>
<td>Bouchabou, B.</td>
<td>65, 66, 67</td>
</tr>
<tr>
<td>Brahham, A.</td>
<td>34, 35, 36</td>
</tr>
<tr>
<td>Breynaert, C.</td>
<td>18</td>
</tr>
<tr>
<td>Brezina, B.</td>
<td>54</td>
</tr>
<tr>
<td>Budimir, I.</td>
<td>13, 88</td>
</tr>
<tr>
<td>Cacic, P.</td>
<td>13, 88</td>
</tr>
<tr>
<td>Caenepeel, C.</td>
<td>14</td>
</tr>
<tr>
<td>Ceuppens, J.</td>
<td>18</td>
</tr>
<tr>
<td>Cichoż-Lach, H.</td>
<td>15, 16, 47, 48</td>
</tr>
<tr>
<td>Cleynen, I.</td>
<td>45, 83</td>
</tr>
<tr>
<td>Clim, A.</td>
<td>32, 53, 68</td>
</tr>
<tr>
<td>Coenen, S.</td>
<td>17</td>
</tr>
<tr>
<td>Cremer, J.</td>
<td>18</td>
</tr>
<tr>
<td>Creyns, B.</td>
<td>18</td>
</tr>
<tr>
<td>Croft, N.</td>
<td>44</td>
</tr>
<tr>
<td>Culafic, D.</td>
<td>74</td>
</tr>
<tr>
<td>Cummings, J.</td>
<td>37</td>
</tr>
<tr>
<td>Dabbèche, R.</td>
<td>10</td>
</tr>
<tr>
<td>Daboussi, O.</td>
<td>11, 19</td>
</tr>
<tr>
<td>Daher, S.</td>
<td>20</td>
</tr>
<tr>
<td>De Haes, P.</td>
<td>17</td>
</tr>
<tr>
<td>De La Revilla Negro, J.</td>
<td>54</td>
</tr>
<tr>
<td>de Meij, T.</td>
<td>44</td>
</tr>
<tr>
<td>De Munter, P.</td>
<td>17</td>
</tr>
<tr>
<td>Deliu, C.</td>
<td>29, 30</td>
</tr>
<tr>
<td>Deliu, I.</td>
<td>21, 22, 23, 24</td>
</tr>
<tr>
<td>Dipasquale, V.</td>
<td>44</td>
</tr>
<tr>
<td>Dix, H.</td>
<td>26</td>
</tr>
<tr>
<td>Djuranovic, S.</td>
<td>64</td>
</tr>
<tr>
<td>Dowling, F.</td>
<td>54</td>
</tr>
<tr>
<td>Downey, L.</td>
<td>37</td>
</tr>
<tr>
<td>Dragasevic, S.</td>
<td>27, 64, 74</td>
</tr>
<tr>
<td>Drazilov Srzentic, S.</td>
<td>27</td>
</tr>
<tr>
<td>Dzhuryak, V.</td>
<td>77</td>
</tr>
<tr>
<td>D’Hoore, A.</td>
<td>82</td>
</tr>
<tr>
<td>Elhendawy, M.</td>
<td>70</td>
</tr>
<tr>
<td>Eliakim, R.</td>
<td>20</td>
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<td>Elleuch, N.</td>
<td>34, 35, 36</td>
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<td>12</td>
</tr>
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<td>Ennaifer, R.</td>
<td>65, 66</td>
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<td>Erne, L.</td>
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<td>63, 79</td>
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<td>37</td>
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<td>Ferrante, M.</td>
<td>14, 17, 18, 45, 46, 82, 83</td>
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<td>26</td>
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<td>Name</td>
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<td>31</td>
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<td>32, 53, 68</td>
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<td>33</td>
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<td>37</td>
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<td>85, 86</td>
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<td>34, 35, 36</td>
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<td>65, 67</td>
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<td>Herber, A.</td>
<td>11, 19</td>
</tr>
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<td>87</td>
</tr>
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<td>Hodges, P.</td>
<td>38</td>
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<tr>
<td>Hoffmann, I.</td>
<td>82</td>
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<td>44</td>
</tr>
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<td>Hrabar, D.</td>
<td>13, 88</td>
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<td>43</td>
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<td>44</td>
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<td>44</td>
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<td>72</td>
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<td>34, 36</td>
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<td>34, 35, 36</td>
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<td>74</td>
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<td>Jovicic, Z.</td>
<td>64</td>
</tr>
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<td>Jurcau, M.</td>
<td>40, 49</td>
</tr>
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<td>41</td>
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<td>7</td>
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<td>42</td>
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<td>Kasztelan-</td>
