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Crossing New Borders in IBD: Thoughts and Demands – From Mechanisms to Treatment

Symposium 210
Lisbon (Portugal), April 20–21, 2018

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Crossing New Borders in IBD: Thoughts and Demands – From Mechanisms to Treatment
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Inflammatory bowel diseases – on the path to targeted personalized therapy

For a long time, the management of inflammatory bowel diseases focused on symptom control. Yet, the therapeutic objectives have long since changed. Nowadays, it is a question of effective and comprehensive disease control with the goal of mucosal healing and even transmural healing and histological remission. The extent to which the diagnostic and therapeutic options can develop even further in the future into a targeted personalized therapy with which such treatment successes can be achieved are exciting, topical questions in gastroenterology.

Suffering from an inflammatory bowel disease (IBD) is generally an enormous burden on affected patients and is associated with a significant loss of quality of life. Furthermore IBDs – which in addition to Crohn’s disease and ulcerative colitis, also include microscopic colitis – are a significant burden on the healthcare system due to the high costs of diagnosis and treatment. Advancements in the diagnosis and treatment of these diseases, including effective prevention of complications which develop, are thus urgently needed.

There are fully justified hopes that the foreseeable future will yield such advancements. Knowledge about the background of IBD has significantly grown recently and also the mechanisms of pathogenesis are increasingly better understood. This gives rise to the expectation of being able to identify biomarkers as an important tool for diagnosis and treatment. Based on this, there are good chances for the development of innovative, targeted and effective therapeutic agents for IBD. As a result, the path to individualized therapy geared towards the patient’s specific clinical picture will also consequently be taken into account in the case of IBDs.

What this path can look like, which steps have already been taken and which are planned was the subject of the lectures and discussions at Symposium 210 of the Falk Foundation e.V. in Lisbon (Portugal). The conference illustrated once again how important the further development of biologically effective therapeutic agents in IBD is. It also made it clear that, despite all of the advancements, the established therapeutic strategies will also still retain their significance for most patients with mild to moderate disease in the future.

There is a significant amount of experience in the management of IBDs with established substances which have an anti-inflammatory effect, such as mesalazine, corticosteroids, thiopurines, and the TNF-alpha blockers, whose efficacy and safety are well known. However, the use of new therapeutic agents inevitably comes with many questions still unanswered regarding long-term efficacy and, above all, safety. The future with regard to the diagnosis and treatment of IBDs will remain exciting and there will also continue to be a great need for interdisciplinary discussions.

The scientific organizers
Prof. A. Dignass and Prof. F. Magro
From understanding disease mechanisms to new therapeutic options

Inflammatory bowel diseases (IBDs) represent very complex clinical pictures whose manifestation and course are influenced by many factors. It is therefore difficult to grasp the specific pathophysiological background of Crohn’s disease and ulcerative colitis as well as microscopic colitis, which can also be attributed to IBDs. Nonetheless, experts hope for diagnostic and therapeutic innovations since the interactions of the various influencing factors are increasingly better understood. The analysis and pooling of the available data are logical prerequisites. The findings on the disease mechanisms can be rapidly implemented in new therapeutic options via “network medicine” – according to the conclusion at Symposium 210 of the Falk Foundation e.V. in Lisbon (Portugal).

For a long time, the dogma was that IBDs develop on the basis of a genetic predisposition, triggered by environmental factors. The perspective on the pathogenesis of IBDs has greatly expanded since then. According to present knowledge, the patient’s immunological situation and the microbiome in particular are thought to play a central role.

Microbiome – the pivotal point in IBDs

The interaction of the various influencing factors appears to play a crucial role in this. Thus, according to H. Sokol, Paris (France), genetics influence the composition of the microbiome, however it can also be modulated by environmental factors and in particular by diet. If there is dysbiosis, it can promote inflammatory reactions to the point of an IBD.

This is clearly mediated through immunological reactions, taking the fact into account that the manifestation of an IBD, has effects on the composition of the microbiome. “It is not clear which is the chicken and which is the egg,” explained H. Sokol. Just as in a vicious cycle, the individual factors can spur each other on through interactions with one another.