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<td>51</td>
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<td>26</td>
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<td>33</td>
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<td>Nakhli, A.</td>
<td>65, 67</td>
</tr>
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<td>Narinskaya, N.</td>
<td>52</td>
</tr>
<tr>
<td>Navas-Lopez, V.</td>
<td>44</td>
</tr>
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<td>Neagoe, D.</td>
<td>21, 22, 23, 24, 25, 30</td>
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<td>Nemteanu, R.</td>
<td>32, 53, 68</td>
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<td>Nikolić, M.</td>
<td>13, 88</td>
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<td>Noor, N.</td>
<td>54</td>
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<td>54</td>
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<td>54</td>
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<td>12</td>
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<td>2</td>
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<td>Ozkan, E.</td>
<td>55, 56</td>
</tr>
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<td>Packham, A.</td>
<td>57</td>
</tr>
<tr>
<td>Parasiris, P.</td>
<td>33</td>
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<tr>
<td>Park, D.</td>
<td>58</td>
</tr>
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<td>Parkes, M.</td>
<td>54</td>
</tr>
<tr>
<td>Patel, K.</td>
<td>54</td>
</tr>
<tr>
<td>Paterson, J.</td>
<td>26, 59</td>
</tr>
<tr>
<td>Pavlovic, S.</td>
<td>27</td>
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<td>74</td>
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<td>60</td>
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<td>61</td>
</tr>
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<td>Petreia, O.</td>
<td>40, 49</td>
</tr>
<tr>
<td>Phan, H.</td>
<td>37</td>
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<td>Pilav, A.</td>
<td>62</td>
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<td>Plehutsa, I.</td>
<td>63</td>
</tr>
<tr>
<td>Plehutsa, M.</td>
<td>63, 77, 79</td>
</tr>
<tr>
<td>Plehutsa, N.</td>
<td>77, 78</td>
</tr>
<tr>
<td>Plehutsa, O.</td>
<td>63, 77, 78, 79</td>
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<td>Plesa, A.</td>
<td>32, 53, 68</td>
</tr>
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<td>Popovic, D.</td>
<td>27, 64</td>
</tr>
<tr>
<td>Pukitis, A.</td>
<td>87</td>
</tr>
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<td>Radwan, P.</td>
<td>15, 16, 47, 48</td>
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<td>14</td>
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<tr>
<td>Rajic, S.</td>
<td>64</td>
</tr>
<tr>
<td>Rankovic, I.</td>
<td>74</td>
</tr>
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<td>44</td>
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<td>Name</td>
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<td>Upponi, S.</td>
<td>54</td>
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<td>44</td>
</tr>
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<td>63, 77, 78, 79</td>
</tr>
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<td>Van Assche, G.</td>
<td>18</td>
</tr>
<tr>
<td>Vancambeke, M.</td>
<td>45, 83</td>
</tr>
<tr>
<td>van Hoeve, K.</td>
<td>82</td>
</tr>
<tr>
<td>Vanhoutvin, T.</td>
<td>17</td>
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<td>14, 17, 18, 45, 46, 82, 83</td>
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<td>85, 86</td>
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<td>84</td>
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<td>85, 86</td>
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<td>38</td>
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<td>44</td>
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<td>54</td>
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<td>44</td>
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<td>44</td>
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<td>13, 88</td>
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<td>62</td>
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</tbody>
</table>
Where medicine and pharmaceuticals meet – a tried and trusted link