Consequently, an attempt should be made to treat IBDs by modulating the microbiome. The use of antibiotics or probiotics and even a fecal microbiota transfer have been tested. However, none of these methods has led to a therapeutic breakthrough yet. According to P. Marteau, Paris (France), this is not least of all due to the complexity of the interactions in which different mediators, such as tryptophan and kynurenine, but also the endogenous bile acids, are involved.

Overview

IBDs present complex clinical pictures which are triggered by various factors, such as the genome, the exposome, the immunosome, and also the microbiome and their interactions. Fig. modified according to Fiocchi C. Dig Dis. 2014;32 Suppl 1:96–102.
Microscopic colitis – underestimated clinical picture

In addition to Crohn’s disease and ulcerative colitis, IBDs also include microscopic colitis, according to A. Münch, Linköping (Sweden). However, the disease is often not considered, even when corresponding symptoms are present. In addition, its importance is still generally underestimated, explained the scientist in a state-of-the-art lecture. Microscopic colitis is characterized by watery, often nocturnal diarrhea, abdominal pain and, to some extent, also unintentional weight loss. Women are affected in particular. Furthermore, microscopic colitis is in no way a rare clinical picture; its prevalence is even higher than that of Crohn’s disease. A differentiation should be made between collagenous and lymphocytic colitis. According to A. Münch, the clinical pictures do not appear to be clearly identifiable inflammatory processes in the large bowel within the scope of a colonoscopy, which is why a random biopsy should always be requested for the diagnosis.

As a result of the disease the impact on patients is often very high, according to S. Miehlke, Hamburg (Germany), which highlights the importance of effective therapy. He named the active substance budesonide as the only evidence-based treatment option at present. Treatment should be given at a dosage of 9 mg daily and the recommended treatment period is initially 6-8 weeks. During this time, there is generally a significant reduction in symptoms. If the symptoms recur after discontinuing the active substance, long-term therapy with 6 mg budesonide daily should be considered. However, this has not yet received approval.

The involved mechanisms still remain largely unclear but this is the subject of intensive research. An ongoing scientific and medical challenge is to analyze and interpret the enormous amount of data which is currently being generated with regard to the mechanisms of the pathogenesis of IBDs, stressed C. Fiocchi, Cleveland (USA).

Rethinking in medicine is required

In Fiocchi’s view, the central objective is to pool the findings from basic research and incorporate them into the development of new therapeutic agents and treatment strategies. Specifically, deciphering patterns in the abundance of data, generating hypotheses, and making “big data” usable for advancements in the diagnosis and treatment of diseases are concerned. “This calls for new technologies, a paradigm shift, and also new thinking in medicine,” stressed C. Fiocchi.

In contrast to previous years, the focus should no longer only be on identifying molecular changes and developing drugs which correct these changes. “Rather, we need ‘network medicine’ which breaks down the multiple interactions between the influencing factors to result in the development of fully new influencing strategies,” says C. Fiocchi.

An increasing variety of therapies is foreseeable

A. Dignass, Frankfurt (Germany), expects advancements, especially with respect to the identification of biomarkers which in turn can be the basis of the development of treatment strategies which have targeted and individualized efficacy. Against this background, a significant expansion in the variety of therapies in IBDs is becoming apparent.

However, this does not in any way mean that established therapeutic agents, such as mesalazine, are becoming less important. Corresponding, mesalazine can achieve a quick and effective remission in around 60-70% of patients with moderate ulcerative colitis. Mesalazine is additionally the first choice for patients in maintenance therapy.

Mesalazine achieves all relevant treatment objectives in UC

- Rapid and effective induction of remission
- Maintenance of remission
- Prevention of complications, such as reduction in surgical interventions, and of dysplasia
- No growth retardation in children
- Mucosal healing
- Dysplasia/cancer prevention
- Improvement of quality of life, normal social life, ability to work
- Avoidance of steroids
- Safe treatment modality

Fig.: Mesalazine has various favorable effects in IBDs and is still the standard therapy in mild to moderate ulcerative colitis. (Source: Prof. Dignass)
IBD – complex relationships and justified hopes for therapeutic advancements

The molecular relationships of the disease manifestation are becoming increasingly better understood in many diseases, including Crohn’s disease and ulcerative colitis. This raises the hope for advancements in treatment through the development of new, targeted treatment strategies which are aimed at the individual pathogenesis.

“Network medicine” is needed

The expectation of further advancements in the treatment of IBD is absolutely realistic, as J. Menche, Vienna (Austria), stated. However, the current strategies in the research of the diseases must be reconsidered. Because of the steadily improving possibilities for analyzing the molecular relationships, there is a flood of new data which must be linked together. This results in a complex network made up of many factors, from genetic predisposition to the multiple environmental factors which interact and mutually influence each other. They mesh with one another like gears, however disruptions can occur and lead to a disease process. According to J. Menche, the challenge is now to understand the relationships within the network – the “interactome”, so to speak – and to find the disruptors on an individual basis. “You can think of such networks like a city map of New York, where the local neighborhood determines the character of the district. The interactome can help us in the development of innovative treatment options and also serve as a disease map,” explained the researcher.

T cells as mediators of chronic inflammation

Chronic inflammatory reactions, according to M.F. Neurath, Erlangen (Germany), are primarily mediated by T cells and immunoregulatory cytokines. The development of disease starts with an acute inflammatory reaction which, through the release of proinflammatory cytokines such as interleukin-6, leads to a chronicification which also generally results in tissue destruction and subsequent complications. A large range of T cell subpopulations and the mediators released by them are involved in this process. These can additionally interact and intensify or weaken each other’s effects. In this regard targeted therapeutic strategies are to be developed based on the findings on pathogenesis, reported S. Schreiber, Kiel (Germany). As an example, he named monoclonal antibodies against T cells as well as adhesion molecule inhibitors and also cell migration inhibitors.
Fibrogenesis – option for therapeutic advancements

Fibrogenesis also plays an important role in IBDs and the development of complications, reported F. Rieder, Cleveland (USA). This is well known for the formation of strictures in the case of Crohn’s disease. In ulcerative colitis as well, fibrogenesis is an important pathogenic factor, which ultimately influences the course of the disease, as in Crohn’s disease, and which can promote complications. “This is a dynamic and multifactorial process,” stressed the physician. A wide variety of factors act on the fibroblasts and accelerate fibrogenesis. Among others, this results in fat storage and interactions with mesenchymal cells, as well as the proliferation of muscle cells. However, the background of fibrogenesis is not yet fully understood. Yet it is clear that the influence of the underlying processes will yield new therapeutic approaches in IBDs. “In this regard, we still have a significant unmet need for medical advancement,” explained F. Rieder.

Microscopic colitis – still often underestimated

D.S. Pardi, Rochester (USA), mentioned microscopic colitis as a clinical picture whose importance is often underestimated and which is not adequately researched. The pathophysiology is still unclear. Causal factors, such as
- disruptions in electrolytes,
- bile acid malabsorption,
- abnormal collagen synthesis or collagen degradation,
- infections,
- autoimmune reactions, and
- the influence of drugs, such as non-steroidal anti-inflammatory drugs (NSAIDs), are discussed.

The administration of proton pump inhibitors (PPIs) and selective serotonin reuptake inhibitors (SSRIs), according to A. Ensari, Ankara (Turkey), may lead to the manifestation of microscopic colitis. The degree to which drugs actually act as disease triggers cannot be specifically measured in individual cases. Therefore, in patients with the clinical picture of colitis, idiopathic colitis should not be hastily concluded, declared P. Borralho, Lisbon (Portugal). For clarification, a random biopsy and histological examination must be performed and it must be ensured that collagenous or lymphocytic colitis can be diagnosed or ruled out by means of the biopsies. The clinical pictures are a part of the IBDs. However, they are frequently not recognized and the clinical symptoms are often misinterpreted as irritable bowel syndrome.

State-of-the-art lecture:
Accelerating translational medicine

Progress is being made faster and faster, thanks to the new possibilities in molecular analysis, and this represents a growing challenge for translational medicine. This must involve bringing the advancements achieved in basic research out of the laboratories quickly and implementing them in therapeutic advancements, declared S. Ghosh, Birmingham (Great Britain), in a state-of-the-art lecture. In the case of IBDs, there is still a significant need for action whereby gastroenterology should learn from the advancements in oncology, in the physician’s opinion. He mentioned breast cancer as an example in which it has been possible to implement new molecular findings in successful therapeutic options. Establishing precision medicine of this type must also be an objective in the case of IBDs. The identification of specific biomarkers by means of which innovative treatment options can be developed and which may also be the basis of a targeted, individual treatment concept in Crohn’s disease and ulcerative colitis is needed for this.
Ulcerative colitis: Regularly classify the degree of severity

Even in ulcerative colitis, the degree of severity of the disease should be classified regularly, explained J. Halfvarson, Orebro (Sweden). However, there are only few valid scores which make this possible. This is further complicated by the fact that the assessment of the clinical situation by the affected patients and the physicians treating them often varies greatly. Physicians therefore take persistent symptoms less seriously than patients do. As a result, they frequently underestimate the degree of severity of the disease and overestimate the therapeutic effects.

According to S. Vermeire, Leuven (Belgium), this should also be taken into account when designing clinical studies. There are various scores, such as the Mayo score and the CDAI, which are primarily used in clinical studies, however these are not very feasible in everyday clinical practice. For this reason, S. Vermeire also touted greater use in practice of PROs in patients with ulcerative colitis, particularly as these data also reflect patients’ expectations with regard to the treatment of their disease.

Crohn’s disease: Monitor the course of the disease closely

The progression of Crohn’s disease is normally based on exacerbations, with the inflammatory processes persisting subclinically during periods of remission, thus determining the further course of the disease, explained G. Fiorino, Rozzano (Italy). Even in this phase of the disease, these processes can contribute to the development of anatomic lesions and structural changes and thus pave the way for strictures and stenoses. This explains the course of the disease which often differs greatly between individuals, and to date there is a lack of criteria for predicting it specifically in individual cases. A regular assessment and disease monitoring are helpful to be able to identify intestinal damage and prevent progression.

According to U. Kopylov, Ramat-Gan (Israel), this includes recording disease activity using the CDAI (Crohn’s Disease Activity Index) as well as the PRO (Patient Reported Outcome) with information on the individual quality of life. These parameters can also be influenced by the effectiveness of the therapy, whereby the treatment objective should always be mucosal healing and, because of the better prognosis, also transmural healing.

State-of-the-art lecture: Caution when interpreting study results

Randomized, controlled clinical trials (RCTs) are currently considered to be the gold standard for identifying the efficacy of a treatment strategy, explained B.E. Sands, New York (USA). However, the data should be interpreted with caution and the results should in no case be generalized. Particular attention should be paid to the inclusion and exclusion criteria for the study participants and the stage of the disease in each case. Children, elderly patients, as well as patients with particular disease sites (upper gastrointestinal tract or proctitis) and those who already have complications, such as strictures or fistula formation, are generally excluded from study participation. In addition, patients with stomas and those with a relevant comorbidity usually do not take part in common RCTs. According to B.E. Sands, a differentiation should also be made regarding whether the patients have already been pretreated and if so, with which therapy. It should also be clarified whether the study collective had immunological changes or whether structural changes were evident which could have influenced the success of the therapy. In the scientist’s view, further investigations are required for most clinical pictures, in addition to the RCTs, in order to obtain valid data. As examples of this, he named large-scale pragmatic studies, head-to-head studies, as well as register studies in which predictive and prognostic biomarkers are also preferably taken into account.
Take drug monitoring seriously

Careful drug monitoring is necessary, particularly in the case of treatment with innovative drugs and those whose active substance levels fluctuate, explained M. Löwenberg, Amsterdam (The Netherlands). The goal of monitoring is to optimize the clinical efficacy and, at the same time, prevent toxicity. Monitoring additionally makes it possible to avoid over- and underdosing and thus also ultimately to save money.

According to P. Michetti, Lausanne (Switzerland), this also applies to treatment with biosimilars, which are currently entering the market in various indications. Biosimilars contribute to lowering the costs of therapy. However, it should be borne in mind that the preparations are always tested in one indication only; if their efficacy is comparable with the original drug, the results can be extrapolated to other indications.

Intraabdominal abscesses: Pros and cons of surgery

The approach to take in the management of intraabdominal abscesses in the case of IBDs was the subject of a pro-and-con discussion.

F. Carbonnel, Le Kremlin Bicêtre (France), primarily called for conservative therapy with antibiotics and, if applicable, percutaneous or surgical drainage, as is also recommended in the ECCO guidelines. If necessary, the abscess can then be surgically corrected at a later point in time. However, about 70% of patients subsequently require resection. Conversely, this means that about one-third of patients can avoid surgery. A. D’Hoore, Leuven (Belgium) argued in favor of a rather broad indication for surgery. Upon initial presentation, 20-30% of Crohn’s patients already have strictures, fistulas or abscesses. A. D’Hoore also stresses that percutaneous drainage is useful, but should be followed by surgery since otherwise a greatly increased chance of recurrent complication can be expected. The decision in favor or against the surgery should always be made within a multidisciplinary team.

Stenosis in Crohn’s disease: Pros and cons of surgery

In the case of stenoses in the small intestine or colon, the question arises whether a primarily conservative or surgical approach should be favoured. Y. Bouhnik, Clichy (France), spoke in favor of initially conservative treatment. The therapy is to be geared towards the symptoms and an attempt should be made to determine the extent of constriction of the lumen by means of comprehensive imaging. Taking this and the inflammatory activity into account, a decision can then be made as to whether anti-inflammatory treatment is sufficient or whether a rapid surgical intervention should be performed. However, particularly in patients with extensive strictures and stenoses and severe symptoms as a result of an obstruction, an immediate surgical procedure is indicated, according to M. Carvello, Rozzano (Italy). Such cases involve patients at high risk of further complications, such as fistula formation. In this case, early resection, is significantly more promising for guarding against such complications than a long course of drug treatment, says the physician.
How should patients with concomitant cancer be treated?

Special treatment situations were also the subject of discussion during the symposium. One challenge, according to L. Beaugerie, Paris (France), is, for example, the treatment of patients with an IBD and concomitant or previous cancer. If a malignant tumor is diagnosed during ongoing IBD treatment, immunosuppressants must be immediately discontinued. Following completion of the cancer treatment, an immunosuppressant-free interval of 2-5 years should be sought. Apart from this, the further treatment of the IBD should be based on the patient’s prognosis, the tumor stage and the aggressiveness of the tumor. Especially in patients with metastatic tumor disease, attention must be paid to maintaining and, if possible, improving quality of life.

Pay attention to extraintestinal manifestations

When treating patients with IBD, attention must always be paid to extraintestinal manifestations. According to S. Vavricka, Zurich (Switzerland), the joints, skin and eyes are often affected. Yet, the inflammatory processes can also manifest in the liver, lungs and pancreas. As examples of extraintestinal manifestations in IBDs, he named erythema nodosum, pyoderma gangraenosum, oral aphthous ulcers, uveitis, as well as primary sclerosing cholangitis, in addition to arthropathy. However, it should be borne in mind that such reactions can also be due to therapy and in particular due to anti-TNF antibodies. If arthritis should occur, a potential reaction to treatment with vedolizumab should also be considered, according to S. Vavricka.

Extraintestinal manifestations in IBDs
The possibility of an infection with cytomegaloviruses (CMV) should also be taken into account, according to B. Siegmund, Berlin (Germany). The majority of adults have probably experienced a CMV infection and thus the viruses may persist in the body. For this reason, there may be a reactivation of the infection during IBD treatment. However, the infection is generally self-limiting, even if the IBD treatment is continued.

State-of-the-art lecture: Advantages and risks of therapy with biologics

The introduction of biologics was, according to J.O. Lindsay, London (Great Britain), an important advancement in the treatment of IBDs through which many more patients than before achieved the therapeutic goal of mucosal healing. Within the scope of the step-up concept, biologics additionally allow intensification of the therapy which is relevant for many patients with a progressive IBD. Nevertheless, the treatment is also associated with risks which one should be aware of, reminded the doctor. Substance-specific adverse effects as well as the possibility of the formation of antibodies against the respective biologic, the appearance of inflammatory skin reactions, but also a potentially increased risk of malignancy as well as an increased risk of opportunistic infections should be taken into account. The benefits and risks of treatment with biologics must therefore be carefully weighed against each other and in doing so, the patient’s age as well as any existing comorbidity must be taken into consideration.

Perspectives on the future in IBD

There will be further advancements in the diagnosis and treatment of Crohn’s disease and ulcerative colitis. Which developments will emerge in the future was another point of discussion in Lisbon. The innovative biologics, according to G. van Assche, Leuven (Belgium), will lead to new treatment strategies and therapy algorithms in IBDs. The objective, according to M. Allez, Paris (France), is to increasingly integrate new options such as an anti-IL-12 and anti-IL-23 treatment in the algorithms in the future. In ulcerative colitis as well as in Crohn’s disease, according to W.J. Sandborn, La Jolla (USA), a variety of additional therapeutic innovations are expected which will make the treatment regimens even more complex in the future.
IBD: From Pathophysiology to Personalized Medicine

March 29–30, 2019
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Scientific Organization
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M. F. Neurath, Erlangen (Germany)
F. Powrie, Oxford (Great Britain)
Poster prizes: Awarding successful scientists

At its symposiums, the Falk Foundation e.V. regularly honors young scientists who present innovative and relevant research work on a poster. At Symposium 210, poster prizes were awarded to:

1st prize: **Vanessa Popp**, University Hospital Erlangen (Germany), for the poster “TH1 transcription factor T-bet as a new target for Crohn’s disease therapy”.

2nd prize: **Dr. Louisa Jeffery**, University of Birmingham (Great Britain), for her work “Ikaros family transcription factors associate with inflammatory switched-Tregs that are elevated in the bowels of IBD patients”.

3rd prize: **Joana Afonso**, University of Porto (Portugal), for the poster “Therapeutic drug monitoring of SB2: The accuracy of three different methods”.

From left to right: Prof. A. Dignass, the winners of the poster prizes V. Popp (1st prize), J. Afonso (3rd prize), Prof. S. Ghosh (on behalf of Dr. L. Jeffery, 2nd prize), Dr. M. Falk (for the Falk Foundation e.V.), Prof. F. Magro

Vanessa Popp, Erlangen (Germany)

Joana Afonso, Porto (Portugal)
“Knowledge about the background of inflammatory bowel diseases is steadily becoming more complex”

There is increasing evidence that progress is currently being made in inflammatory bowel diseases and that the therapeutic regimens will change in the future. Established therapeutic agents such as mesalazine will still retain their importance, however the algorithms will become more complex with the introduction of new therapeutic agents. Professor Dr. Axel Dignass, Frankfurt (Germany), one of the scientific organizers of Symposium 210, explains what specifically can be expected.

Editorial staff: Professor Dignass, are there relevant innovations in the diagnosis and therapy of inflammatory bowel diseases?

Prof. Dignass: There are no significant innovations which we would have to implement immediately in the diagnosis and therapy of ulcerative colitis and Crohn’s disease in our everyday clinical practice. However, a change in perspective for the future which may also influence our daily practical work in the long term is becoming quite clear. Knowledge about the molecular background of the disease and the better understanding of immunological parameters as well as other factors such as the microbiome has considerably increased. At present, more and more new data on this subject are being generated at a fast pace. As a result, the knowledge available continues to grow, but it is also becoming far more complex.

What are the consequences of this?

Currently, a wealth of data on the physiology and also the pathophysiology is generated and make it increasingly difficult for physicians to keep track and use these data for daily clinical practice. To do so, we need modern computer technologies and the support of experts who process the new findings for us. These experts are not physicians or scientists but rather data processing experts who, in close cooperation with physicians and scientists, extract the essence from the data and make it usable for us. We are virtually generating “big data” – this is the current buzzword for this development – and we need partners for this who assist us in processing the abundance of data.

How might this look like?

In cooperation with the experts, we can attempt to develop targeted hypotheses and on this basis identify mechanisms which may provide a foundation for developing new drugs with innovative mechanisms of action.

To what extent does this represent a shift in perspective?

Previously, we mainly focused on the symptoms and attempted to treat them. Clinical studies were also generally laid out in this way. In the future, we will have to take another path and design clinical studies in a far more targeted manner and with a direct view to the mechanisms of pathogenesis. Currently, in many cases the scientists performing basic research and the clinicians are working in parallel but practically isolated. We have to change this and join forces to be able to take new therapeutic approaches in a targeted way. Last but not least, this also calls for new thinking from us clinicians – to look beyond our own horizons.

Which results do you specifically expect in the foreseeable future?

It is to be expected that we will initially see progress in the search for relevant biomarkers in inflammatory bowel diseases. Examples from oncology show that the biomarkers are very important and can be the basis for personalized and more effective therapy. Treatment will thus be administered in an increasingly targeted manner. We are already on this path now with biologics and in the foreseeable
future, there will be additional new therapeutic principles with innovative mechanisms of action in inflammatory bowel diseases.

**Will the conventional therapeutic options then be passé?**

No, not at all. The conventional therapeutic options, such as mesalazine, are effective and well tolerated treatment options with which a majority of patients with UC can achieve good disease control. As a result, 60-70% of patients with moderate ulcerative colitis can be satisfactorily treated with mesalazine. In contrast to the established therapeutic strategies whose efficacy and safety we have known well for many years, there are currently still unanswered questions with regard to the innovative active substances. In addition, the high costs of therapy are not without problems and thus it can be assumed that these options should initially be reserved for serious cases.

**Who then ultimately decides which patient receives which drug and when?**

There are patients with Crohn’s disease or ulcerative colitis who can be treated effectively with the established therapeutic agents. In such cases, the non-hospital-based gastroenterologist is undoubtedly the one who manages the therapy. On the other hand, the modern therapeutic algorithms are very complex when there is a difficult disease course and serious complications occur. This will not change in the future. By contrast, if new therapeutic substances become available, the treatment will become even more complex. From my viewpoint, the less specialized colleagues are well advised to network early on with a corresponding specialised IBD center and treat these patients in cooperation with the center. Also apart from this, our work will have to be more interdisciplinary in the future, as it is also already being done in other countries with multidisciplinary team meetings.

**Who should take part in a multidisciplinary team meeting of this type?**

Definitely the gastroenterologist, a surgeon, if applicable a pediatrician and, for example, also a pathologist if microscopic colitis is suspected. Therapists to provide psychological care to patients as well as therapists from the field of nutritional medicine should also be included.

**Is microscopic colitis also an inflammatory bowel disease?**

Yes, this is in fact an inflammatory bowel disease and we are still seeing a significant need for training and continuing education regarding this clinical picture. Microscopic colitis is often overlooked, because the level of awareness of this clinical picture is still not very high and also because no abnormalities are seen during routine colonoscopy. If microscopic colitis is suspected, biopsies must be taken to rule out or confirm the suspected diagnosis. However, the suspected diagnosis should also be pointed out to the pathologist, since definitive detection of changes requires special stains. Yet, a reliable diagnosis is very important, since with budesonide, we have the possibility of effective therapy for the disease.

**Based on which symptoms microscopic colitis needs to be considered?**

The suspected diagnosis should be made in any case if elderly patients, especially women, indicate that they suffer from at least five episodes of primarily watery diarrhea every day. It is also necessary to pay attention when patients mention nocturnal diarrhea. In such cases, a corresponding diagnostic clarification is always indicated. Unfortunately, this happens all too rarely and more often, the diagnosis of irritable bowel syndrome is hastily made. Apart from this, in patients who complain of watery diarrhea, it is also important to take a careful drug history, since quite a few active substances can cause diarrhea as a side effect.

**Professor Dignass, thank you very much for the interview.**
IBD: From Diagnosis to Therapy

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